Primary Arthroplasty

Five-Year Experience of Vitamin E–Diffused Highly Cross-Linked Polyethylene Wear in Total Hip Arthroplasty Assessed by Radiostereometric Analysis

Audrey K. Nebergall, BA a, *, Anders Troelsen, MD, PhD a, b, Harry E. Rubash, MD a, Henrik Malchau, MD, PhD a, Ola Rolfson, MD, PhD a, c, Meridith E. Greene, PhD a

a Department of Orthopaedics, Harris Orthopaedic Laboratory, Massachusetts General Hospital, Boston, Massachusetts
b Department of Orthopaedics, Copenhagen University Hvidovre Hospital, Hvidovre, Denmark
c Department of Orthopaedics, Institute of Clinical Sciences at Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

A R T I C L E   I N F O

Article history:
Received 15 September 2015
Received in revised form 17 November 2015
Accepted 1 December 2015
Available online 17 December 2015

Keywords:
total hip arthroplasty
radiostereometric analysis
polyethylene
vitamin E
patient-reported outcome measures

A B S T R A C T

Background: Vitamin E–diffused highly cross-linked polyethylene (VEPE) was developed to reduce oxidation without compromising mechanical strength. The purpose of this study was to evaluate VEPE in vivo using radiostereometric analysis (RSA) and patient-reported outcome measures (PROMs).

Methods: Fifty-one hips were enrolled. Each patient received a VEPE liner, a porous titanium shell, and an uncemented stem with a 32-mm cobalt–chrome femoral head. Tantalum beads were inserted into the VEPE to measure femoral head penetration using RSA. RSA radiographs and PROMs were obtained preoperatively immediately after surgery, 6 months, 1, 2, 3, and 5 years after surgery.

Results: Forty-seven hips returned at 3 years, and 42 hip at 5 years. The mean ± standard error of the mean proximal head penetration into the polyethylene was 0.06 ± 0.01 at 5 years. The amount of head penetration did not change significantly with increasing time in vivo. The mean ± standard error of the mean Harris Hip Score was 58 ± 2 preoperatively, which improved significantly to 93 ± 2 at 5 years (P < .001).

Conclusion: The head penetration into VEPE liners was low compared with non-VEPE at 5 years. After settling of the liners in the early period, no significant head penetration occurred from 2- to 5-year follow-up. All PROMs improved significantly from preoperative to postoperative and remained very favorable at 5 years. This study documents the longest-term evaluation of in vivo wear performance of VEPE.

© 2015 Elsevier Inc. All rights reserved.

Long-term performance of total hip arthroplasty (THA) is often compromised by implant loosening secondary to osteolysis caused by wear of the ultrahigh molecular weight polyethylene (UHMWPE) lining the acetabular shell [1–4]. Cross-linking of UHMWPE through irradiation lowers wear compared with conventional nonirradiated polyethylene but also produces free radicals, which induces oxidation [5,6]. The highly cross-linked UHMWPE (HXLPE) may be subjected to a melting process, which allows further cross-linking of the material, thereby reducing the presence of free radicals [4,7]. However, melting after irradiation diminishes the strength of the material which may increase the risk for fracture in the future [8,9]. Alternatively, if HXLPE is annealed, fatigue strength is not as compromised as it is during melting, but free radicals remain, which may cause oxidation [4,8,10–14].

Vitamin E–diffused HXLPE (VEPE) was developed to address some of the shortcomings of HXLPE; namely to maintain low wear and eliminate free radicals while not compromising fatigue strength [8,10,12,15]. The added vitamin E stabilizes the residual free radicals by hindering the oxidative chain reactions of primary and secondary free radicals, thereby eliminating the need for
melting [5]. Comprehensive in vitro evaluation has shown that the antioxidant properties of vitamin E improve performance by stabilizing free radicals while retaining the physical properties and strength of HXLPE [14,16,17].

Because the wear of HXLPE is very low compared with conventional polyethylene and wear of VEPE is expected to be comparable with that of HXLPE, it is necessary to use the most accurate and sensitive measurement method to detect penetration early. Radiostereometric analysis (RSA) was used in this study as it is the most accurate method of measuring femoral head penetration over time in THA [18,19]. Because of the accuracy of RSA, it is a valuable tool for early prediction of long-term implant prognosis in small cohorts [18-21]. This highly sensitive method allows for the use of smaller cohorts than other wear measurement techniques. Other techniques require much larger sample sizes to show the same effect as RSA. In addition, small cohort RSA studies are a critical step in evaluating new technologies according to Malchau’s stepwise introduction [22]. The purpose of this prospective clinical study of 51 THAs was to evaluate femoral head penetration into the VEPE liners up to 5 years postoperatively. RSA was used to accurately measure relative displacement of the center of the femoral head compared with the polyethylene liner over time. Patient-reported outcome measures (PROMs) were evaluated at each follow-up interval to determine the patient’s perception of their outcome at 5 years.

