Research Protocol

A Prospective, Randomized Clinical Study Comparing Marathon Polyethylene and Enduron Polyethylene Acetabular Liners Used in Total Hip Arthroplasty at Long-Term Follow-up

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Background and Purpose

In 1999, the Anderson Orthopaedic Research Institute (AORI) initiated a prospective, Institutional Review Board-approved study to compare the clinical outcome of total hip arthroplasty (THA) patients who were randomized to either crosslinked Marathon or non-crosslinked Enduron polyethylene liners. During an 18-month enrollment period, 226 patients who received 236 THAs consented to participate in the study. Six patients (6 THAs) were excluded intra-operatively, leaving 230 THAs implanted with a Duraloc acetabular shell (DePuy) coupled with a 28-mm cobalt-chrome femoral head (DePuy). At 5-year outcome, we found that crosslinked Marathon polyethylene liners were wearing 95% less than the non-crosslinked Enduron liners [1]. In fact, the Marathon wear rates were so low at 5-year follow-up that the mean was not statistically different than zero. Several other institutions have also reported very low wear rates with highly crosslinked polyethylene based on early clinical outcome data [2-8]. However, since osteolysis typically appears after 5-year follow-up, the reduction in the incidence and extent of periprosthetic bone loss among THA patients with Marathon liners, compared to those with Enduron liners, was not as dramatic as the wear reduction [9]. Despite the substantial reduction in wear that we observed at 5-year follow-up, the patients' perceptions of their outcomes remained similar among the Marathon and Enduron groups [1]. At an average follow-up interval of at least 10-years (using outcome data for individual study participants obtained at a minimum of 9-year follow-up), we anticipated that the reduction in wear associated with Marathon polyethylene would be associated with significant reductions in periprosthetic osteolysis. Our findings [10] confirmed this hypothesis and indicated that the wear rate of Marathon polyethylene remained substantially lower than conventional Enduron polyethylene through 10-year follow-up.

Because crosslinking is accompanied by a reduction in the ultimate tensile strength, fatigue strength, and elongation to failure of ultra high molecular weight polyethylene [11-13], characterizing the long-term clinical performance of Marathon polyethylene is also important. Concerns have been expressed about the potential for the liner fracture, in vivo polyethylene oxidation or accelerated wear at long-term follow-up, the effects of femoral head roughening over time and the bioreactivity of crosslinked polyethylene debris particles [14-23]. Ultimately, the best way to address these concerns is in the context of well-controlled, long-term clinical outcome studies. As part of our efforts to follow patients throughout their lives to obtain long-term outcome data, we will continue to obtain routine follow-up at 5-year intervals from the date of surgery for each patient. Because we anticipate that the reduced incidence of wear and osteolysis will result in a lower incidence of revision surgery among the patients randomized to Marathon liners, implant revision for reasons related to wear will be our primary outcome measure at long-term follow-up.

Primary Hypothesis:

- Primary THAs prospectively randomized to Marathon liners will demonstrate a lower rate of revision for wear-related complications and higher survivorship compared to primary THAs randomized to Enduron liners.

Additional Hypotheses:

- Primary THAs prospectively randomized to Marathon liners will demonstrate substantially reduced polyethylene wear compared to primary THAs randomized to Enduron liners.
- THAs prospectively randomized to Marathon liners will demonstrate a reduced incidence of clinically important osteolysis with an area of at least 1.5 square centimeters compared to primary THAs prospectively randomized to Enduron liners.
- THAs prospectively randomized to Marathon liners will demonstrate higher rates of patient satisfaction and better Harris Hip Scores compared to primary THAs randomized to Enduron liners.
- All the THAs prospectively randomized to Marathon and Enduron liners will demonstrate constant wear rates over time.

Study Population

Inclusion criteria

- Patient consented to participate in this study
- Implanted on the acetabular side with a Duraloc 100 cup incorporating a 4-mm lateralized polyethylene liner that was randomized to either Marathon or Enduron
- Implanted on the femoral side with an extensively porous-coated (AML/Solution or Prodigy) stem with a 28-mm cobalt-chrome femoral head

Exclusion criteria

- Intra-operative considerations related to implant stability, leg length correction or bone quality led to the implantation of THA components other than a Duraloc 100 cup, 4-mm lateralized liner, extensively porous-coated stem and 28-mm cobalt-chrome femoral head
- Patient refused reconsent for continued follow-up

Anticipated Study Population Size

The 230 THAs randomized to a Marathon or Enduron polyethylene liner will comprise the study population for our survivorship analyses. Based on our previously published data, we found 9 THAs among deceased patients at a mean follow-up of 5.7 years [1] and 32 THAs among deceased patients at a mean follow-up of 10 years [10]. Based on this data, we anticipate that approximately 12% of the patients enrolled in the study will pass away every five years.

