HIGHLY CROSSLINKED POLYETHYLENES: *HOPES VS. REALITIES*

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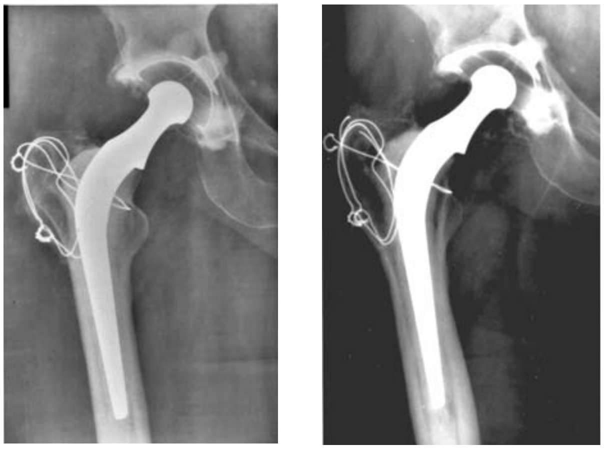
A REALITY CHECK

The enduring success of the low-friction arthroplasty first advanced by Sir John Charnley as a solution for severe hip arthritic problems may be appreciated from the fact that in 2003 more than 800,000 hip and knee arthroplasties were performed in the United States. The prevalence of aseptic loosening attributed to ultra-high molecular weight polyethylene (UHMWPE) debris-induced osteolysis has been in the single digits in most contemporary series, with some reports describing prostheses surviving for 20 to 30 years and represents the gold standard against which contemporary material improvements will be measured over time. (Figure 1)



(a) (b)

Figure 1: *Radiographs of a Charnley cemented hip replacement: (a) immediate post-operative; (b) 25 years post-operative.*

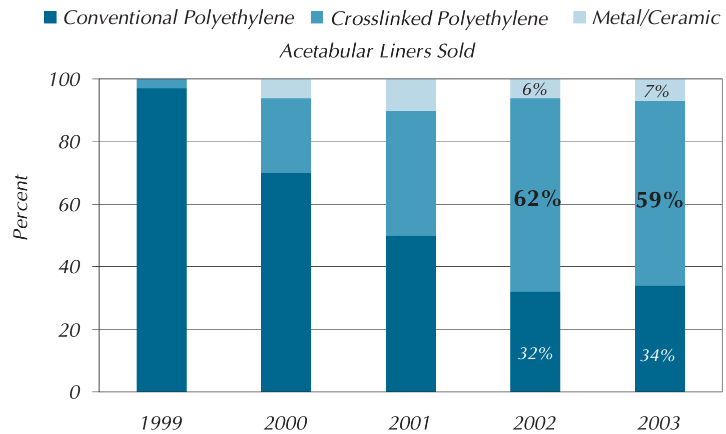


Figure 2: *Histogram illustrating the growth of highly crosslinked UHMWPE acetabular component sales in the United States. From: Orthopaedic Network News, July 2004.*

Beginning in 1997, the FDA approved a series of UHMWPE's with elevated crosslinking for use in prosthetic joints. Their stated benefit is to dramatically decrease the generation of UHMWPE wear debris, confirmation of which finds support in wear simulator reports for hip and knee components. The commercial adaptation of these new UHMWPE's has been aggressively marketed particular to acetabular components (Figure 2) well in advance of now emerging short-term clinical reports.

What follows is a descriptor of the clinical evolution of UHMWPE bearing surfaces: the good, the bad and the hopeful.

STRUCTURE

The UHMWPE used in hip and knee components results from polymerization of ethylene gas into a fine resin powder of sub-micron and micron size distribution. It is consolidated with the use of ram-extrusion or compression-molding techniques. Structurally, the polymer is made up of repeating carbon-hydrogen (-CH_2-) units that are arranged in ordered (crystalline) and disordered (amorphous) regions. Gamma irradiation breaks the polymer chains, creating free radicals, (Figure 3) which in an air environment combine with oxygen, facilitating ongoing oxidative degradation of the polymer.

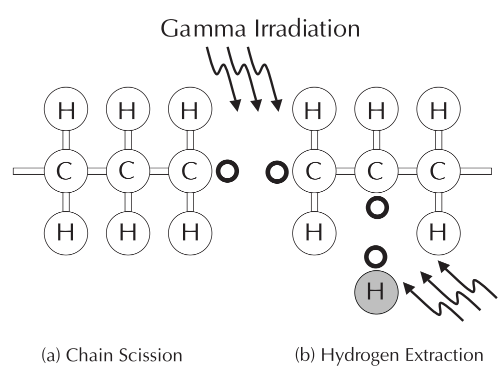


Figure 3: *Depicted polymer chain breakage following gamma irradiation.*

STRUCTURE (Cont.)

