Gamma-irradiation Sterilization in an Inert Environment A Partial Solution

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Abstract

Background In the mid to late 1990s, to sterilize UHMWPE bearings, manufacturers changed from gamma-irradiation-in-air (gamma-air) sterilization, which initiated oxidation leading to bearing fatigue, to gamma-irradiation sterilization in an inert environment (gamma-inert). The change to gamma-inert sterilization reportedly prevented shelf oxidation before implantation but not in vivo oxidation.

Questions/purposes We asked: (1) Has the change to gamma-inert sterilization prevented shelf oxidation that led to early in vivo fatigue damage in gamma-air-sterilized tibial inserts? And (2) has the change to gamma-inert

sterilization prevented the occurrence of fatigue secondary to in vivo oxidation?

Methods We rated 183 retrieved gamma-air- and 175 retrieved gamma-inert-sterilized tibial inserts for clinical fatigue damage and analyzed 132 gamma-air- and 174 gamma-inert-sterilized tibial inserts for oxidation by Fourier transform infrared spectroscopy.

Results Oxidation led to decreased mechanical properties in shelf-aged gamma-air-sterilized tibial inserts. Barrier packaging prevented shelf oxidation in gamma-inert-sterilized tibial inserts. Gamma-air- and gamma-inert-sterilized inserts oxidized in vivo. Fatigue damage (delamination) occurred more frequently in inserts retrieved after longer time in vivo. Longer in vivo time correlated with higher oxidation and more accumulated cycles of use. **Conclusions** Published oxidation projections suggest gamma-inert-sterilized tibial inserts would reach the critical oxidation for the onset of fatigue after 11 to 14 years in vivo. These retrievals appear to follow the projected oxidation trends. Frequency of fatigue damage increased with increasing oxidation.

Clinical Relevance Fatigue of tibial inserts becomes more likely, especially in active patients, after more than a decade of good clinical performance.

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Introduction

For more than four decades, gamma-irradiation has been the industry standard sterilization method [11]. In the mid to late 1990s, manufacturers changed from gamma sterilization in air (gamma-air) to gamma sterilization in an inert environment (gamma-inert; eg, ArCom®, gamma vacuum foil, gamma-N2, etc). This change was an effort to exclude oxygen from the sterilization environment after reports

showing gamma-air sterilization initiated UHMWPE oxidation [5, 14]. Long shelf aging time of gamma-air-sterilized bearings before implantation reportedly led to reduced mechanical properties of UHMWPE, resulting in early fatigue damage, especially in tibial inserts [7].

Studies of never-implanted gamma-inert-sterilized acetabular liners and tibial inserts suggested gamma-inert sterilization in a barrier package prevented shelf oxidation before implantation [4, 6], although some instances of leaking in early multilayer polymer film packaging leading to shelf oxidation were reported [6]. Short-term retrieval studies showed sterilization in an inert environment did not prevent in vivo oxidation. These studies projected exponentially increasing in vivo oxidation of gamma-inert tibial inserts (average in vivo time, 2.8 years) [12] or tibial inserts and acetabular liners combined (average in vivo time, 3.4 years) [9]. Based on projections of oxidation increase with time, these studies suggested an in vivo service life of 12 years or more before the critical oxidation for the onset of fatigue damage (ketone peak height oxidation > 1) was reached [9].

To confirm previous findings, we evaluated the projections from those earlier studies in light of measured oxidation and in vivo fatigue damage of longer in vivo time retrieved tibial inserts. We addressed the following questions: (1) Has the change in packaging from air-permeable packaging to barrier packaging (resulting in a change from gamma-air to gamma-inert sterilization) prevented the shelf oxidation that led to early in vivo fatigue damage in gamma-air-sterilized inserts? (2) Has the change to gamma-inert sterilization in barrier packaging prevented in vivo fatigue? And (3) do previously published projections of oxidation versus in vivo time for gamma-inert retrievals [9, 12] accurately predict the oxidation measured in longer in vivo time retrieved tibial inserts? We therefore determined: (1) the effect of oxidation on the mechanical properties of UHMWPE and the occurrence of fatigue damage in retrieved gamma-air-sterilized inserts; (2) the oxidation that occurred during shelf storage for a series of barrier-packaged, gamma-inert-sterilized tibial inserts and the occurrence of fatigue damage in retrieved gamma-inert-sterilized inserts; and (3) the oxidation of gamma-air- and gamma-inert-sterilized retrievals after in vivo time.

