■ HIP

Polyethylene manufacturing characteristics have a major effect on the risk of revision surgery in cementless and hybrid total hip arthroplasties

AN ANALYSIS OF THE NATIONAL JOINT REGISTRY OF ENGLAND, WALES, NORTHERN IRELAND AND THE ISLE OF MAN

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Aims

The aim of this study was to identify the effect of the manufacturing characteristics of polyethylene acetabular liners on the survival of cementless and hybrid total hip arthroplasty (THA).

Methods

Prospective cohort study using linked National Joint Registry (NJR) and manufacturer data. The primary endpoint was revision for aseptic loosening. Cox proportional hazard regression was the primary analytical approach. Manufacturing variables included resin type, crosslinking radiation dose, terminal sterilization method, terminal sterilization radiation dose, stabilization treatment, total radiation dose, packaging, and face asymmetry. Total radiation dose was further divided into G1 (no radiation), G2 (> 0 Mrad to < 5 Mrad), G3 (≥ 5 Mrad to < 10 Mrad), and G4 (≥ 10 Mrad).

Results

A total of 5,329 THAs were revised, 1,290 of which were due to aseptic loosening. Total radiation dose, face asymmetry, and stabilization treatments were found to significantly affect implant survival. G1 had the highest revision risk for any reason and for aseptic loosening and G3 and G4 the lowest. Compared with G1, the adjusted hazard ratio for G2 was 0.74 (95% confidence interval (CI) 0.64 to 0.86), G3 was 0.36 (95% CI 0.30 to 0.43), and G4 was 0.38 (95% CI 0.31 to 0.47). The cumulative incidence of revision for aseptic loosening at 12 years was 0.52 and 0.54 per 100 THAs for G3 and G4, respectively, compared with 1.95 per 100 THAs in G1. Asymmetrical liners had a lower revision risk due to aseptic loosening and reasons other than aseptic loosening compared with symmetric (flat) liners. In G3 and G4, stabilization with vitamin E and heating above melting point performed best.

Conclusion

Polyethylene liners with a total radiation dose of ≥ 5 Mrad, an asymmetrical liner face, and stabilization with heating above the melting point demonstrate best survival.

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Introduction

Total hip arthroplasty (THA) is a highly successful procedure for restoring mobility, improving quality of life, and relieving pain.[1] While infection and recurrent dislocation are the most common indications for revision surgery, historically, the most common indication for revision has been reported as prosthesis loosening associated with wear of the bearing surface.[2] Recent studies report encouraging results on the longevity of modern THA.[3] The demand for arthroplasty surgery in younger patients is increasing and younger patients are reported to have a much higher lifetime risk of revision.[4,5]

Modified polyethylene, commonly labelled crosslinked polyethylene (XLPE), was introduced in the late 1990s in order to reduce wear debris and associated loosening at later stages.[6] Among

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Table I. Characteristics of acetabular liners.

Characteristic	Value
Resin type	1020
	1050
Radiation source	Gamma
	Ebeam
	None
Multiple crosslinking treatments	Yes
	No
Crosslinking dose	In Mrad
Terminal sterilization method	Gamma
	EtO
	Gas plasma
Terminal sterilization radiation dose	In Mrad
Stabilization treatment (free radical scavenging)	None
	Heated below melting point
	Heated above melting point
	Vitamin E infused
	Vitamin E blended
	Heated below + mechanical deformation
Total radiation dose	Derived, crosslinking dose + terminal sterilization radiation dose in Mrad
Packaging	In air/air permeable
	Inert gas/non-air permeable
Liner face asymmetry	Asymmetrical ('lip')
	Flat

EtO, ethylene oxide.

products labelled as XLPE, there is significant variation in the process of manufacture, including differences in the type of resin used, the dose of radiation applied, the treatment used to stabilize the polyethylene, the sterilization process, packaging, and the shape of the final product. Each step in the manufacturing process affects the properties of the polyethylene end product,[7] and, possibly, its long-term performance. Beyond simple division into conventional polyethylene (PE) and XLPE using a cut-off of 5 Mrad of radiation, little is known about the effect of polyethylene manufacturing process modifications on the risk of revision of THAs.

This study is an analysis of the survival of 292,920 primary THAs using cementless acetabular components. Cemented acetabular components were excluded from this analysis, because failure mechanisms unrelated to polyethylene wear have been proposed that might confound the results of a combined analysis.[8,9] Data from the National Joint Registry for England, Wales, Northern Ireland and the Isle of Man (NJR) were linked with polyethylene acetabular liner manufacturing information obtained from the implant manufacturers. The aim of the study was to assess the effect of different manufacturing characteristics on the risk of revision for aseptic loosening.

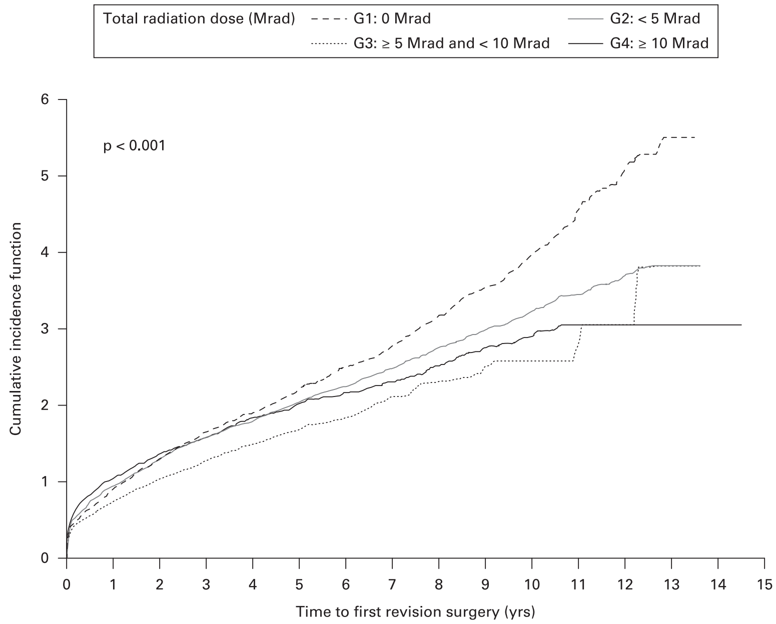
Methods

Two data sources were combined: demographic and outcome (survival) data from the NJR, and manufacturing information on polyethylene acetabular liners. The NJR outcomes were obtained for all primary THAs between 1 January 2004 and 28 July 2016 that used a cementless acetabulum and a polyethylene liner. Manufacturing details of 31 different polyethylene liner brands were obtained from the manufacturers. For each liner, information was obtained on the manufacturing characteristics listed in Table I.

Linkage between NJR data and liner manufacturing data was performed using the liner catalogue number, and was highly successful. There were 316,449 records of primary THA using a cementless acetabulum and a polyethylene liner. Of these, 1,101 constrained and 308 dual-mobility liners were excluded. Of the remaining 315,040 primary THAs, liner manufacturing data were available and were successfully linked for 299,958 (95.2%) primary THAs. A further 7,038 records were excluded for missing or erroneous follow-up and covariate information. The final sample included 292,920 primary THAs.

