

Crosslinked polyethylene compared to conventional polyethylene in total hip replacement

Pre-clinical evaluation, in-vitro testing and prospective clinical follow-up study

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Background Polyethylene wear-induced osteolysis is a major cause of implant loosening in total hip arthroplasty. New crosslinked polyethylenes are presumed to give lower wear rates, but no long-term clinical results are available yet.

Patients and methods We compared basic material characteristics and MTS hip joint simulator wear rates of a crosslinked polyethylene (Duration) to those of conventional polyethylene. In a randomized double-blind 5-year clinical follow-up study, 133 hips (67 conventional, 66 Duration) in 127 patients were followed-up for an average of 5 (3–6) years. Wear rates were measured using a computer-based edge detection method. The radiographic appearances of wear-related phenomena were recorded.

Results The Duration polyethylene showed a significantly lower in-vitro wear rate in the simulator study (mean 22 (SD 2.3) vs. 40 (SD 1.5) mm³/106 cycles). Also, the in-vivo wear was lower for Duration (mean 0.083 (SD 0.056) mm/year) than for conventional polyethylene (mean 0.123 (SD 0.082) mm/year). All radiographic signs of osteolysis were less frequent in the Duration group.

Interpretation Our study has given a substantial body of evidence—from lower wear rates, less frequent signs of osteolysis, and higher survival rates after a mean follow-up of 5 years—that Duration provides better clinical outcomes than conventional polyethylene.

In total hip arthroplasty, wear particle-induced osteolysis is a major cause of aseptic implant loosening. The osteolytic effect of the wear debris depends on the cytotoxicity of the material (polyethylene, ceramic or metal), the size and morphology of the debris particles, the pathways available for particle migration, and the volume of wear particles produced and released into the periprosthetic tissue. Several authors have established that lower wear rates substantially reduce the incidence of osteolysis and increase the survival of the implants (Barrack et al. 1997, Shih et al. 1997, Sochart 1999, Dumbleton et al. 2002, Dumbleton and Manley 2003, Harris 2003, Orishimo et al. 2003).

The resistance of ultra-high-molecular-weight polyethylene to adhesive and abrasive wear can be increased by increasing the degree of crosslinking, the formation of covalent bonds between the backbone molecular chains (Wang et al. 1998). Polyethylene crosslinking for clinical application is achieved by irradiation. During the irradiation process, the level of crosslinking can be influenced by the type of radiation (e.g. Co60 gamma, electron beam), the dose (20–100 kGy), the atmosphere (air, nitrogen, argon), and/or post-radiation treatment (e.g. sequential radiation, annealing, remelting). These process parameters also influence the degree of unwanted side effects of radiation crosslinking, such as the creation of free radicals which

lead to oxidation, embrittlement and accelerated wear during ageing. Annealing can induce further crosslinking by promoting recombination of free radicals.

Early polyethylene was irradiated mainly for the purpose of sterilization at low doses (ca 20–30 kGy) and in air, leading only to low crosslink densities and to oxidation and embrittlement during ageing. This “conventional” polyethylene was used clinically until the late 1990s when it was gradually replaced by subsequent generations of moderately and highly crosslinked polyethylenes. These highly crosslinked materials show promisingly low wear rates in hip simulator studies (McKellop et al. 1999), but due to their relative novelty, there have been relatively few clinical studies, either with a follow-up that has been too short (Heisel et al. 2004) or patients have not been randomized to a well-matched control. This is a problem, as clinical wear rates can vary enormously depending on patient demographics; even sophisticated computer-based wear measurement methods produce errors, making follow-up times of less than 3 years unreliable (Collier et al. 2003). In addition, comparison of wear rates from different studies using different techniques must also be interpreted with caution (Devane et al. 1995).

This study compares the wear rates and radiographic signs of osteolysis of conventional polyethylene with those of Duration—a new, moderately crosslinked polyethylene—in a 5-year randomized clinical follow-up study. Wear of both materials was assessed in a hip simulator study and by basic characterization of their material properties, to assess the advantages (or disadvantages) of the elevated crosslink density of the newer polyethylene. Our hypothesis was that the Duration polyethylene produces lower clinical wear rates and fewer radiographic signs of osteolysis, and that this superior wear resistance in-vivo is reflected by the in-vitro test results.