Materials and Methods

We evaluated the effect of oxidation on the mechanical properties (ultimate tensile strength [UTS] and ultimate elongation [UE]) of three shelf-aged, never-implanted tibial inserts (two gamma-air sterilized, one gamma-inert

sterilized) and compared them to ASTM specified minima for surgical implants [3].

To measure mechanical properties, we performed uniaxial tensile tests on thin sections taken from the three never-implanted tibial bearing that had sufficient size and thickness for sampling. Thin sections were prepared using a technique developed to permit static mechanical testing of the surface, subsurface, and bulk regions of the tibial bearings [5]. Two sagittal cuts, 6 mm apart, were made from the anterior to the posterior surface of the tibial bearings using a band saw. Thin sections (200 μ m thick) of these specimens were cut parallel to the nonarticular surface using a Jung microtome (Leica Microsystems, Wetzlar, Germany), producing a series of horizontal sections [5]. A sequence of thin sections representing a depth of approximately 4 mm (20 sections) was taken from each sample. Before uniaxial tensile testing, oxidation measurements were made on the series of horizontal thin sections using a PerkinElmer® Spectrum® BXII (PerkinElmer Inc, Shelton, CT, USA), each representing a sequential depth into a tibial bearing. Oxidation was reported as ketone peak height ratio, and a crossplot of ASTM oxidation index (OI) [1] and ketone peak height ratio was included for reference (Fig. 1).

We then cut the thin sections with a die into ASTM Type V samples [2]. Uniaxial tensile testing was carried out on an Instron 5544 load frame (Instron Corp, Norwood, MA, USA) equipped with a 2-kN load cell, pneumatic sample grips, and video extensometer. Samples were loaded at a rate of 25.4 mm/minute [2], corresponding to a strain rate of 100%/minute. Before the start of the test, the video extensometer was used to record the actual gauge length marked on the sample. Throughout the test, sample

Fig. 1 A crossplot shows ASTM OI correlated with ($R^2 = 1.00$) ketone peak height ratio from never-implanted tibial insert analyses. ASTM OI is a factor of 1.32 higher than ketone peak height ratio.

elongation was recorded using the video extensometer (accurate to 0.5% of the reading), and data were collected through the Bluehill[®] software interface (Version 2.15; Instron Corp).

We analyzed 306 (132 gamma-air-sterilized, 174 gamma-inert-sterilized) retrieved tibial and unicondylar inserts and four gamma-inert-sterilized, never-implanted tibial inserts from two manufacturers (DePuy Orthopaedics, Inc, a Johnson & Johnson company, Warsaw, IN, USA; and Zimmer, Inc, Warsaw, IN, USA) using Fourier transform infrared (FTIR) spectroscopy to determine oxidation of the inserts. The pedigree of the inserts included sterilization method and date, shelf time before implantation, time in vivo, and ex vivo shelf time. The inserts analyzed for oxidation in this study had a shelf time of 6 months or less after retrieval before analysis (mean $\pm$ SD, 2.6 ± 1.2 months; range, 0.2–6 months) to minimize postretrieval oxidation. Twenty-nine gamma-inert-sterilized tibial inserts from three manufacturers (Biomet, Inc, Warsaw, IN, USA; DePuy Orthopaedics, Inc; and Zimmer, Inc) were retrieved after less than 1.5 years in vivo. They had a preimplantation shelf storage time ranging from 0.5 to 77.2 months. We