The primary endpoint was time to first revision, defined as the exchange of one or more implant components. If no revision occurred until the last follow-up date of 28 July 2016, the observation was censored at this date. Participants who died before undergoing revision were censored at the time of death. We investigated risk of revision for any reason (5,329 revisions), for aseptic loosening (1,290 revisions), and for reasons other than aseptic loosening (4,039). The same revision can have multiple reasons reported.

Exploratory statistical analysis was based on Kaplan-Meier product limit estimator. First, a series of exploratory Kaplan-Meier analyses were performed to identify manufacturing characteristics possibly associated with general and cause-specific revisions. These exploratory analyses were followed by multivariate Cox proportional hazard regression survival analyses. Based on exploratory review of Kaplan-Meier cumulative incidence functions, a time-specific Cox regression model using an exploratory defined cut-off at 4.5 years was run as well. Finally, a statistical sensitivity analysis was performed using a parametric



Total rad group (Mrad)	Y_0	Y_1	Y_2	Y_3	Y_4	Y_5	Y_6	Y_7	Y_8	Y_9	Y_10	Y_11	Y_12	Y_13	Y_14
G1: 0	26,526	25,835	25,078	24,296	23,378	21,346	18,549	15,179	11,706	8,166	5,295	2,917	1,147	224	1
G2: < 5	56,847	54,616	51,943	48,625	44,790	40,620	35,872	30,688	25,011	18,714	12,616	7,379	3,498	835	1
G3: ≥ 5 and < 10	136,057	112,522	86,160	63,488	45,147	30,107	18,978	10,091	4,480	1,643	656	338	149	7	1
G4: ≥ 10	73,490	61,138	47,802	35,726	26,003	18,123	12,343	8,332	5,021	3,160	1,757	753	252	26	3

Fig. 1a

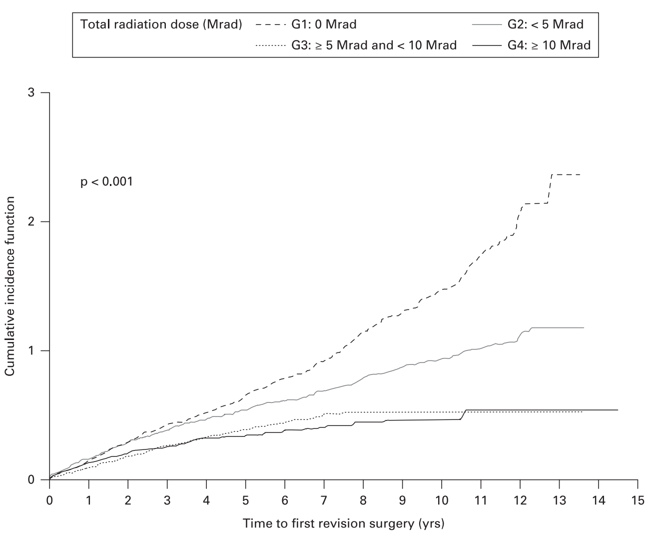


Fig. 1b

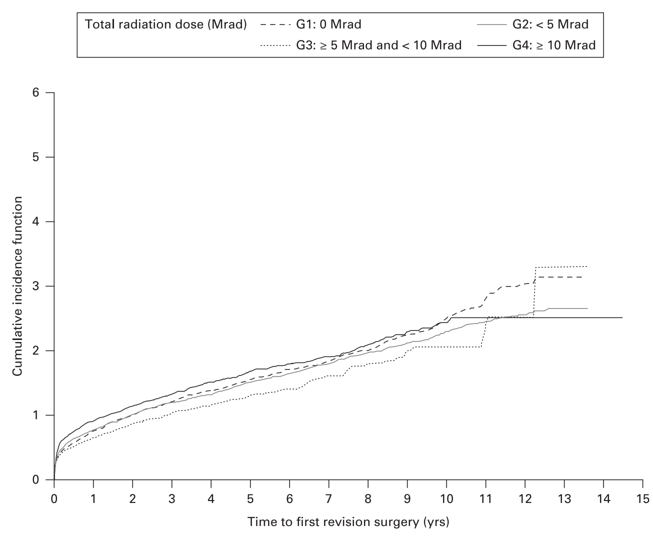


Fig. 1c

a) Cumulative incidence function of revision due to any reason by polyethylene acetabular liner total radiation dose. b) Cumulative incidence function of revision due to aseptic loosening by polyethylene acetabular liner total radiation dose. c) Cumulative incidence function of revision due to reasons other than aseptic loosening by polyethylene acetabular liner total radiation dose.

life regression survival analysis (PROC LIFEREG) model. The best parametric model fit was achieved using gamma distribution. All survival analyses were performed accounting for a competing risk of death in order to obtain cumulative incidence function (CIF) estimates utilizing a Gray CIF method.[10]

Cause-specific analyses treated revisions for other causes as competing risks as well. The full Cox multivariate proportional hazards regression and the life hazard models were built following exploration of individual candidate variables in age- and sex-adjusted models. The following variables were

Table II. Descriptive information by acetabular liner group.

Variable	Radiation (Mrad)			
	G1: No radiation	**G2: < 5**	**G3: ≥ 5 and < 10**	**G4: ≥ 10**
n	26,526	56,847	136,057	73,490
Female sex, n (%)	16,820 (63.4)	35,202 (61.9)	80,393 (59.1)	44,480 (60.5)
Mean age, yrs (SD)	70.5 (9.1)	70.5 (9.4)	69.3 (10.1)	69.3 (10.5)
Age group, n (%)				
< 55 yrs	1,140 (4.3)	2,785 (4.9)	10,539 (7.8)	6,368 (8.7)
55 to < 65 yrs	5,328 (20.1)	10,793 (19.0)	27,985 (20.6)	14,812 (20.2)
65 to < 75 yrs	11,067 (41.7)	23,418 (41.2)	53,980 (39.7)	27,893 (38.0)
≥ 75 yrs	8,991 (33.9)	19,851 (34.9)	43,553 (32.0)	24,417 (33.2)
Osteoarthritis indication	25,233 (95.1)	53,430 (94.0)	125,813 (92.5)	67,502 (91.9)
Liner, n (%)				
Face asymmetry: yes	17,918 (67.6)	24,111 (42.4)	76,439 (56.2)	35,358 (48.1)
Resin type: 1020	4,934 (18.6)	6,692 (11.8)	70,335 (51.7)	13 (0.02)
Terminal sterilization, n (%)				
Gamma	4,937 (18.6)	56,847 (100.0)	0 (0.0)	20,923 (28.5)
EtO	3,231 (12.2)	0 (0.0)	4,526 (3.3)	52,555 (71.5)
Gas plasma	18,358 (69.2)	0 (0.0)	131,531 (96.7)	12 (0.02)
Stabilization treatment, n (%)				
Any	0 (0.0)	1,518 (2.7)	136,057 (100.0)	73,355 (99.8)
Heated below melting point	0 (0.0)	1,518 (2.7)	58,142 (42.7)	198 (0.3)
Heated above melting point	0 (0.0)	0.0 (0.0)	76,338 (56.1)	61,451 (83.6)
Vitamin E infused	0 (0.0)	0.0 (0.0)	0 (0.0)	11,693 (15.9)
Vitamin E blended	0 (0.0)	0.0 (0.0)	233 (0.2)	0 (0.0)
Heated below + mechanical deformation	0 (0.0)	0.0 (0.0)	1,344 (1.0)	0 (0.0)
None	26,526 (100.0)	55,329 (97.3)	0.0 (0.0)	13 (0.2)
Head size ≤ 32 mm, n (%)	26,526 (100.0)	56,787 (99.89)	93,125 (68.5)	46,712 (63.6)
Cementless stem fixation, n (%)	18,751 (70.7)	30,334 (53.4)	82,674 (60.8)	38,670 (52.6)
Head composition, n (%)				
Ceramic or oxinium	4,513 (17.0)	14,113 (24.8)	44,214 (32.5)	31,214 (42.5)
Metal	22,013 (83.0)	42,734 (75.2)	91,843 (67.5)	42,276 (57.5)
Follow-up				
Mean person-time, yrs (SD)	7.3 (2.9)	6.9 (3.3)	3.1 (2.3)	3.3 (2.6)
Maximum follow-up, yrs	13.5	13.6	13.6	14.5
Outcome, n (%)				
Not revised	20,440 (77.1)	44,353 (78.0)	126,302 (92.8)	67,146 (91.4)
Revised	884 (3.3)	1,534 (2.7)	1,720 (1.3)	1,191 (1.6)
Revised due to aseptic loosening*	318	437	345	190
Revised due to aseptic loosening socket*	117	229	119	75
Revised due to aseptic loosening stem*	243	243	250	126
Expired	5,202 (19.6)	10,960 (19.3)	8,035 (5.9)	5,153 (7.0)