Methods

Enrolled Patients

Forty-seven patients (32 males and 15 females), all of whom suffered from osteoarthritis, were recruited into a 5-year prospective, institutional review board—approved, RSA, and clinical outcome study. Inclusion criteria were patients with a diagnosis of osteoarthritis who required primary THA between the ages of 20-75 years. Any patient with a limited lifespan, difficulty in comprehending the study protocol, females who may become pregnant, or those who required a femoral head size other than 32 mm, were excluded from the study. Informed consent was obtained from all patients. Four patients had both hips enrolled in the study, for a total of 51 observed hips. All surgeries were performed at 1 center by 4 arthroplasty surgeons. The average age at the time of surgery was 59 years (range, 26-75 years).

Each patient received a VEPE liner (E1 antioxidant infused technology), a highly porous titanium acetabular shell (Regenerex), a lateralized, proximally porous-coated uncemented femoral stem (Taperloc), and a modular 32-mm cobalt–chromium femoral head (all components were from Zimmer Biomet Holdings, Inc, Warsaw, IN). Screws were inserted into the acetabular shell according to surgeon preference and either a posterolateral or anterolateral approach was used. A customized jig was used to press-fit 12 or 14 (depending on cup size) tantalum beads (1.0-mm diameter) into predrilled holes of each antirotational tab of the VEPE liner during surgery. Biplanar RSA radiographs were taken in the immediate postoperative period before discharge from the hospital, or if this was not possible, at the 2- to 6-week follow-up appointment. The average (range) of postoperative follow-up was 15 days (0-43 days). Additional RSA radiographs were obtained postoperatively at 6 months, 1, 2, 3, and 5 years. The total number of hips included in the RSA analysis at each interval was 47 hips at 6 months and 1 year; 46 at 2 years; 47 at 3 years, and 42 at 5 years (Fig. 1). As this was an efficacy study to establish early safety of VEPE, a control cohort was not recruited. At the time of study design, retrieval reports showed midterm oxidation of HXLPE; therefore, historical RSA wear measurements of HXLPE were used for comparison with this cohort [6,23].

Radiostereometric Analysis

Biplanar RSA views of the patient’s operated hip were captured simultaneously using 2 fixed x-ray sources and a uniplanar calibration cage (cage 43; RSA Biomedical, Umeå, Sweden) with digital cassettes positioned beneath the examination table and the patient’s operative hip. Each patient was oriented with their hip and the implant centered within calibration cage in both foci, which served as a frame of reference for the measurements over time. The UmRSA 6.0 software (RSA Biomedical) was used to analyze patient films. A three-dimensional reconstruction of the acetabular unit segment at each subsequent follow-up visit was derived from the calibration cage and the tantalum beads.

The backside of the shell was combined with the beads in the liner to make one segment that used a greater point count in the analysis than using the liner alone, thus allowing for more precise RSA measurements [24]. This acetabular unit (shell + liner) segment consisted of up to 6 matched beads (visible in both foci) in the liner and 3 points automatically assigned to the backshell by the software using edge detection. The center of the femoral head was defined as a single point, which was calculated from automated detection. Using the postoperative film as the baseline, the relative motion of the center of the femoral head to the acetabular unit was compared in all subsequent image pairs to determine femoral head penetration over time. The normal course for wear measurements involves an initial settling/bedding-in period (up to 1 year), followed by a more linear wear pattern (penetration after 1 year). To differentiate settling from true wear, penetration was defined by comparing all films back to the immediate postoperative film (as such, penetration included the settling period).

<table>
<thead>
<tr>
<th>Preoperative</th>
<th>Postoperative</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 50 hips</td>
<td>N/A</td>
</tr>
<tr>
<td>n = 47 hips</td>
<td>N/A</td>
</tr>
<tr>
<td>n = 46 hips</td>
<td>n = 51 hips</td>
</tr>
<tr>
<td>n = 45 hips</td>
<td>n = 40 hips</td>
</tr>
<tr>
<td>n = 42 hips</td>
<td>n = 45 hips</td>
</tr>
<tr>
<td>n = 40 hips</td>
<td>n = 42 hips</td>
</tr>
</tbody>
</table>

* The number of PROMs in each time period excludes patients who missed their appointment (a missed follow-up showed for each interval), refused the surveys, had technical difficulties with survey administration tool, or the research coordinator was unavailable to administer the survey.