These free radicals can also combine with adjacent molecules forming crosslinks, a process enhanced by increasing radiation dose. This has been shown in laboratory hip simulators to dramatically lower the wear rate of these materials. (Figure 4)

Further, residual free radicals, which are generated during irradiation of the polymer, can be suppressed by several different post-irradiation processes. Kinetic recombination at increased temperature in an oxygen-free environment or quenching through remelting, are currently used methods to eliminate these retained free radicals. Eliminating oxygen from the final component sterilization process further contributes to this material improvement.

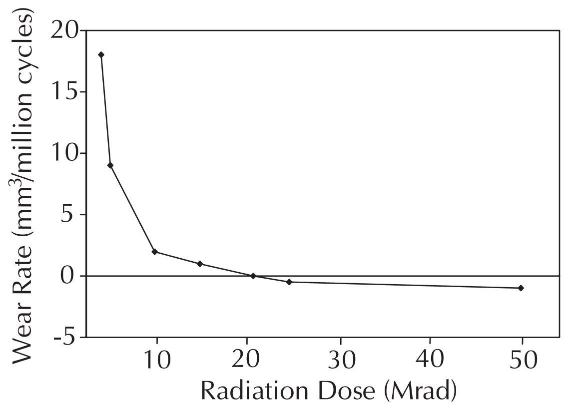
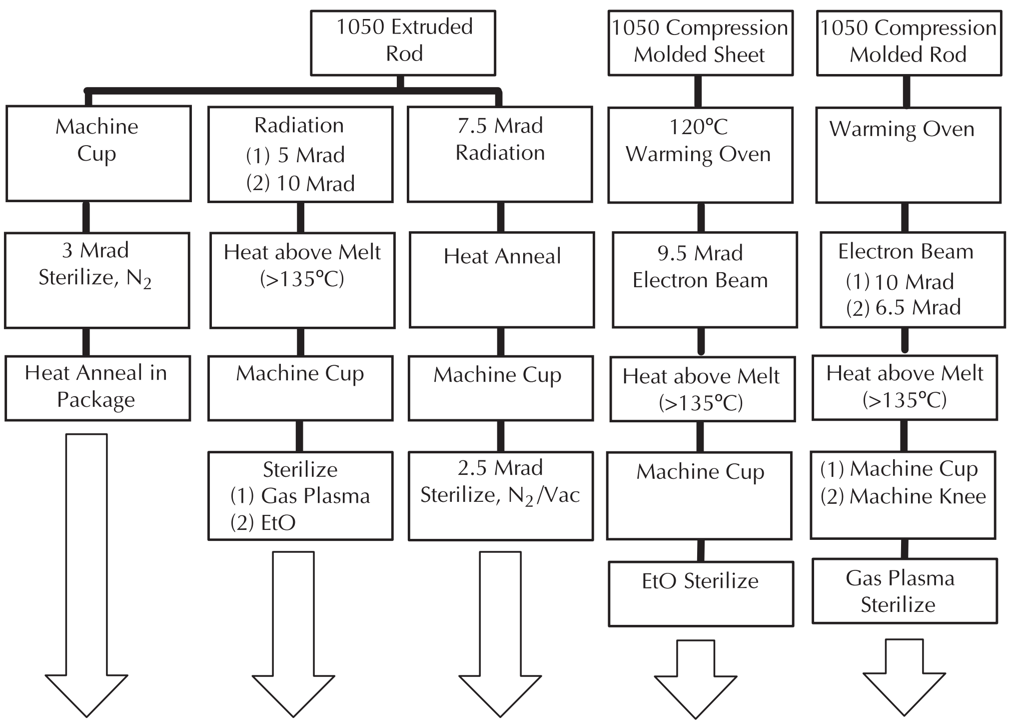


Figure 4: *Mean acetabular cup wear rates versus gamma dose level. From McKellop, et al., J Orthop Res 17: 160, 1999.*

CONTEMPORARY CROSSLINKED UHMWPE's

The new generation of crosslinked UHMWPE's represents contemporary alternatives whose common denominator is an appreciation of the importance of increased crosslinking to minimize oxidative degradation and reduce wear. Process differences include: 1) heating above or below the melt temperature of the polyethylene, 2) the radiation source, 3) dose level and 4) end-point sterilization. (Figure 5)