*Categories are not mutually exclusive.
EtO, ethylene oxide.

considered for inclusion: indication for implantation (osteoarthritis vs other); yearly cohort effect (e.g. 2004, 2005, etc.); femoral head composition (metal, ceramic, or ceramicized metal); type of stem fixation (cemented or cementless); liner/head size; and liner manufacturing characteristics (resin type, terminal sterilization method, packaging, liner face asymmetry, and radiation dose). Following exploratory analysis showing similar risk, ceramicized metal and ceramic femoral head composition groups were merged together. The total radiation dosage used in the polyethylene manufacturing process was classified into four categories: G1 (no radiation), G2 (> 0 Mrad to < 5 Mrad), G3 (≥ 5 Mrad to < 10 Mrad), G4 (≥ 10 Mrad). Translated into the clinical practice of dividing polyethylene into conventional (PE) and highly crosslinked (XLPE), G1 and G2 are conventional (PE) and G3 and G4 are crosslinked (XLPE). G3 and G4 were created in order to evaluate the effect of radiation dose within XLPE. The effect of stabilization treatment was evaluated in liners irradiated with total radiation dose of ≥ 5 Mrad. All analyses were done using SAS/STAT software, version 9.4 for PC (SAS Institute, Cary, North Carolina, USA). Approvals were received from the NJR Research Committee and the Trust Research & Development (R&D) Department.

Results

Exploratory Kaplan-Meier analyses identified that the largest magnitude of effect on the risk of revision is associated with total radiation dose grouping. Kaplan-Meier estimated