compared shelf time and oxidation of these retrieved inserts to those of the never-implanted gamma-inert-sterilized tibial inserts (shelf storage time, 2–74 months) using Student's t-test (IBM[®] SPSS[®] Statistics, Version 19; SPSS Inc, an IBM company, Chicago, IL, USA). Nonparametric correlations (IBM[®] SPSS[®] Statistics, Version 19) were used to assess the effect of shelf time and in vivo time on maximum oxidation measured in all retrieved tibial inserts. Maximum oxidation was plotted as a function of time since sterilization for the gamma-air-sterilized retrievals and since implantation for the gamma-inert-sterilized retrievals. We obtained FTIR absorbance spectra using a PerkinElmer[®] AutoIMAGE[®] infrared microscope connected to a PerkinElmer[®] Spectrum[®] 100 spectrometer (PerkinElmer Inc). Oxidation measurements with the infrared microscope were made versus depth from the nonarticular (backside) surface to the articular surface of thin sections from inserts. FTIR spectroscopy measurements were made midway in the anterior-posterior direction of vertical cross sections of the retrieved inserts, except in cases of severe delamination when a nondelaminated section of the articular surface was measured to obtain the full oxidation profile of the insert.

Table 1. Retrieved tibial inserts by manufacturer and sterilization method

Manufacturer	Component	Sterilization method	Number	Gamma-inert sterilization method	Number
Biomet Inc (Warsaw, IN, USA)	Tibial	Gamma-air	1	ArCom [®]	14
	Uni	Gamma-air	0	ArCom [®]	5
DePuy Orthopaedics, Inc, a Johnson & Johnson company (Warsaw, IN, USA)	Tibial (fixed)	Gamma-air	24	Gamma-N2	7
	Tibial (MB)	Gamma-air	11	Gamma-N2 3 GVF	13
	Uni	Gamma-air	1	GVF	3
	Tibial	Gamma-air	11		
Howmedica (now Stryker Corp, Mahwah, NJ, USA)					
Intermedics (now Zimmer, Inc, Warsaw, IN, USA)	Tibial	Gamma-air	2		
Johnson & Johnson (now DePuy Orthopaedics, Inc)	Tibial (fixed)	Gamma-air	101	GVF	96
	Tibial (MB)	Gamma-air	0	GVF	31
	Uni	Gamma-air	0	GVF	1
Orthomet (now Wright Medical Technology, Inc, Arlington, TN, USA)	Tibial	Gamma-air	2		
Osteonics (now Stryker)	Tibial	Gamma-air	4		
Richards (now Smith & Nephew, Inc, Memphis, TN, USA)	Tibial	Gamma-air	10	Nongamma (EtO)	
Wright Medical Technology, Inc	Tibial	Gamma-air	5	Nongamma (EtO)	
Zimmer, Inc (Warsaw, IN, USA)	Tibial	Gamma-air	15	Gamma-N2	2

Uni = unicondylar; MB = mobile bearing; gamma-air = gamma-irradiation-in-air sterilization; gamma-inert = gamma-irradiation sterilization in an inert environment; gamma-N2 = gamma-irradiation sterilization in nitrogen; GVF = gamma vacuum foil; EtO = ethylene oxide.

Parameters for the measurements were 32 scans/100- μm depth interval, using a wave number interval of 2 cm^{-1} and an aperture of $100\text{ }\mu\text{m}^2$. FTIR spectroscopy results were reported using a ketone peak height ratio technique (ketone peak height, $1713\text{--}1718\text{ cm}^{-1}$) normalized to the $1368\text{--}1371\text{ cm}^{-1}$ peak height thickness proxy ($1365\text{--}1371\text{ cm}^{-1}$) [8, 9]. The oxidation value reported for each retrieved insert is the maximum ketone value measured 0.5 to 2.5 mm below the articular surface of the bearing (maximum articular oxidation).