**Fig. 1.** Total number of hips included in the radiostereometric (RSA) and patient-reported outcome measure (PROM) analyses at each interval, with any necessary RSA exclusions and missed follow-up listed as branches. After taking the missed follow-up into account, all other patients missing PROMs either refused the surveys or the clinic had difficulty in administering the survey tool. Preoperative RSA films and postoperative PROMs are not applicable (N/A). THA, total hip arthroplasty.
and the steady state wear was defined by comparing all films back to the 1-year film (eliminating the settling period).

Double examinations (2 sets of RSA films taken 10 minutes apart) were performed at the 6-month and 2-year follow-up visits to establish the precision of the RSA measurements. The precision of the setup was defined as the standard deviation of the difference between the double examinations, multiplied by the critical value (t), from a t distribution table [24]. The mean error (ME) tolerance was set at 0.25 mm and the condition number tolerance was set at <110; results obtained beyond these parameters were deemed too high and thus unreliable [21].

Patient-Reported Outcome Measures

All patients also completed a set of PROMs preoperatively and at each aforementioned visit after surgery excluding the immediate postoperative visit. PROMs allowed patients to describe their own perception of their disease and nondisease health states before and after THA. The PROMs collected were Harris Hip Score (HHS), the EuroQol group’s EQ-5D (The EuroQol Group’s 5 dimension health-related quality of life measure), the University of California Los Angeles (UCLA) activity score, the 36-item short-form survey (SF-36), and a pain and satisfaction visual analog scale. The HHS ranges from 0 to 100 with the high end corresponding to the best health-related quality of life [25]. The EQ-5D, the UCLA activity score, and the SF-36 were used as general health measures. The EQ-5D has a weighted index score ranging from −0.109 to 1.000 and a visual analog scale (VAS) from 0 to 100 where the high end of each scale corresponds to the best health-related quality of life [26]. The UCLA activity score ranges from 1 (wholly inactive; dependent on others; and cannot leave residence) to 10 (regularly participates in impact sports) and the SF-36 describes health states on a range from 0 to 100 with 0 being the worst health state [27,28]. The pain and satisfaction VAS ranges from 0 to 10 where 0 is no pain and complete satisfaction, respectively. Not all patients who completed RSA follow-up also completed the PROM follow-up because of missed appointment, refusal to fill out questionnaires, and technical difficulties in administering the questionnaires (Fig. 1).

Statistical Analysis

Thirty-six hips were needed to detect a difference of 0.02 mm in penetration from 6 months to 5 years, with 80% power, assuming a 0.07-mm standard deviation. However, 51 hips were enrolled to account for loss to follow-up. The Shapiro–Wilk test was used to determine normality in both the RSA penetration and the PROM data. A paired t-test was used to determine if changes in femoral head penetration into VEPE and steady state wear were significant between intervals. This test was also used to determine differences in patient-reported outcome scores over time. The level of significance was set at P < .05 for all tests.

Results

Radiostereometric Analysis

The mean ± standard error of the mean (SEM) proximal head penetration into the VEPE was 0.06 ± 0.01 mm at 5 years (Fig. 2). There were statistically significant differences between the 6-month interval and 2, 3, and 5 years (P < .021 for all comparisons) as well as between 1 and 2 years (P = .022) and between 1 and 3 years (P = .014). Neither was there any difference between 1 and 5 years nor was there any difference between 2 years and the later time points. Differences were observed in the medial and/or lateral plane between 6 months at all later time points (P < .044 for all comparisons), but there were no further differences in penetration after 6 months (Table 1). No significant differences were observed between any time points in the anterior/posterior plane (Table 1). The mean ± SEM proximal steady state wear was 0.005 ± 0.01 at 5 years. Steady state wear at all intervals was imperceptible as it was below the threshold of detection by RSA (Fig. 3). There were no significant differences over time in steady state wear in any plane throughout the 5 years.