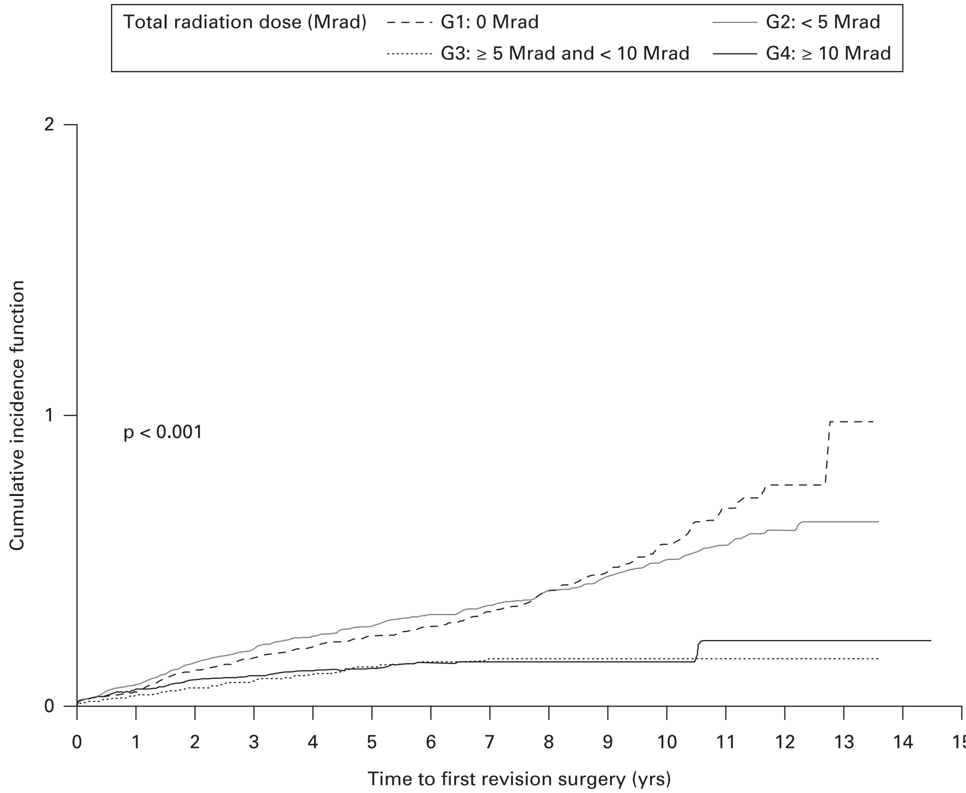


Fig. 2a

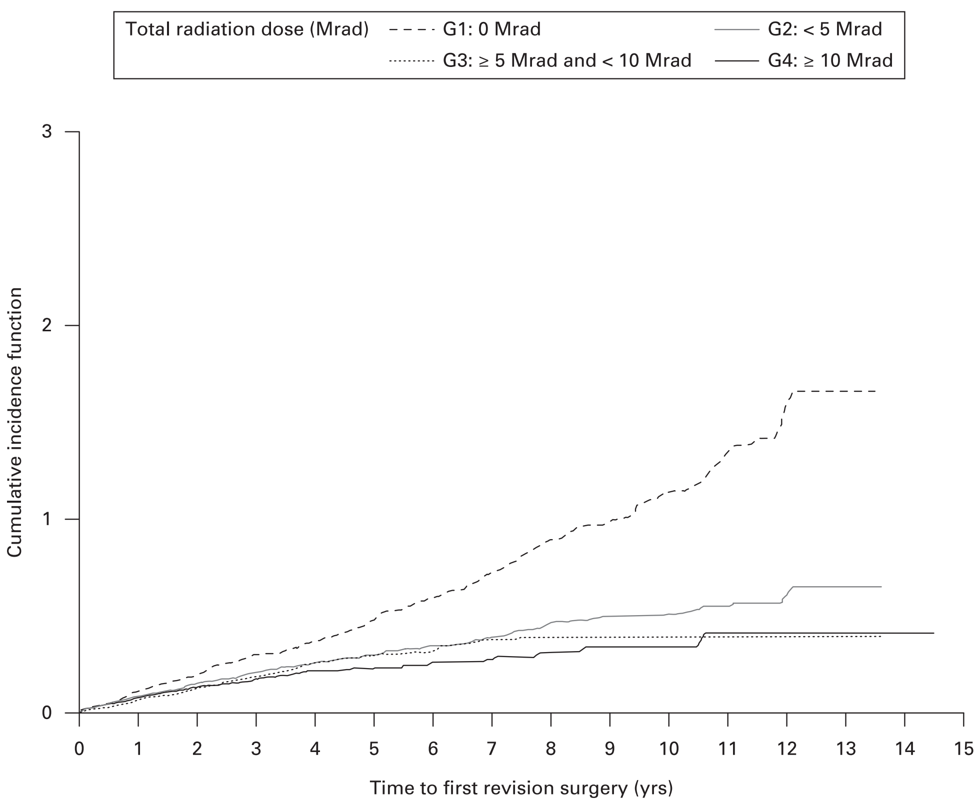


Fig. 2b

a) Cumulative incidence function of revision of the acetabulum due to aseptic loosening by polyethylene acetabular liner total radiation dose.
b) Cumulative incidence function of revision of the stem due to aseptic loosening by polyethylene acetabular liner total radiation dose.

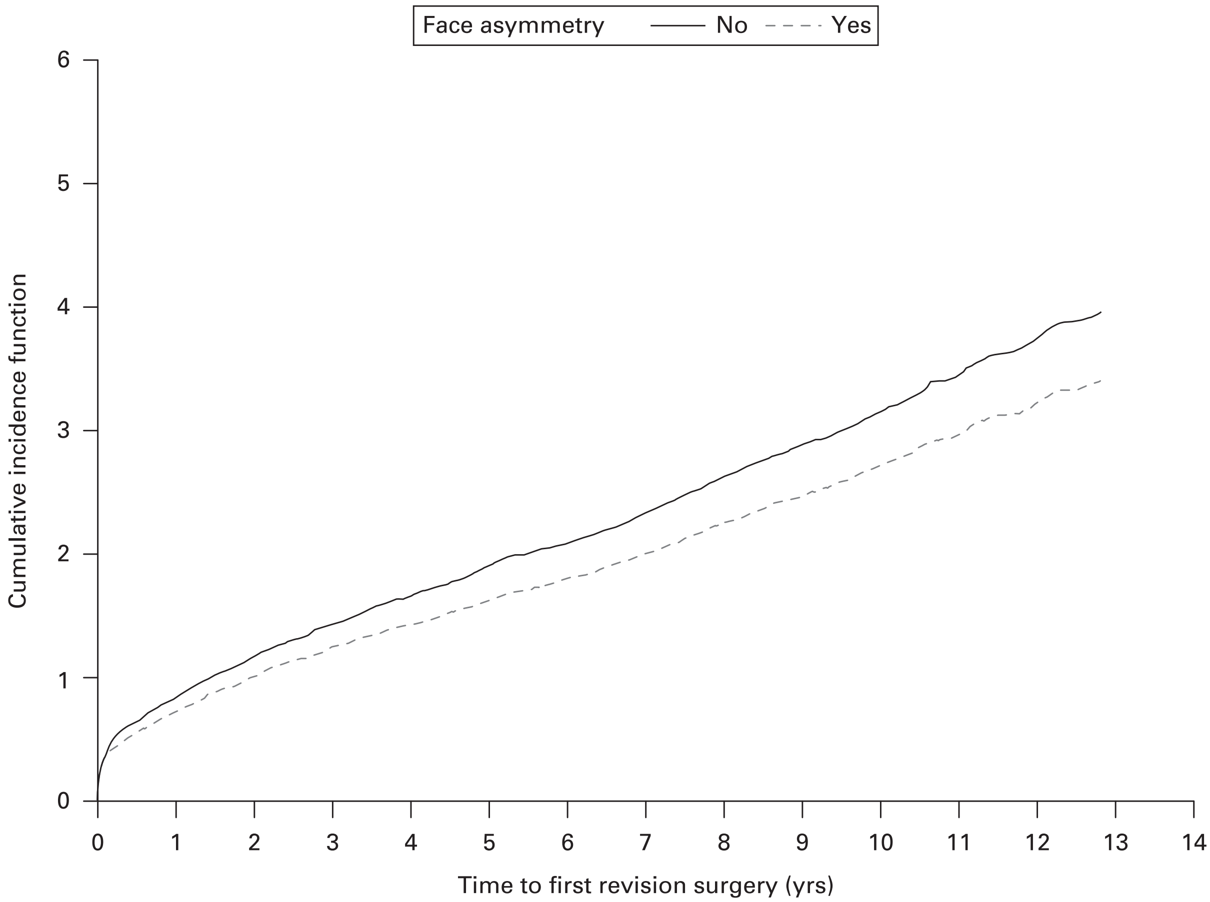


Fig. 3

Cox regression cumulative incidence function of revision for any reason by acetabular liner face asymmetry adjusted for age and sex.

cumulative incidence of revision differed among the irradiation groups ($p < 0.001$; Figure 1a). At 13 years post-THA, the cumulative incidence of revision for any reason was highest in G1 (5.48 per 100 THAs) and lowest in G4 (3.04 per 100 THAs). Descriptive statistics by acetabular liner total radiation dose are shown in Table II. G3 and G4 (XLPE) had shorter mean follow-up times compared with G1 and G2 (PE). A total of 1.8% THAs (5,329/292,920) were revised. Of these, 24% (1,290/5,329) were due to aseptic loosening.

There was a marked difference in cumulative incidence of revision for aseptic loosening among the irradiation groups (Figure 1b). The cumulative incidence of revision due to reasons other than aseptic loosening increased linearly in all irradiation groups (Figure 1c). Figures 2a and 2b show cumulative incidence of revision due to aseptic loosening in the acetabulum and stem groups per liner total radiation dose.

After adjustment for age and sex, asymmetrical (lipped) face liners had a lower risk of any revision than flat face liners (Figure 3). The difference in the risk of revision was present for aseptic loosening and for reasons other than aseptic loosening (Table III). Liners stabilized with heating below melting point had a higher risk of revision for aseptic loosening (Figure 4a) but a lower risk of revision for other reasons (Figure 4b).

Manufacturing variables were analyzed for association with a risk of revision due to aseptic loosening in age- and sex-adjusted Cox regression. Type of terminal sterilization and resin type were not a risk factor. There was no interaction between the total radiation dose and liner face symmetry. Cemented stems had better survival than cementless stems. Male sex, younger age, and larger head sizes were associated with a higher risk of revision due to aseptic loosening.

A validation model using life hazard gamma model showed similar hazard ratios to the Cox regression model (Table IV). A time-specific Cox regression model showed marked separation of risk of revision due to aseptic loosening among the groups after 4.5 years following primary surgery.

The effect of G3 and G4 in reduced risk of revision was noted in the risk of aseptic loosening for acetabular and stem components. G2 had a lower risk of aseptic loosening for the femoral stem but not the acetabular component. In this component-specific analysis, male sex was associated with a reduced risk of aseptic loosening of the acetabular component, but a higher risk of loosening of the femoral stem.

Asymmetrical (lipped) liners had a lower risk of revision for any reason compared with flat liners (Table III). Lipped liners had a lower risk of revision due to aseptic loosening and due

Table III. Cox regression hazard ratios for revision due to any reason, to aseptic loosening, and to reasons other than aseptic loosening.