Material and methods

Preparation of material

All acetabular cup inserts were manufactured from ram-extruded rods converted from Hoechst GUR 415 resin by the Standard Specification for Ultra-

Table 1. Methods for derivation of basic properties of polyethylene

Method / Property
Tensile test (ASTM D638) ^a
Yield strength
Ultimate strength
Elongation to break
Creep test (ASTM D621)
Creep strain
Izod impact test (double notch, ASTM D256)
Impact double notch
Small punch test (ASTM F2183-02)
Load at break
Work to failure
Density gradient column (ASTM D1505)
Density
Differential scanning calorimetry
Crystallinity
High temperature gel permeation chromatography
Molecular weight M _n
Molecular weight M _w

^a Standard test method for tensile properties of plastics

High-Molecular-Weight-Polyethylene Powder and Fabricated Form for Surgical Implants (Poly-Hi Solidur), with a molecular weight between 5 and 6 106 g/mol. Two materials, conventional and Duration polyethylene were produced by different radiation and sterilization processes in order to be used in preclinical testing and the clinical study.

The inserts to be named conventional polyethylene were packaged and sealed into a double plastic blister surrounded by air, and the package was then irradiated at a dose of 30 kGy. The inserts to be labeled Duration were placed in two blisters which were evacuated and then flushed with nitrogen prior to sealing. The oxygen concentration in the inner blister was less than 0.5% (v/v) and the concentration in the outer blister was less than 5% (v/v) at the time of packaging. The completed package was then gamma-irradiated at a dose of 30 kGy. Following irradiation, the package was placed in an oven for annealing at a temperature of 50°C for 144 h. The annealing was meant to increase crosslink density by promoting free radical recombination.

Characterization of materials

For a basic comparison, preclinical tests of a physical, chemical and mechanical nature were performed (Table 1) on both the conventional polyethylene and the Duration polyethylene, with a view

to measuring differences in crosslink density using the Small Punch Test (Standard Test Method for Tensile Properties of Plastics, ASTM D 638-95). For each test, 4 samples were analyzed and compared using the unpaired two-sided Student t-test.

Hip simulator

Tribological tests were performed on an MTS hip joint simulator with biaxial rocking through a 23° load angle according to a Paul-type physiological curve. Peak load was 2,450 N and load frequency was 1 Hz. Sterile-filtered bovine calf serum (Sigma) was used as a lubricant, with the addition of 0.3% sodium azide to prevent degradation. Test chambers were sealed with polyethylene bags to prevent contamination and evaporation. Wear was determined gravimetrically every 250,000 cycles using soak controls to compensate for fluid sorption. The test was terminated after 10 million cycles and the average linear and volumetric wear rates were calculated.

Randomized clinical study

After obtaining informed consent and ethical approval, 127 patients (133 hips) were included in a randomized prospective clinical study performed at 3 hospitals by 3 surgeons. We included patients with osteoarthritis, rheumatoid arthritis, avascular necrosis of the femoral head, or posttraumatic arthritis of the hip. The mean age was 63 (37–74) years. Patients were excluded if they had had prior hip surgery at the site of operation.

Following inclusion, patients were assigned to either a conventional insert or the Duration insert by double-blind block randomization. Both inserts were of the same hemispherical design and were mated to an ABG-II hydroxyapatite-coated hemispherical acetabular shell made of titanium alloy (Stryker, Mahwah, NJ). The femoral implant was not controlled, but consisted of either a press-fit hydroxyapatite-coated stem or a cemented ABG-II stem. All femoral heads were of CoCr alloy and measured 28 mm in diameter; thus, a major factor influencing wear was standardized.