We evaluated the presence or absence of in vivo fatigue damage, specifically delamination, in 358 retrieved tibial and unicondylar inserts (183 gamma-air sterilized, 175 gamma-inert sterilized) from 10 manufacturers (Table 1). The reasons for retrieval for the inserts varied (Table 2). The frequency of occurrence of in vivo fatigue in gamma-air- and gamma-inert-sterilized inserts was compared over in vivo time intervals of 0 to 5 years, greater than 5 to 10 years, and greater than 10 years. To assess in vivo damage, each of the retrieved inserts was examined visually using a Nikon Binocular Dissecting Microscope (Nikon Corp, Tokyo, Japan) with $10\times$ magnification or a Keyence Digital Microscope VHX-1000 (Keyence Corp, Osaka, Japan) at $10\times$ magnification. We rated all inserts

for clinical damage on a scale of 0 (none) to 3 (severe) [10], focusing on delamination to indicate fatigue damage to the polyethylene material of some portion of the insert.

We evaluated factors potentially influencing delamination (sterilization method, shelf time before implantation, in vivo time, oxidation, patient age, and patient BMI) using nonparametric correlations (IBM® SPSS® Statistics, Version 19). We compared the maximum oxidation measured in the retrieved inserts plotted as a function of time since sterilization for the gamma-air-sterilized retrievals and since implantation for the gamma-inert-sterilized retrievals to published projections of oxidation versus time [9, 12].

Results

Barrier packaging of gamma-sterilized tibial inserts prevented the embrittlement caused by oxidation during shelf storage measured in gamma-sterilized in air-permeable packaging tibial inserts. Never-implanted gamma-sterilized tibial inserts, removed from air-permeable packages after years of shelf aging, showed UTS (Fig. 2A) and UE (Fig. 2B) that decreased with increasing oxidation. Measured UTS decreased by 60%, to below the ASTM specified minimum UTS for surgical implants at ketone peak height oxidation of 1.2 (ASTM OI = 1.6). Measured UE decreased by greater than 75%, to below the ASTM specified minimum UE for surgical implants at ketone peak height oxidation of 1.2 (ASTM OI = 1.6). The never-implanted barrier-packaged tibial insert (gamma-inert sterilized) had UTS and UE that were above the ASTM minima for surgical implants.

Barrier packaging prevented oxidation during shelf storage for up to 5 years. The 29 retrieved gamma-inert-sterilized tibial inserts in vivo less than 1.5 years and four never-implanted gamma-inert-sterilized tibial inserts had similar ranges of preimplantation shelf storage times (Fig. 3) and equivalent ($p = 0.139$) mean shelf storage time (Table 3). The retrieved and the never-implanted inserts had similar ranges of oxidation values and equivalent ($p = 0.879$) mean oxidation values (Table 3). Oxidation of the combined groups correlated (Spearman's $\rho = 0.371$, $p = 0.034$) with preimplantation shelf time. The 33 inserts (29 retrieved and 4 never-implanted) were separated into two groups based on shelf storage time (< 5 years and > 5 years). Oxidation measured in the inserts that were shelf-stored for less than 5 years before implantation or analysis did not correlate (Spearman's $\rho = 0.134$, $p = 0.489$) with shelf storage time (Table 4). Mean oxidation of tibial inserts with shelf storage time of greater than 5 years was almost 70% higher than those shelf-stored less than 5 years.

Table 2. Number of retrieved gamma-air- and gamma-inert-sterilized inserts listed by reason for retrieval

Reason for retrieval	Gamma-air sterilized	Gamma-inert sterilized
Amputation	1	0
Dislocation	3	3
Failed polyethylene (patella)	4	
Failed polyethylene (tibia)	15	
Instability	3	13
Laxity (giving way)	1	2
Fracture of bone	3	3
Fracture of implant (tibial tray)	2	3
Loose	18	53
Infection	8	30
Limited ROM	1	1
Fall, injury		2
Malposition	4	5
Osteolysis	34	9
Pain	27	21
Other	3	5
Polyethylene disassociation (patella)	3	
Polyethylene wear	38	15
Synovitis	2	
Subsidence	3	3
Unknown	10	7
Total	183	175

More than 40% of gamma-air-sterilized inserts retrieved after 5 years or less in vivo exhibited delamination at retrieval (Fig. 4). The percentage increased with longer times in vivo to greater than 75% after more than 10 years in vivo. In contrast, only 2% of gamma-inert-sterilized