Parameter	Hazard ratio (95% confidence interval)		
	Any revision	**Aseptic loosening**	**Other reasons**
Age, yrs			
< 55	1.00 (reference)	1.00 (reference)	1.00 (reference)
55 to < 64	0.88 (0.79 to 0.98)	0.77 (0.63 to 0.94)	0.92 (0.81 to 1.05)
65 to < 75	0.73 (0.66 to 0.82)	0.52 (0.42 to 0.63)	0.84 (0.74 to 0.95)
≥ 75	0.66 (0.59 to 0.73)	0.33 (0.26 to 0.41)	0.82 (0.72 to 0.93)
Sex			
Female	1.00 (reference)	1.00 (reference)	1.00 (reference)
Male	1.16 (1.10 to 1.23)	1.22 (1.09 to 1.36)	1.15 (1.08 to 1.22)
Indication			
Osteoarthritis	1.00 (reference)	1.00 (reference)	1.00 (reference)
Other	1.47 (1.34 to 1.62)	1.24 (1.01 to 1.53)	1.54 (1.38 to 1.71)
Head composition			
Metal	1.00 (reference)	1.00 (reference)	1.00 (reference)
Ceramic/ceramicized metal	0.77 (0.72 to 0.82)	0.70 (0.61 to 0.80)	0.79 (0.73 to 0.85)
Total radiation, Mrad			
No radiation	1.00 (reference)	1.00 (reference)	1.00 (reference)
< 5	0.85 (0.78 to 0.93)	0.74 (0.63 to 0.86)	0.93 (0.83 to 1.03)
≥ 5	0.71 (0.66 to 0.77)	0.38 (0.32 to 0.44)	0.88 (0.79 to 0.97)
Liner asymmetry			
No	1.00 (reference)	1.00 (reference)	1.00 (reference)
Yes	0.84 (0.80 to 0.89)	0.88 (0.79 to 0.99)	0.83 (0.78 to 0.89)
Stem implantation			
Cemented	1.00 (reference)	1.00 (reference)	1.00 (reference)
Cementless	1.32 (1.24 to 1.40)	2.01 (1.76 to 2.28)	1.17 (1.09 to 1.25)
Internal diameter, mm			
< 36	1.00 (reference)	1.00 (reference)	1.00 (reference)
≥ 36	1.09 (1.01 to 1.18)	1.09 (1.01 to 1.18)	0.98 (0.90 to 1.07)

to reasons other than aseptic loosening (Table III). There was no interaction between polyethylene modification groups and liner asymmetry; asymmetrical liners irradiated with < 5 Mrad and those irradiated with ≥ 5 Mrad had a lower risk of revision. Liners stabilized with heating above melting point and liners stabilized with vitamin E had a lower risk of revision due to aseptic loosening (Table V). Our study included a low number of vitamin E stabilized products with shorter follow-up, so these results should be interpreted with caution.

Discussion

Our results show an association between polyethylene manufacturing characteristics and implant survival following cementless and hybrid THA. Exploration of the individual manufacturing characteristics revealed that radiation dose, liner asymmetry, and stabilization treatment had a significant effect on implant survival. The effect of radiation dose was further investigated after grouping the products according to total radiation dosage. G3 and G4 (XLPE) were associated with a marked reduction of risk of revision for aseptic loosening. G4 (high radiation) was not associated with an additional reduction in the risk of revision at the 14-year follow-up compared with G3. This is a novel finding in the registry literature. The effect of stabilization treatment was investigated within G3 and G4 (XLPE), and stabilization with vitamin E and heating above melting point performed best.

Our findings are supported by basic science literature on polyethylene modifications.[7,11] Irradiation of polyethylene is associated with a higher degree of crosslinking density up to the magnitude of 10 Mrad with an associated decrease in wear.[12] Irradiation of polyethylene with high doses is also associated with a decrease in tensile and fracture toughness.[13] The optimal amount of irradiation has been sought extensively in vitro with most early (first-generation) XLPE products irradiated with 5 Mrad to 10.5 Mrad.[7,14] The deterioration in tensile and fracture toughness at high radiation doses may translate to mechanical and clinical failure.[15,16] This was not identified during our analysis, where G4 (highly irradiated) performed as well as G3 (moderately irradiated) at maximum follow-up of 14 years.

The free radicals generated during the crosslinking process can affect the properties of the finished product. Oxidation ex vivo (preimplantation) or in vivo can affect the mechanical properties of polyethylene. A critical degree of oxidation is required to negatively affect the mechanical properties of the material.[17,18] The products that have had a single thermal treatment post-irradiation have been classified as first-generation XLPE.[7] Alternative treatments include sequential thermal and mechanical treatments or antioxidant infusion. Retrieval studies have demonstrated increased oxidation of the exposed rim of annealed polyethylene liners.[19] In our study, the majority of products included in G2 (< 5 Mrad) were irradiated as part of the sterilization process and did not undergo stabilization