Clinical follow-up parameters were assessed at postoperative patient visits after less than 6 weeks, and at 1, 2, 3 and 5 years postoperatively. Standard radiographs were obtained for measurement of wear and identification of migration, loosening,

and potentially wear-related phenomena such as radiolucencies and osteolysis in both the femur and acetabulum. Findings were expressed according to the 7 Gruen regions for the femur and the 3 DeLee and Charnley regions for the acetabulum. The zero-wear baseline radiographs were obtained at more than 28 days and less than 6 weeks postoperatively, in order to minimize the effects of joint laxity on the seating of the femoral head into the acetabular liner.

Wear was measured by a single observer using a validated computer-based edge-detection technique, which has been described previously (Martell and Berdia 1997). The technique uses sequentially applied custom convolution kernels to the region of interest, thereby extracting the best-fit circles defining the femoral head and the acetabular shell. Edge detection and extraction is performed in a completely automated manner, thereby reducing inter- and intraobserver errors. While both anteroposterior (AP) and lateral radiographs were obtained at each interval, only the AP radiographs were used to assess wear (Martell et al. 2003). Volumetric wear was calculated from the 2D anterior-posterior radiograph based on the amount of linear wear, the wear angle with respect to the cup face (beta angle), and the size of the femoral head, using a modified version of previously described geometric relationships (Kabo et al. 1993).

Statistics

Linear and volumetric wear rates were compared using the non-paired, two-tailed Student t-test and the Mann-Whitney U test. Survival analysis was performed with radiographic evidence of the onset of osteolysis as the endpoint.

Results

Characterization of material

All material properties measured were not statistically significantly different between the conventional polyethylene and the Duration polyethylene, apart from the “load at break” in the Small Punch Test (Table 1). While the average “load at break” for conventional polyethylene was mean 84 (SD 2.2) N, the Duration material scored mean 94 (SD 3.3) N, giving evidence of elevated crosslink den-

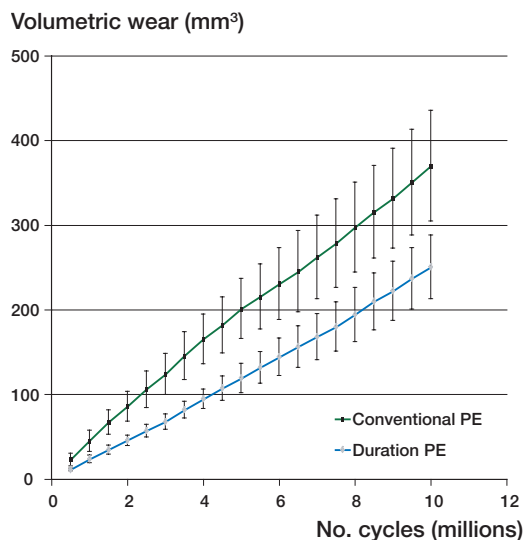


Figure 1. Accumulated wear volumes during hip simulator testing for conventional polyethylene (black) and Duration polyethylene (gray); mean \pm SD.

sity. Virgin, non-irradiated polyethylene tested as reference showed a mean “load at break” of 71 (SD 2.2) N, indicating the level of additional crosslink density achieved.

Hip simulator

The mean volumetric wear rate measured after 2 million cycles was 40 (SD 1.5) $\text{mm}^3/10^6$ cycles for the conventional polyethylene, and only 22 (SD 2.3) $\text{mm}^3/10^6$ cycles for the Duration inserts, a 45% reduction ($p = 0.03$). The difference in wear rates diminished with time, so that at 10 million cycles the reduction in wear rate achieved by the Duration inserts was down to 32% (Figure 1).

Randomized clinical study

127 patients with 133 implants (67 conventional, 66 Duration) had a mean follow-up of 4.7 (3–6) years. 6 patients (3 conventional, 3 Duration) died after a mean follow-up period of 3.5 years. The cause of death was unrelated to the prosthesis. 2 stems paired to conventional polyethylene inserts were revised after a mean period of 3 years because of excessive thigh pain, but no osteolysis was observed in these cases. No Duration insert had to be revised.