The ME and condition numbers were all low, with a mean ± SEM of 0.19 ± 0.01 mm and 28 ± 1, respectively. The low ME measurements demonstrated strong stability and rigid body fitting of the beads within the patients. The low condition numbers suggested excellent spatial dispersion and visualization of the tantalum beads defining the segments and consistent patient positioning through the various follow-up intervals. Forty-nine double examinations indicated a high precision in the proximal direction of 0.115 mm.

Clinical Outcomes

All postoperative patient-reported outcomes improved significantly from the preoperative scores (all P < .001; Table 2). There was no significant difference in any outcome scores from 6 months to 5 years, demonstrating that patients improved significantly by 6 months and maintained favorable outcomes to 5 years. At 5 years, 82% of patients had a HHS above 90, with a mean ± SEM of 93 ± 2, suggesting an excellent midterm outcome. The patient-reported pain VAS was also very favorable at 5 years with mean scores of 1 ± 0.3. Patients reported a high level of functionality with a UCLA score of 6 ± 0.3 and a SF-36 physical function score of 49 ± 2 at the latest follow-up. Finally, a high general health state was reported with an EQ-5D score of 0.9 ± 0.01 at 5 years. One hip was revised at the 6-month follow-up for an infection and was consequently removed from the study.

Discussion

This study demonstrated low femoral head penetration into VEPE liners with up to 5-year follow-up. The early head penetration, probably due to settling of the liner, is low relative to that reported for non–vitamin E-stabilized liners measured by similar techniques [29]. Although variability was seen from some early time points to the later intervals, the penetration is still less than what was seen in the first generation of HXLPE [3,11,12]. Furthermore, steady state wear (wear without the initial bedding-in
period) was undetectable throughout the follow-up period. Digas et al [30] reported proximal head penetration measured by RSA of 0.08 mm into HXLPE at 5 years. The penetration of the VEPE in this cohort measured by the same technique showed less wear than that demonstrated by HXLPE at the same interval of 5 years. In addition, the wear observed in this study was well below the reported level (0.1 mm/year) at which osteolysis becomes a serious concern [31].

The study cohort used in this analysis was powered to detect wear differences between VEPE penetration over time. If other available wear measurement methods were implemented, substantially more patients (often several hundreds) would be needed to have the same power that was obtained in this RSA cohort. Therefore, the use of RSA to monitor new technologies puts the fewest patients at risk and allows for safe examination of wear without sacrificing statistical power [18]. As a result, it is not necessary to wait for late-term failures to identify problems with new technologies should they arise.

There have been a few reports of rim fractures of HXLPE, particularly in large head articulations and malpositioned cups, providing evidence for the reduced fatigue strength of HXLPE [32–34]. Two of these reports describe rim fractures in liners that were in vivo for approximately 2 years and the third notes a fracture at approximately 5 years in vivo. In addition to superior wear performance of VEPE compared with HXLPE, in vitro studies have shown that VEPE has improved fatigue strength over irradiated and melted HXLPE [4]. Oral et al [4] reported that even with suboptimal cup positioning, which subsequently leads to impingement, there were no fractures observed and no differences in wear or damage between conventional and large head sizes articulating with VEPE on a hip simulator [4]. Therefore, VEPE appears to maintain mechanical strength unlike some formulations of HXLPE. Although none of the acetabular components in our series had as steep anteversion angles (data not shown) as those included in the reports of rim fracture, it is nevertheless encouraging that no polyethylene fractures were observed at 5 years. Because retrieval and accelerated aging studies on HXLPE have shown that oxidation does occur, particularly in formulations that were annealed after irradiation, the long-term outcome of HXLPE is uncertain [6,23]. Oral et al showed that the oxidative stability of VEPE was not influenced by the accelerated aging process, which further substantiates the promise of VEPE as an improvement over HXLPE [4].

At 5 years, patients showed a high level of functional outcome according to patient-administered questionnaires. There was a slight drop (not significant) in the EQ VAS and satisfaction VAS from 6 months to 5 years. However, these changes are not clinically significant to the THA and are to be expected during the course of follow-up as patients continue to age [35]. All patients who reported unfavorable satisfaction scores (11 patients reported scores above 5) reported favorable scores on all other surveys. There is some concern that 0 being high satisfaction is perhaps unconventional and was therefore an oversight as patients completed surveys very quickly. Furthermore, the HHS, UCLA activity score, and the SF-36 physical function remain favorable at 5 years.