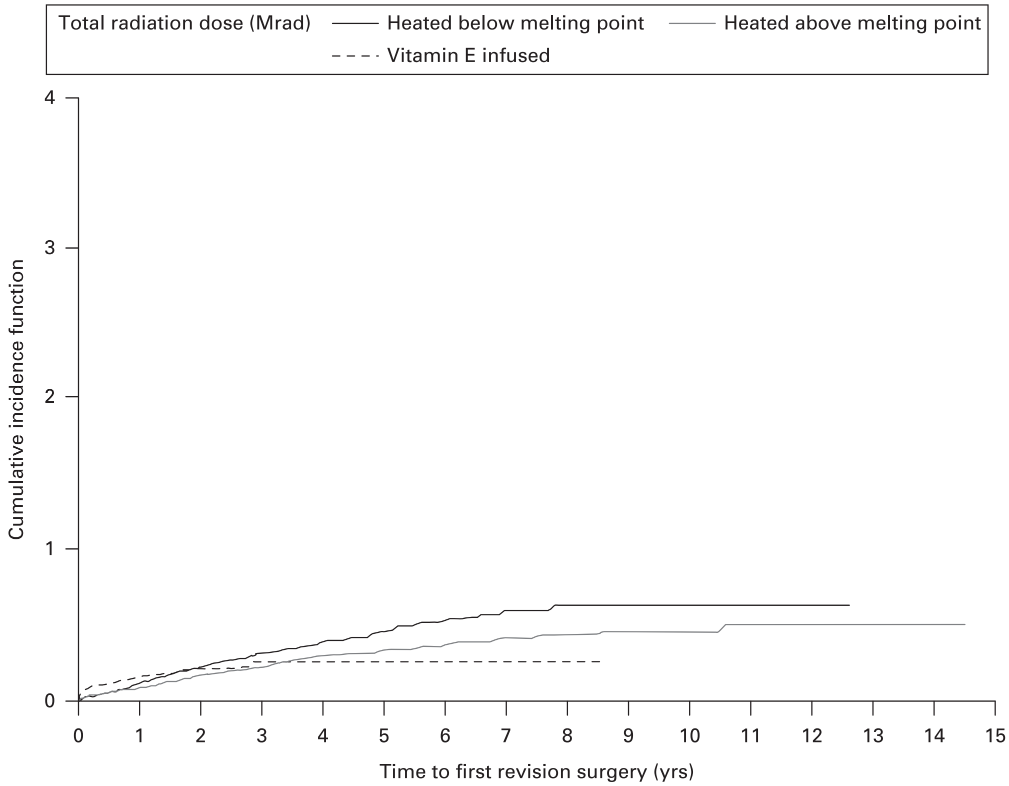


Fig. 4a

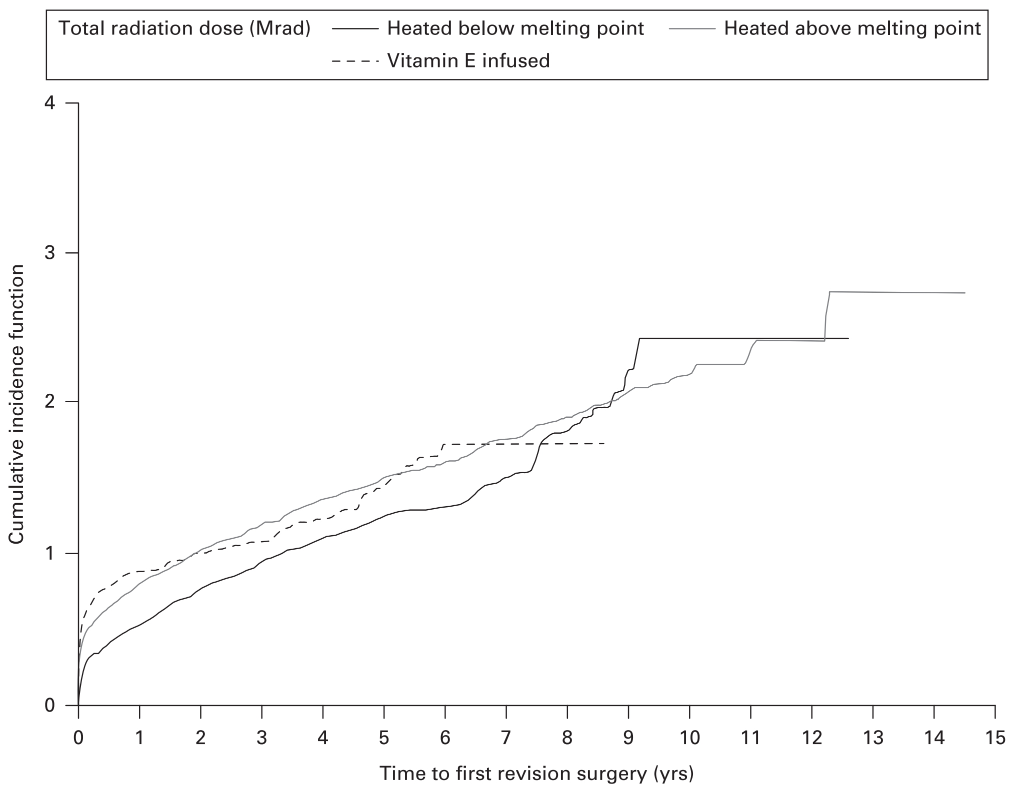


Fig. 4b

a) Cumulative incidence function of revision due to aseptic loosening in liners with total radiation dose of ≥ 5 Mrad by stabilization treatment.
b) Cumulative incidence function of revision due to reasons other than aseptic loosening in liners with total radiation dose of ≥ 5 Mrad by stabilization treatment.

Table IV. Cox regression and Gamma model hazard ratios (HR) for revision due to aseptic loosening.

Parameter	Cox HR (95% CI)			Gamma model HR (95% CI)
	Entire period	**0 to 4.5 yrs**	**> 4.5 yrs**	**Entire period**
Age, yrs				
< 55	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
55 to < 64	0.77 (0.63 to 0.94)	0.79 (0.62 to 1.02)	0.70 (0.50 to 0.99)	0.75 (0.60 to 0.94)
65 to < 75	0.51 (0.42 to 0.63)	0.60 (0.47 to 0.76)	0.38 (0.27 to 0.54)	0.49 (0.39 to 0.61)
≥ 75	0.32 (0.26 to 0.40)	0.45 (0.35 to 0.79)	0.14 (0.09 to 0.22)	0.75 (0.60 to 0.94)
Sex				
Female	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Male	1.22 (1.09 to 1.36)	1.16 (1.01 to 1.32)	1.36 (1.12 to 1.67)	1.27 (1.12 to 1.43)
Indication				
Osteoarthritis	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Other	1.24 (1.01 to 1.53)	1.30 (1.02 to 1.65)	1.21 (0.80 to 1.83)	1.37 (1.09 to 1.72)
Head composition				
Metal	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Ceramic/ceramicized metal	0.69 (0.61 to 0.79)	0.73 (0.63 to 0.86)	0.61 (0.47 to 0.80)	0.67 (0.58 to 0.78)
Total radiation, Mrad				
G1: No radiation	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
G2: < 5	0.74 (0.64 to 0.86)	1.01 (0.82 to 1.25)	0.50 (0.40 to 0.62)	0.72 (0.61 to 0.85)
G3: ≥ 5 and < 10	0.36 (0.30 to 0.43)	0.48 (0.38 to 0.60)	0.22 (0.14 to 0.34)	0.33 (0.27 to 0.40)
G4: ≥ 10	0.38 (0.31 to 0.47)	0.53 (0.42 to 0.69)	0.16 (0.14 to 0.34)	0.35 (0.28 to 0.44)
Liner asymmetry				
Yes	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
No	1.16 (1.04 to 1.30)	1.11 (0.97 to 1.27)	1.28 (1.05 to 1.57)	1.15 (1.02 to 1.32)
Stem implantation				
Cemented	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
Cementless	1.99 (1.75 to 2.26)	2.26 (1.93 to 2.64)	1.52 (1.21 to 1.92)	2.17 (1.85 to 2.50)
Internal diameter, mm	1.06 (1.03 to 1.08)	1.07 (1.04 to 1.09)	1.04 (0.99 to 1.10)	Not evaluated

CI, confidence interval; HR, hazard ratio.

treatment. A further analysis of a subgroup of products (G3 and G4) was performed to investigate the stabilization treatment effect. Stabilization with vitamin E and heating above melting point performed best. This is in keeping with recent radiostereometric analysis (RSA) studies on the wear profile of vitamin E diffused polyethylene demonstrating in vivo wear below the reported osteolysis threshold.[20,21]

There are several reports on the in vivo radiological wear rates of XLPE products, both remelted and annealed, with rates consistently reported to be lower than the proposed osteolysis threshold.[6,22-25] A recent analysis of wear rates of a remelted product versus a sequentially annealed polyethylene demonstrated similar rates at two-year follow-up.[26] First-generation annealed products showed some oxidation in vivo in a retrieval study.[27] The potential for in vivo oxidation of first-generation annealed products might be related to the increased risk of revision due to aseptic loosening as seen in our analysis. The annealed group in our analysis was also seen to have a reduced risk of revision for reasons other than aseptic loosening. This reduced risk of revision could be a result of improved fatigue crack propagation resistance that annealed products demonstrate compared with highly irradiated and remelted products,[15] which may make remelted polyethylene liners susceptible to early failure due to liner fracture.[28]

A recent study used registry data from the Australian Joint Registry (AOANJRR) on XLPE and classified polyethylene as conventional (PE) and crosslinked (XLPE) based on the radiation dose with a cut-off of 5 Mrad.[29] The authors showed a marked improvement in the risk of revision for any reason when XLPE was compared with PE. Our findings are in agreement with the AOANJRR study. Further, our analysis shows that this difference is almost exclusively due to aseptic loosening. Our analysis includes a number of additional variables and adds clarity to the effects of polyethylene modifications. We analyzed cementless acetabular components with a polyethylene liner, while the AOANJRR analysis included all-polyethylene components. The mechanism of failure of all-polyethylene acetabular components can be different and has previously been linked to surgical technique and early radiological findings.[8,9] We therefore limited our study to cementless acetabular components with polyethylene liners.