Process Name	**Heat Stabilized**	**CISM** (Cold Irradiated Subsequent Melt)	**CIAN** (Cold Irradiated Annealed Non-melt)	**WIAM** (Warm Irradiated Adiabatic Melting)	**WISM** (Warm Irradiated Subsequent Melt)
Product Name	*Duration™*	*(1) Marathon™* *(2) XLPE™*	*Crossfire™*	*Durasul®*	*(1) Longevity®* *(2) Prolong™*
Company	*Stryker Orthopaedics*	*(1) DePuy/J&J* *(2) Smith+Nephew*	*Stryker Orthopaedics*	*Zimmer*	*Zimmer*

Figure 5: *Current methods used to manufacture moderately to highly crosslinked UHMWPE.*

EARLY CLINICAL EXPERIENCES

A number of early, *in vivo* and retrieval experiences demonstrate a significant reduction in wear volume and rate for these contemporary crosslinked UHMWPE's. Radiographic techniques involving radiostereometric analysis (RSA), and two- and three-dimensional measurements suggest that these materials perform better than conventional UHMWPE over the short-term. It is important to appreciate that these results are promising, but must manifest over the long-term in their comparison to the gold standard of conventional UHMWPE usage. If they do so, these materials will contribute significantly to the longevity of joint arthroplasty.

Digas, et al., Clin Orthop 429:6-16, 2004.

Heisel, et al., J Bone Joint Surg 86-A(4):748-751, 2004.

Hopper, et al., J Arthroplasty 18(7 Suppl 1):60-67, 2003.

Martell, et al., J Arthroplasty 18(7 Suppl 1):55-59, 2003.

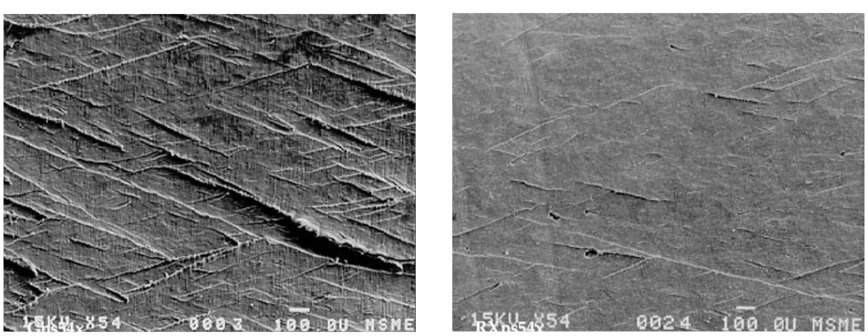
Muratoglu, et al., J Arthroplasty 18(7 Suppl 1):42-47, 2004.

Sychterz, et al., J Arthroplasty 19(2):258, 2004.

NOTES OF CAUTION

These processes, however, change either the amorphous or both the amorphous and crystalline regions of the resulting polymers, potentially affecting mechanical properties and fatigue characteristics.

There is laboratory evidence to suggest that processing methods utilized to increase cross-linking decrease resistance to fatigue crack propagation (Figure 6), a finding that could have implications for modular acetabular cup designs (Figure 7) as well as the suitability of highly crosslinked materials in knee application.



(a) (b)

Figure 6: *SEMs of UHMWPE fatigue fracture specimens: (a) gas-plasma-sterilized specimen demonstrating ductile tearing associated with plastic deformation and slowing fatigue crack growth; (b) radiation crosslinked specimen demonstrating the relative absence of ductile tearing mechanisms. From Pruitt, et al., J Biomed Mater Res, 46: 573-581, 1999.*

Figure 7: *Crack propagation failure of a retrieved conventional UHMWPE liner associated with an inadequate locking mechanism design.*

NOTES OF CAUTION (Cont.)

It is important to appreciate that the principal modes of hip and knee material damage differ. While abrasion and adhesion are the prevalent mechanisms of hip wear, fatigue-induced delamination and pitting predominate in the knee, a reality universally appreciated in clinical retrievals. (Figure 8)

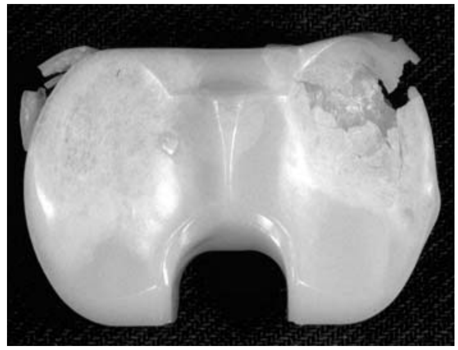


Figure 8: *A retrieved conventional UHMWPE tibial insert demonstrating typical knee failure patterns of gross delamination and pitting.*