Fig. 2A–B (A) Gamma-sterilized tibial inserts were removed from their packages after years of shelf aging. Gamma-air-sterilized tibial inserts showed loss of UTS to below the ASTM minimum at a ketone peak height ratio of greater than 1.2. Barrier-packaged, gamma-inert-sterilized tibial inserts had a UTS above the ASTM minimum and could be expected to resist fatigue damage in vivo. (B) Gamma-sterilized tibial inserts were removed from their packages after years of shelf aging. Gamma-air-sterilized tibial inserts showed loss of UE to below the ASTM minimum at a ketone peak height ratio of greater than 1.2. Barrier-packaged, gamma-inert-sterilized tibial inserts had a UE above the ASTM minimum and could be expected to resist fatigue damage in vivo.

retrievals in vivo 5 years or less exhibited delamination at retrieval, demonstrating barrier packaging effectively prevented in vivo fatigue secondary to preimplantation shelf oxidation. However, 20% of retrieved gamma-inert-sterilized inserts in vivo more than 10 years exhibited delamination (Fig. 5), showing gamma-inert sterilization did not prevent fatigue secondary to in vivo oxidation and cycles of use (Fig. 6). Occurrence of delamination in gamma-air-sterilized inserts correlated with shelf time before implantation ($p < 0.001$), time in vivo ($p = 0.002$), and articular oxidation ($p < 0.001$). Delamination in gamma-inert-sterilized inserts correlated with time in vivo ($p = 0.001$) articular oxidation ($p < 0.001$), and patient BMI ($p = 0.039$). Patient age and BMI (evaluated as proxies for cycles of use) did not correlate with delamination (Table 5).

Comparison of measured oxidation to published projections of oxidation versus time [9, 12] showed the projections satisfactorily described the increase in oxidation with time for most of retrievals (Fig. 7). Maximum oxidation measured in retrieved inserts increased exponentially with time since sterilization for gamma-air-sterilized retrievals and

Fig. 3 Retrieved gamma-inert-sterilized tibial inserts ($n = 29$) from three manufacturers were in vivo less than 1.5 years and had a wide range of shelf time before implantation. These retrievals all had similar oxidation that was comparable to the oxidation measured in four never-implanted shelf-aged gamma-inert-sterilized tibial inserts. Barrier packaging appeared to have been effective in preventing shelf oxidation.

Table 3. Shelf storage time, in vivo time, and articular oxidation in four never-implanted and 29 retrieved gamma-inert-sterilized tibial inserts with in vivo times of less than 1.5 years

Variable	Retrieved	Number	Never-implanted	Number	p value
Shelf storage time (years)	1.47 ± 1.80 (0.05–6.4)	29	2.99 ± 2.52 (0.2–6.2)	4	0.139
In vivo time (years)	0.76 ± 0.40 (0.04–1.46)	29	0	4	< 0.001
Articular oxidation	0.06 ± 0.04 (0.02–0.12)	29	0.06 ± 0.03 (0.03–0.11)	4	0.879

Values are expressed as mean ± SD, with range in parentheses.

Table 4. Shelf storage time, in vivo time, and articular oxidation for tibial inserts with preimplantation shelf time of less than 5 years and more than 5 years

Variable	< 5 years' shelf time	Number	> 5 years' shelf time	Number	p value
Shelf storage time (years)	1.04 ± 1.00 (0.05–3.6)	29	6.09 ± 0.38 (5.6–6.4)	4	< 0.001
In vivo time (years)	0.66 ± 0.43 (0–1.46)	29	0.75 ± 0.64 (0–1.38)	4	0.706
Mean articular oxidation	0.06 ± 0.03 (0.02–0.11)	29	0.10 ± 0.02 (0.09–0.12)	4	0.011

Values are expressed as mean ± SD, with range in parentheses.

Fig. 4 Gamma-inert-sterilized retrievals showed gamma sterilization in barrier packaging was effective in preventing the early fatigue damage (0–5 years after implantation) seen in gamma-air-sterilized retrievals. Both gamma-air- and gamma-inert-sterilized retrievals showed increasing frequency of delamination with increased time in vivo.

with time since implantation for gamma-inert-sterilized retrievals.