Our analysis also investigated the effect of polyethylene liner asymmetry in addition to the modification variables. Symmetric (flat) liners had a higher cumulative risk of revision compared with asymmetrical (lipped) liners. The New Zealand Orthopaedic Association Joint Registry reported a similar finding, although that analysis did not include polyethylene modifications.[30] Our multivariate model confirmed that use of asymmetrical (lipped) liners is associated with reduced risk of revision for any reason, for aseptic loosening, and for reasons other than aseptic loosening. A decreased risk of aseptic loosening for asymmetrical (lipped) liners goes against previous concerns regarding increased polyethylene wear due to impingement against the elevated rim, leading to osteolysis and aseptic loosening.[31] A recent study from AOANJRR is in agreement with our

Table V. Cox regression hazard ratios for revision due to any reason, to aseptic loosening, and to reasons other than aseptic loosening in total hip arthroplasty utilizing liners with irradiation of 5 Mrad or more.

Parameter	Hazard ratio (95% confidence interval)		
	Any reason	**Aseptic loosening**	**Reasons other than aseptic loosening**
Age, yrs			
< 55	1.00 (reference)	1.00 (reference)	1.00 (reference)
55 to < 64	0.76 (0.66 to 0.88)	0.71 (0.53 to 0.96)	0.78 (0.66 to 0.92)
65 to < 75	0.70 (0.61 to 0.80)	0.55 (0.41 to 0.72)	0.75 (0.65 to 0.88)
≥ 75	0.68 (0.59 to 0.79)	0.38 (0.28 to 0.53)	0.78 (0.66 to 0.91)
Sex			
Female	1.00 (reference)	1.00 (reference)	1.00 (reference)
Male	1.10 (1.02 to 1.19)	1.19 (0.99 to 1.42)	1.09 (1.00 to 1.18)
Head composition			
Metal	1.00 (reference)	1.00 (reference)	1.00 (reference)
Ceramic/ceramicized metal	0.80 (0.73 to 0.87)	0.79 (0.65 to 0.96)	0.81 (0.73 to 0.86)
Liner asymmetry			
No	1.00 (reference)	1.00 (reference)	1.00 (reference)
Yes	0.82 (0.76 to 0.89)	0.84 (0.70 to 1.02)	0.82 (0.75 to 0.89)
Stem implantation			
Cemented	1.00 (reference)	1.00 (reference)	1.00 (reference)
Cementless	1.28 (1.18 to 1.39)	2.56 (2.06 to 3.17)	1.11 (1.01 to 1.22)
Internal diameter, mm			
< 36	1.00 (reference)	1.00 (reference)	1.00 (reference)
≥ 36	1.12 (1.03 to 1.22)	1.56 (1.27 to 1.90)	1.03 (0.94 to 1.13)
Stabilization treatment			
Vitamin E	1.00 (reference)	1.00 (reference)	1.00 (reference)
Heated above melting point	1.06 (0.90 to 1.24)	1.30 (0.86 to 1.96)	1.01 (0.84 to 1.20)
Heated below melting point	0.99 (0.83 to 1.18)	1.96 (1.28 to 3.01)	0.83 (0.69 to 1.01)

findings, showing reduced risk of revision both for all reasons and for aseptic loosening with asymmetrical liners.[32] We further confirmed that reduction in risk of revision with use of asymmetrical liners is independent of polyethylene modification.

Age and sex are known risk factors for revision and are confirmed in this study.[2] Cemented versus cementless stem use was associated with a lower risk of revision after adjustment for other factors, which concurs with a previous analysis of the NJR dataset.[2,33] In previous NJR reports, ceramic-on-polyethylene outperformed metal-on-polyethylene, as well as ceramic-on-ceramic combinations.[2] In our analysis, head composition included ceramicized metal along with ceramic in a single group. Ceramicized metal was not analyzed independently due to the low numbers of ceramicized metal components used with other than G4 liners.

Our study has several limitations. The observational nature means that all potential factors contributing to the risk of revision cannot be controlled for. Selection bias may be considered a significant confounding factor within this analysis despite the modelling performed in an attempt to control for confounding variables. Selection bias may certainly have some effect on surgeons' choices between conventional polyethylene (G1 and G2) and modified (crosslinked) polyethylene (XLPE) (G3 and G4). However, it is difficult to conceive that surgeons would differ in their choices of XLPE depending on patient factors. The endpoint, revision, fails to capture cases where the prosthesis is malfunctioning but has not led to revision. Duration of follow-up is critical in polyethylene analysis. The effect of some modifications of polyethylene, such as free radical scavenging treatment, is aimed at reducing oxidation which is a time-dependent process. All groups in our analysis had acceptable numbers of risk at ten-year follow-up. The under-reporting of revision procedures within NJR has been well-documented; therefore, the absolute revision numbers may be higher than those reported here.[2] However, the overall effect of under-reporting on the relative revision rates between groups would be small.

In conclusion, this is the first study to investigate the effect of polyethylene manufacturing process modifications on THA survival using NJR data. Total radiation dosage is associated with the lowest risk of revision due to aseptic loosening. At 14 years following primary THA, the moderately and highly irradiated components are performing equally well. Asymmetrical liners (lipped) outperform symmetric (flat) liners. Polyethylene liners with a total radiation dosage of ≥ 5 Mrad, an asymmetrical liner face, and stabilization with heating above melting point are associated with the best implant survival. The risk of revision for aseptic loosening in cementless and hybrid THAs has been markedly reduced at 14-year follow-up with the use of XLPE.

Take home message

- Irradiation of polyethylene with > 5 Mrad was associated with a marked reduction in the risk of revision for aseptic loosening.
- Irradiation with ≥ 10 Mrad was not associated with further risk reduction at 12-year follow-up.
- An asymmetrical liner face and polyethylene stabilization by heating above melting point further improves survival.