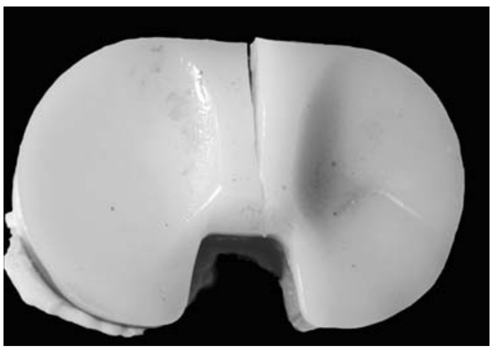


Figure 9: *A retrieved conventional UHMWPE tibial insert demonstrating an anterior-posterior fracture of the non-articulating portion of the insert.*

Additionally, reduced fracture properties in highly crosslinked UHMWPE's raise concerns of gross fracture in knee components, a condition relatively rare with conventional UHMWPE. (Figure 9)

Although contemporary hip and knee simulator data for these materials suggest favorable wear characteristics, it is important to appreciate that current simulators do not replicate all *in vivo* loading conditions that may lead to mechanical failure.

There are short-term case and retrieval reports that describe caution in the use of these materials.

Bradford, et al., J Bone Joint Surg 86-A(6):1271-1282, 2004.

Bradford, et al., J Bone Joint Surg 86-A(5):1051-1056, 2004.

Halley, et al., J Bone Joint Surg 86-A(4):827-830, 2004.

These reports suggest that *in vivo* material longevity of highly crosslinked UHMWPE's is dependent on counter-surface interaction, altered material properties and component placement.

Although the short-term clinical efficacy in the published reports to date for the hip is encouraging, this is not sufficient for its extrapolation to assuring *in vivo* longevity. There is no contemporary evidence-based clinical report that supports the latter with these FDA-approved materials.

LEST WE FORGET

There have been a number of alternatives to improve the performance of UHMWPE components, which have not stood the test of clinical longevity despite promising laboratory results. These include carbon-fiber reinforcement (Poly-2) and, more recently, polymer reprocessing to enhance mechanical properties by hot isostatic pressing (Hylamer). The former was withdrawn from the market because of an unexpectedly high wear rate (Figure 10) while the latter has been linked to debris-induced osteolytic response, especially when sterilized by gamma irradiation in air, in early reports. (Figure 11) Heat pressing was yet another attempt to improve the finish of the articular surface, but was associated with polymer fatigue and early delamination. (Figure 12)

Figure 10: *A failed Poly-2 tibial insert retrieved 5 years after implantation.*

Figure 11: *A failed Hylamer acetabular cup insert retrieved 3 years after implantation.*

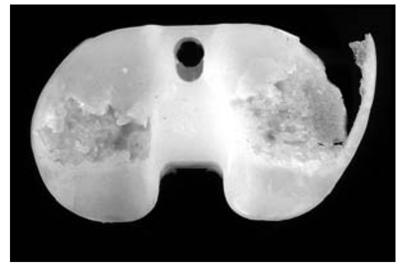


Figure 12: *A heat pressed tibial component retrieved 6 years after implantation.*

TAKE HOME MESSAGE

- For the past three decades, UHMWPE hip and knee components have been predominantly sterilized by gamma irradiation in air and have shown remarkable overall resilience in terms of clinical function.
- Nevertheless, aseptic loosening attributed to UHMWPE debris-induced osteolysis is of contemporary concern. As the indications for total joint replacement expand to younger patients and life expectancy increases, the interest in alternative bearing materials has accelerated.
- Beginning in 1997, the FDA approved a series of UHMWPE's with elevated crosslinking for use in prosthetic joints. Their stated benefit is to dramatically decrease the generation of UHMWPE wear debris, confirmation of which finds strong support in wear simulator reports.
- These pre-clinical studies have been buttressed by recent short-term clinical reports describing the *in vivo* efficacy of these materials in reducing wear.
- It is known, however, that the processing of these polymers changes the chemical structure affecting both static mechanical and fatigue characteristics. This suggests that conventional damage mechanisms for hip and knee design be fully appreciated when considering these new materials.
- The commercial adaptation of these new UHMWPE's has been aggressively marketed particular to acetabular components well in advance of the now emerging short-term clinical reports.
- The clinical use of highly crosslinked UHMWPE's is an ongoing, concurrent laboratory and human experiment that shows promise in early hip replacement reports, but is not without its caveats.
- The orthopaedic community should still exercise caution in the use of contemporary highly crosslinked UHMWPE's as the tincture of *in vivo* time is requisite for the demonstration of long-term efficacy.