The RSA setup of this study was precise, including excellent dispersion and subsequent visualization of the tantalum beads within each of the segments. Double examinations at 2 follow-up intervals allowed for a thorough precision analysis of the RSA measurements and quantified the reliability of the measurements. In addition, obtaining the immediate postoperative film pair as soon after surgery as possible was crucial to establishing the baseline implant positions to monitor any and all penetrations that occurred over the study period. Furthermore, because the wear was negligible at the midterm in this cohort, the limits of RSA were tested. Because RSA is the most accurate and sensitive method of measuring wear, detecting wear at these very low levels makes it imperative to obtain baseline films as early as possible as measuring motion at this level using any other method would have been very difficult. In the future, increasing the number of patients who receive their postoperative films as an inpatient rather than returning 2–6 weeks after surgery will ensure that the most accurate baseline for comparison with all future films is collected.

Although the RSA protocol for study was well designed and executed, there were a few limitations. First, the patient-reported

Table 1
Mean ± SEM (mm) of Femoral Head Migration into the VEPE in 3 Orthogonal Planes at Each Follow-Up Interval.

<table>
<thead>
<tr>
<th>Plane</th>
<th>6 Mo ± SEM</th>
<th>1 Y ± SEM</th>
<th>2 Y ± SEM</th>
<th>3 Y ± SEM</th>
<th>5 Y ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial/lateral</td>
<td>0.01 ± 0.01</td>
<td>0.03 ± 0.01</td>
<td>0.05 ± 0.01</td>
<td>0.05 ± 0.01</td>
<td>0.04 ± 0.01</td>
</tr>
<tr>
<td>Proximal/distal</td>
<td>0.02 ± 0.01</td>
<td>0.03 ± 0.02</td>
<td>0.05 ± 0.01</td>
<td>0.05 ± 0.01</td>
<td>0.06 ± 0.01</td>
</tr>
<tr>
<td>Anterior/posterior</td>
<td>−0.02 ± 0.02</td>
<td>0.05 ± 0.04</td>
<td>−0.01 ± 0.04</td>
<td>0.01 ± 0.04</td>
<td>0.01 ± 0.04</td>
</tr>
<tr>
<td>Count</td>
<td>47 ± 47</td>
<td>46 ± 47</td>
<td>47 ± 47</td>
<td>47 ± 47</td>
<td>42 ± 42</td>
</tr>
</tbody>
</table>

The positive directions are medial, proximal, and anterior.

SEM, standard error of the mean; VEPE, vitamin E–diffused highly cross-linked polyethylene.

![Fig. 3.](image) Mean proximal steady state wear (mm) of the VEPE liners over time with standard error bars.
outcomes follow-up rate was lower than anticipated because of equipment malfunction within the clinic, patient refusal to complete forms, and occasional unavailability of the study coordinator to administer the surveys. Second, the highly porous acetabular shell did not project as clear of an edge around the backside of the shell compared with a less porous shell. Because the RSA software used edge detection of the shell to add 3 extra points to the acetabular unit segment, a less porous shell may have allowed for a tighter definition of the shell. Finally, the lack of a control group limits the direct comparison of the wear of VEPE with HXLPE. However, by comparing our group with others assessing wear of HXLPE using RSA in the literature, the measured head penetration was lower [30].

This study documents the longest-term evaluation of in vivo wear performance of VEPE. At the midterm follow-up of 5 years, the wear remained low compared with non-VEPE using the measurement tool of RSA. After settling of the liners in the early period, no significant head penetration occurred. All PROMs improved significantly from preoperatively to postoperative and remained favorable at 5 years. Diffusing vitamin E into HXLPE appears to be an alternative to melting and annealing because of its ability to simultaneously restore oxidative stability while maintaining low wear and fatigue strength. Long-term RSA follow-up is necessary to determine if this low midterm wear is maintained over time.

Acknowledgements

Thank you to Dr Andrew Freiberg and Dr Young-Min Kwon for allowing the enrollment of their patients to this study. In addition, thank you to Dr Ebru Oral for providing her expertise on vitamin E—diffused HXLPE.

References

学霸图书馆
www.xuebalib.com

本文献由“学霸图书馆-文献云下载”收集自网络，仅供学习交流使用。

学霸图书馆（www.xuebalib.com）是一个“整合众多图书馆数据库资源，
提供一站式文献检索和下载服务”的24小时在线不限IP图书馆。
图书馆致力于便利、促进学习与科研，提供最强文献下载服务。

图书馆导航：
图书馆首页 文献云下载 图书馆入口 外文数据库大全 疑难文献辅助工具