For the remaining 125 implants, 10 cases (4 conventional, 6 Duration) were lost due to inadequate

Table 2. Patient demographics

	Conventional polyethylene n = 54	Duration polyethylene n = 45
Age (years) ^a	63 (37–72)	64 (45–74)
BMI ^a	27 (22–49)	28 (21–40)
Follow-up (years) ^a	4.7 (3.3–5.9)	4.7 (3.1–5.5)
Ratio stem uncemented/cemented	42/12	36/9
Cup diameter (mm) ^a	54 (48–60)	54 (48–60)
Liner thickness (mm) ^a	9.0 (6–12)	9.0 (6–12)
Primary diagnosis:		
Osteoarthritis	51	43
Posttraumatic arthritis	2	2
^a mean (range)		

follow-up (< 36 months) and a further 15 were lost because the quality of the radiographs was insufficient for accurate wear measurement (5 conventional, 10 duration). This left 54 conventional implants and 45 Duration implants for statistical analysis. The two groups were well matched for age, body mass index, follow-up time, liner thickness, cup diameter, use of uncemented or cemented stem, and primary diagnosis (Table 2).

Polyethylene wear

Between baseline and last follow-up, conventional polyethylene produced a linear wear rate of 0.12 (SD 0.082) mm/year and a volumetric wear rate of 60 (SD 43) mm^3/year . The Duration polyethylene wore significantly more slowly, at a linear rate of 0.083 (SD 0.056) mm/year and a volumetric rate of 44 (SD 34) mm^3/year , a reduction of 33% and 28% respectively ($p = 0.008$ and $p = 0.04$; Mann-Whitney U-test). No correlation between wear rate and age, body mass index, liner thickness, cup diameter or method of stem fixation (uncemented/cemented) could be found.

The distribution of linear wear rates was narrower with Duration polyethylene and it lacked the high value outliers observed for conventional polyethylene (Figure 2).

Radiographic evaluation

Phenomena that are potentially wear particle-induced, such as radiolucencies in the proximal Gruen regions 1 and 7, acetabular radiolucencies,

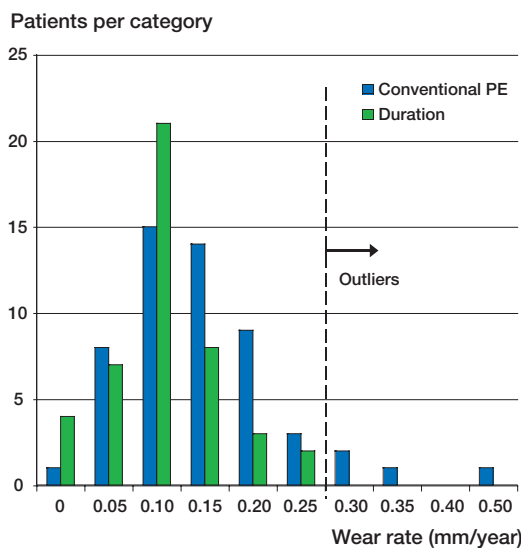


Figure 2. Histogram of in-vivo linear wear rates for conventional polyethylene (blue) and Duration polyethylene (green).

femoral osteolysis and femoral aseptic loosening, were much more common with conventional polyethylene than with the Duration material. Polyethylene penetration occurred 2.4 times more often in conventional inserts than in Duration inserts (Table 3). The survival rates for not having femoral osteolysis at 5-year follow-up were 92% for conventional polyethylene and 98% for Duration polyethylene.

Discussion

Crosslink density and wear resistance of the new polyethylene Duration could be raised without increasing the radiation dose above the conventional sterilization levels, but by modification of the process only (nitrogen atmosphere, annealing at 50°C for 144 h). At the same time, other mechanical properties such as crystallinity, creep strain, yield strength and elongation at break remained unchanged, suggesting that elevated crosslink density was achieved without increasing brittleness.