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References

1. **Learmonth ID, Young C, Rorabeck C.** The operation of the century: total hip replacement. *Lancet*. 2007;370(9597):1508–1519.
2. **No authors listed.** 14th Annual Report, 2017. National Joint Registry for England, Wales, Northern Ireland and the Isle of Man (NJR). https://www.hqip.org.uk/wp-content/uploads/pelerous_media_manager/public/253/NJR/NJR%2014th%20Annual%20Report%202017.pdf (date last accessed 18 October 2019).
3. **Evans JT, Evans JP, Walker RW, Blom AW, Whitehouse MR, Sayers A.** How long does a hip replacement last? A systematic review and meta-analysis of case series and national registry reports with more than 15 years of follow-up. *Lancet*. 2019;393(10172):647–654.
4. **Bayliss LE, Culliford D, Monk AP, et al.** 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. *Lancet*. 2017;389(10077):1424–1430.
5. **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):2606–2612.
6. **Kurtz SM, Gawel HA, Patel JD.** History and systematic review of wear and osteolysis outcomes for first-generation highly crosslinked polyethylene. *Clin Orthop Relat Res*. 2011;469(8):2262–2277.
7. **Kurtz SM.** *UHMWPE Biomaterials Handbook: Ultra-High Molecular Weight Polyethylene in Total Joint Replacement and Medical Devices*. Third ed. Waltham, Massachusetts: William Andrew, Elsevier. 2016.
8. **Ranawat CS, Deshmukh RG, Peters LE, Umlas ME.** Prediction of the long-term durability of all-polyethylene cemented sockets. *Clin Orthop Relat Res*. 1995;(317):89–105.
9. **Flivik G, Kristiansson I, Kesteris U, Ryd L.** Is removal of subchondral bone plate advantageous in cemented cup fixation? A randomized RSA study. *Clin Orthop Relat Res*. 2006;448:164–172.
10. **Gray RJ.** A class of K-sample tests for comparing the cumulative incidence of a competing risk. *The Annals of Statistics*. 1988:1141–1154.
11. **Bracco P, Bellare A, Bistolfi A, Affatato S.** Ultra-high molecular weight polyethylene: influence of the chemical, physical and mechanical properties on the wear behavior. A review. *Materials (Basel)*. 2017;10(7):E791.
12. **Muratoglu OK, Bragdon CR, O'Connor DO, et al.** Unified wear model for highly crosslinked ultra-high molecular weight polyethylenes (UHMWPE). *Biomaterials*. 1999;20(16):1463–1470.
13. **Gomoll A, Wanich T, Bellare A.** J-integral fracture toughness and tearing modulus measurement of radiation cross-linked UHMWPE. *J Orthop Res*. 2002;20(6):1152–1156.
14. **Sobieraj MC, Rimnac CM.** Ultra high molecular weight polyethylene: mechanics, morphology, and clinical behavior. *J Mech Behav Biomed Mater*. 2009;2(5):433–443.
15. **Atwood SA, Van Citters DW, Patten EW, Furmanski J, Ries MD, Pruitt LA.** Tradeoffs amongst fatigue, wear, and oxidation resistance of cross-linked ultra-high molecular weight polyethylene. *J Mech Behav Biomed Mater*. 2011;4(7):1033–1045.
16. **Tower SS, Currier JH, Currier BH, Lyford KA, Van Citters DW, Mayor MB.** Rim cracking of the cross-linked longevity polyethylene acetabular liner after total hip arthroplasty. *J Bone Joint Surg Am*. 2007;89-A(10):2212–2217.
17. **Currier BH, Currier JH, Mayor MB, Lyford KA, Van Citters DW, Collier JP.** In vivo oxidation of gamma-barrier-sterilized ultra-high-molecular-weight polyethylene bearings. *J Arthroplasty*. 2007;22(5):721–731.
18. **Currier BH, Currier JH, Collier JP, Mayor MB.** Effect of fabrication method and resin type on performance of tibial bearings. *J Biomed Mater Res*. 2000;53(2):143–151.
19. **Kurtz SM, Hozack W, Turner J, et al.** Mechanical properties of retrieved highly cross-linked crossfire liners after short-term implantation. *J Arthroplasty*. 2005;20(7):840–849.
20. **Galea VP, Rojanasopondist P, Laursen M, Muratoglu OK, Malchau H, Bragdon C.** Evaluation of vitamin E-diffused highly crosslinked polyethylene wear and porous titanium-coated shell stability: a seven-year randomized control trial using radiostereometric analysis. *Bone Joint J*. 2019;101-B(7):760–767.
21. **Galea VP, Connelly JW, Shareghi B, et al.** Evaluation of in vivo wear of vitamin E-diffused highly crosslinked polyethylene at five years: a multicentre radiostereometric analysis study. *Bone Joint J*. 2018;100-B(12):1592–1599.
22. **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):649–661.
23. **Takada R, Jinno T, Koga D, Hirao M, Muneta T, Okawa A.** Comparison of wear rate and osteolysis between annealed and remelted highly cross-linked polyethylene in total hip arthroplasty. A case control study at 7 to 10 years follow-up. *Orthop Traumatol Surg Res*. 2016;102(6):717–721.
24. **Takada R, Jinno T, Koga D, Miyatake K, Muneta T, Okawa A.** Comparison of wear rate and osteolysis between second-generation annealed and first-generation remelted highly cross-linked polyethylene in total hip arthroplasty. A case control study at a minimum of five years. *Orthop Traumatol Surg Res*. 2017;103(4):537–541.
25. **Teeter MG, Lanting BA, Naudie DD, McCalden RW, Howard JL, MacDonald SJ.** Highly crosslinked polyethylene wear rates and acetabular component orientation: a minimum ten-year follow-up. *Bone Joint J*. 2018;100-B(7):891–897.
26. **Suraci A, Louati H, Culliton KN, Beaulé PE.** Comparing In Vivo Performance of Two Highly Cross-Linked Polyethylene Thermal Treatments: Remelting vs Annealing in Acetabular Liners. *J Arthroplasty*. 2019;34(7):1509–1513.
27. **Kurtz SM, MacDonald DW, Mont MA, Parvizi J, Malkani AL, Hozack W.** Retrieval analysis of sequentially annealed highly crosslinked polyethylene used in total hip arthroplasty. *Clin Orthop Relat Res*. 2015;473(3):962–971.
28. **Ast MP, John TK, Labbisiere A, Robador N, Valle AG.** Fractures of a single design of highly cross-linked polyethylene acetabular liners: an analysis of voluntary reports to the United States Food and Drug Administration. *J Arthroplasty*. 2014;29(6):1231–1235.
29. **De Steiger R, Lorimer M, Graves SE.** Cross-Linked Polyethylene for Total Hip Arthroplasty Markedly Reduces Revision Surgery at 16 Years. *J Bone Joint Surg Am*. 2018;100-A(15):1281–1288.
30. **Insull PJ, Cobbett H, Frampton CM, Munro JT.** The use of a lipped acetabular liner decreases the rate of revision for instability after total hip replacement: a study using data from the New Zealand Joint Registry. *Bone Joint J*. 2014;96-B(7):884–888.
31. **Gerhardt DM, Sanders RJ, De Visser E, van Susante JL.** Excessive polyethylene wear and acetabular bone defects from standard use of a hooded acetabular insert in total hip arthroplasty. *Int Orthop*. 2014;38(8):1585–1590.
32. **Bauze A, Agrawal S, Cuthbert A, De Steiger R.** Are Hooded, Crosslinked Polyethylene Liners Associated with a Reduced Risk of Revision After THA? *Clin Orthop Relat Res*. 2019;477(6):1315–1321.
33. **Kandala NB, Connock M, Pulikottil-Jacob R, et al.** Setting benchmark revision rates for total hip replacement: analysis of registry evidence. *BMJ*. 2015;350:h756.

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