Discussion

In the mid to late 1990s, manufacturers changed to gamma-inert sterilization of UHMWPE bearings from gamma-air sterilization, which reportedly initiates oxidation leading to bearing fatigue [9, 11]. Gamma-inert sterilization prevented shelf oxidation before implantation but not subsequent in vivo oxidation. Our goals were (1) to confirm gamma-inert sterilization in barrier packaging was effective in preventing shelf oxidation before implantation; (2) to determine whether gamma-inert sterilization prevented in vivo fatigue damage; and (3) to verify previously published in vivo oxidation rate projections effectively predicted the timing when critical oxidation would be reached for gamma-inert-sterilized inserts. We found a ketone peak height ratio of greater than 1, where mechanical properties decreased below the ASTM specified minima for surgical implants.

Fig. 5A–B (A) A retrieved DePuy Sigma® STB tibial insert (gamma vacuum foil sterilized) was shelf stored 0.6 months before implantation. It was in vivo 12.5 years before being retrieved for polyethylene wear. Maximum articular oxidation was 2.2, and it exhibited delamination on retrieval. (B) A retrieved Biomet Maxim® CR tibial insert (ArCom® sterilized) was shelf stored 6.7 months before implantation. It was in vivo 10.5 years before being retrieved for instability. Maximum articular oxidation was 1.6, and it exhibited delamination on retrieval.

Limitations of this study are (1) this was a retrieval study; (2) sterilization dates for retrieved inserts were not available from all implant manufacturers; and (3) the retrievals were received from 117 different surgeons.

Retrieval studies are able to report on observed phenomena in retrievals but are unable to put those results in the context of all implanted devices. Typically the number

For gamma-air-sterilized bearings:

For gamma-inert-sterilized bearings:

Fig. 6 While barrier packaging used in gamma-inert sterilization prevents shelf oxidation before implantation, the in vivo steps leading to fatigue remain the same as for gamma-air sterilization.

Fig. 7 Oxidation measured in gamma-air- and gamma-inert-sterilized tibial inserts increased exponentially with time since sterilization (gamma-air) or time since implantation (gamma-inert). Oxidation values are compared to previously published trend lines for ketone peak height [9] and ASTM OI [12].

Table 5. Factors correlated with occurrence of delamination (Spearman's correlation)

Variable	Gamma-air sterilized (Spearman's rho, p value)	Number	Gamma-inert sterilized (Spearman's rho, p value)	Number
Preimplantation shelf time	0.442, $p < 0.001$	182	0.035, $p = 0.649$	175
In vivo time	0.225, $p = 0.002$	182	0.258, $p = 0.001$	175
Articular oxidation	0.697, $p < 0.001$	129	0.336, $p < 0.001$	173
Patient BMI	0.192, $p = 0.039$	116	0.103, $p = 0.354$	83
Patient age	0.017, $p = 0.816$	180	0.091, $p = 0.234$	174

of retrievals represents some fraction of 1% of the number of similar devices implanted. The observations and comparisons within a retrieval dataset can show relative frequency of occurrence of an observed phenomenon (eg, delamination in tibial inserts) and whether the phenomenon occurs in multiple designs by a number of manufacturers or is specific to a design or manufacturer. Tracing the pedigree of retrievals depends on the retrieving surgeon having access to implant records from the original surgery and manufacturers being able to tie historical lot numbers to fabrication and sterilization records. The gamma-inert sterilization methods we evaluated are limited to those methods used by manufacturers that were able to provide information on retrieved devices. A broad surgeon base complicates calibrating surgeon-supplied information, such as reason for retrieval.

This study evaluated whether the change in packaging from air-permeable packaging to barrier packaging (resulting in a change from gamma-air to gamma-inert sterilization) prevented the shelf oxidation that led to early in vivo fatigue damage in gamma-air-sterilized inserts. Never-implanted gamma-sterilized tibial inserts, removed from air-permeable packages after years of shelf aging,

showed oxidation of the UHMWPE during shelf aging resulted in degraded mechanical properties [4, 9] (Table 6). We confirmed barrier packaging of gamma-sterilized tibial inserts prevented preimplantation shelf oxidation for up to 5 years [6]. By preventing preimplantation oxidation, gamma-inert-sterilized inserts were not embrittled by shelf oxidation, and delamination fatigue damage was essentially eliminated in barrier-packaged inserts over the first 5 years in vivo. We did find evidence that some barrier packaging may begin to lose its effectiveness beyond 5 years.