The annealing process accelerates recombination of radicals formed during irradiation. If annealing is performed in an inert atmosphere such as nitrogen, the recombining radicals form additional crosslinks rather than bind with oxygen

Table 3. Radiographic observations at maximum follow-up

Radiographic phenomenon	Counts ^a	
	Conventional n = 54	Duration n = 45
Femoral radiolucencies		
None	28 (0.5)	28 (0.6)
Gruen region 1 or 7	7 (0.1)	2 (0.04)
Gruen regions 2–6	31 (0.5)	28 (0.6)
Acetabular radiolucencies		
None	50	44
DeLee and Charnley zone 1	2 (0.04)	1 (0.02)
DeLee and Charnley zone 2	1 (0.02)	0
DeLee and Charnley zone 3	1 (0.02)	0
Femoral osteolysis	5 (0.08)	1 (0.02)
Femoral aseptic loosening	3 (0.05)	1 (0.02)
Acetabular aseptic loosening	0	0
PE penetration	8 (0.1)	3 (0.1)
Femoral hypertrophy		
Cancellous	23 (0.4)	30 (0.7)
Cortical	17 (0.3)	12 (0.3)
Corticocancellization	23 (0.4)	24 (0.5)

^a Figures in parentheses are rates

(Streicher 1988). This increases crosslink density further—instead of forming hydroperoxy radicals in an atmosphere of air, causing continual chain scission, long-term degradation and shelf ageing (Edidin et al. 2000). While the newest generation of polyethylenes for orthopedic application has now reached radiation levels of approximately 100 kGy, beyond which no further increase in crosslinking can be expected (product information from Sulzer Medica, Orthopedic Division, Winterthur, Switzerland), further optimization may come from process modifications such as annealing, which reduces the number of non-crosslink chemical events that tend to occur during irradiation.

Our study has given a chain of evidence from lower wear rates, less frequent signs of osteolysis and higher survival, to suggest that Duration can provide better clinical outcomes than conventional polyethylene.

In comparison to the newest generation of highly crosslinked polyethylenes, the Duration material can only be considered to be moderately crosslinked. However, we found that even the relatively small step from conventional polyethylene gamma-sterilized in air to polyethylene gamma-sterilized in nitrogen with subsequent annealing was sufficient to reduce wear rates, diminish high-value

outliers, reduce radiographic evidence of osteolysis, and to increase survival during a randomized 5-year study.

One deficiency in our clinical study was the relatively high loss to follow-up because of radiographs of insufficient quality. The wear measurement method we used is superior to the established manual methods such as the Livermore method, but requires well-centered radiographs with highly congruent patient alignment between follow-up points (Martell et al. 1997). This led to the exclusion of several radiographs, some of which could have been measured with a conventional manual method. However, we decided to prioritize consistency and accuracy of the method over limitation of loss to follow-up.

The advantage of Duration over conventional polyethylene in terms of clinical wear rate was confirmed in our wear simulator study, with the relative reduction in vitro being only slightly higher than in vivo. This adds strength to the clinical evidence and suggests that the even lower simulator wear rates reported for the newest highly crosslinked polyethylene (McKellop et al. 1999) can produce corresponding clinical advantages at mid-term follow-up.

We found that the absolute wear rates measured in vivo were higher than in vitro. This could be expected from other studies comparing laboratory and clinical results (McKellop et al. 1981, McKellop and Clarke 1984, Wang 2001). Clinical wear rates tend to be elevated by individual patient outliers whose wear rates are many times the mean (Martell et al. 2000, Schmalzried et al. 2000).

Our simulator study showed that the reduction in wear of Duration relative to conventional polyethylene became less with increasing number of cycles. Long-term clinical measurements of wear will be required to determine whether the benefits of Duration polyethylene diminish over time in the same way as in the hip simulator, and whether wear debris leading to osteolysis and implant loosening also remains significantly reduced during a long-term follow-up.

Contributions of authors

CHG performed data analysis and wrote the manuscript. BG performed data analysis and gave statistical support. RR per-

formed the wear simulator study and examined basic material properties. JJR operated patients in Zwolle. AJV operated patients in Sittard. AJT operated patients in Heerlen.

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