Material and Methods:

- Patients due for routine 15-year follow-up will be contacted by Anderson Orthopaedic Institute personnel who will schedule follow-up appointments. Attempts will be made to obtain follow-up for all enrolled patients who have not had a follow-up evaluation at the Anderson Clinic within one year before the 15-year anniversary of their original surgery date. This procedure will be repeated at five-year intervals (20 years, 25 years, etc.).

Study interval	Minimum follow-up date for study interval	End date
15-year	DOS + 14 years	DOS + 19 years -1 day
20-year	DOS + 19 years	DOS + 24 years -1 day
25-year Continue every 5 years	DOS + 24 years, etc.	DOS + 29 years -1 day, etc.

- At the initial follow-up visit associated with this long-term study, the subjects will be informed of changes to the protocol and asked to sign a reconsent.
- At the time of each follow-up visit, patients will complete the clinic patient questionnaire per current protocols and the physician will complete a standardized evaluation.
- Standardized x-rays will be obtained during follow-up visits per current standard of care.
- Subjects who have already come to the clinic for a routine follow-up visit within one year preceding each 5-year anniversary and have not yet signed a reconsent for this long-term follow-up study will be sent a copy of the reconsent in the mail. Designated research personnel will call the subject to review the consent when the subject is able to read along, answer any questions, and ask the subject to send back the signed form if the subject is willing to reconsent.
- Subjects unable to return to the Anderson Clinic for follow-up will be asked to complete the clinic patient questionnaire and a prescription for x-rays will be sent to them after a reconsent has been obtained by telephone as outlined above.
- If a subject does not request to be withdrawn from this study but a fully executed reconsent cannot be obtained (potentially because the subject cannot be contacted), a waiver of informed consent and HIPAA Authorization is requested from the IRB to use the subject's existing medical records for the purposes of this study.
- Serial anteroposterior (AP) pelvic x-rays will be analyzed to evaluate femoral head penetration into the polyethylene liner for each THA using a computer-assisted, validated software application (Hip Analysis Suite, Chicago, IL) [24]. A least-

squares linear regression analysis based on the head penetration versus time in situ will be used to calculate a wear rate for each THA [25]. The Hip Analysis Suite software will also be used to calculate the volumetric wear of the polyethylene liner based on the femoral head penetration data. Wear rates among the Marathon and Enduron groups will be compared using an Independent samples t-test or Mann-Whitney U, depending on the normality of the data.

- Serial x-rays for each THA will be analyzed to identify regions of femoral and acetabular osteolysis. The area of each osteolytic region will be measured on the AP pelvic x-ray with Martell's Hip Analysis Suite software. The incidence of osteolysis will be compared using a chi-square or Fisher's Exact test, depending on the cell counts. The size of osteolytic lesions will be compared using an Independent samples t-test or Mann-Whitney U, depending on the normality of the data. X-rays will also be used to evaluate radiographic complications such as periprosthetic fracture and implant loosening. The incidence of radiographic complications among the Marathon and Enduron groups will be compared using a chi-square or Fisher's Exact test, depending on the cell counts.
- Kaplan-Meier survivorship analysis will be used to compare the outcome of the Marathon and Enduron groups using revision for any reason as an endpoint. Survivorship analyses using revision for specific diagnoses, such as wear and osteolysis or implant loosening, will also be performed.
- Clinical outcome data among the Marathon and Enduron groups will queried from AORI's institutional database and compared based on the nature and distribution of the data. Specifically, we anticipate that patient satisfaction will be compared with a Fisher's Exact test and Harris Hip scores will be compared with the use of a Mann-Whitney U.
- A manuscript summarizing the results of this study will be submitted for publication in a peer-reviewed orthopaedic journal. The results of this study will also be presented at orthopaedic meetings and conferences.
- Subjects will continue to be followed for life.

Source of Funding

Partial funding for this study will be provided by DePuy Orthopaedics. Study costs in excess of the funding provided by DePuy will be supported internally by the Anderson Orthopaedic Research Institute.

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