While the change to gamma-inert sterilization in barrier packaging has effectively prevented preimplantation shelf oxidation, it has not eliminated in vivo fatigue [12]. The frequency of delamination fatigue damage was lower in gamma-inert-sterilized retrievals than in gamma-air-sterilized retrievals; however, the likelihood of fatigue increases as oxidation reduces the mechanical properties of the UHMWPE.

Previously published projections of oxidation versus in vivo time for gamma-inert-sterilized retrievals [9, 12] reasonably predict the oxidation measured in longer in vivo time retrieved tibial inserts. Critical oxidation, defined as the oxidation at which strength and ductility of the

Table 6. Summary of literature results

Study	Sterilization method	Shelf storage time (years)	In vivo time (years)	Oxidation	UTS (MPa)	UE (%)	In vivo delamination
Bargmann et al. [4]	Gamma-air	7.8		1.3	28	27	
	Gamma-inert	1.9		0.01	59	451	
Collier et al. [5]	Gamma-air	Unknown	< 4				27%
	Gamma-air	Unknown	> 4				66%
Costa et al. [6]	Gamma-inert	< 5		0.17 (0.06–0.32)			
	Gamma-inert	> 5		0.17 (0.11–0.26)			
Currier et al. [7]	Gamma-air	7.3	0.6				Yes
	Gamma-air	0.1	7				Yes
Currier et al. [9]	Gamma-air	15		1.0*	<27	50	Yes
	Gamma-air	6		1.5†	<27	50	Yes
Medel et al. [12]	Gamma-air	0.3	12.9	1.7			Yes
	Gamma-air	0.2	8.3	2.1			Yes
	Gamma-air	2.8	5.7	3.0			Yes
	Gamma-inert	0.7	6.5	1.0			No
	Gamma-inert	6	3.7	2.1			Yes
	Gamma-inert	1.0	7.8	1.4			No
	Gamma-inert	1.9	0.6	0.2			No
	Gamma-inert						
Current study	Gamma-air	7.8		1.2‡	<27	50	
	Gamma-inert	6.2		0.10	57	340	
	Gamma-inert	2.1		0.04			
	Gamma-inert	0.05	12.5	2.2			Yes
	Gamma-inert	0.6	10.5	1.6			Yes

* 1900 resin results; †GUR 412/415 resin results; ‡1020 resin results; UTS = ultimate tensile strength; UE = ultimate elongation.

UHMWPE are reduced to below the ASTM minima for surgical implants, is reached in 11 to 14 years according to the projections. Delamination requires cycles of use on increasing degraded UHMWPE. Patient factors such as activity level and potentially BMI [13] could be expected to influence timing of insert fatigue.

Shelf storage time before implantation was a concern for gamma-air-sterilized inserts [4, 7, 9] where shelf oxidation led to early in vivo fatigue damage. Some early barrier packaging did not effectively prevent shelf oxidation [6], but the change from gamma-air to gamma-inert sterilization largely prevented the shelf oxidation that led to fatigue after less than 4 years in vivo [5]. In vivo oxidation was predicted to increase exponentially with time [9, 12]. The predictions of time to reach critical oxidation were reasonable for most retrieved inserts in this study; however, retrieved inserts (both gamma-air and gamma-inert sterilized) that reached critical oxidation much earlier than the predicted 11- to 14-year time frame have been reported [7, 12]. Delamination resulted from oxidation-weakened UHMWPE coupled with cycles of use in vivo. Gamma-inert sterilization clearly reduced the incidence of delamination over the first 10 years in vivo but did not prevent it

entirely. Monitoring patients for signs of insert fatigue continues to be necessary.

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