In Vivo Oxidative Stability and Clinical Performance for 1st – and 2nd – Generation Highly Crosslinked Polyethylene

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Background

- Highly crosslinked polyethylenes have shown improved \textit{in vivo} wear performance.
  - Significantly reduced osteolysis rates
- 1\textsuperscript{st} Generation HXLPEs Concerns
  - Annealed $\rightarrow$ Oxidative Stability
  - Remelted $\rightarrow$ Reduced Mechanical Properties
### 2\textsuperscript{nd} Generation HXLPE

<table>
<thead>
<tr>
<th></th>
<th>Crosslinking Dose</th>
<th>Post-irradiation stabilization</th>
<th>Sterilization Modality</th>
<th>Total Irradiation Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sequentially Annealed</strong></td>
<td>30 kGy in 3 steps</td>
<td>Annealing after each crosslinking dose</td>
<td>Gas Plasma</td>
<td>90 kGy</td>
</tr>
<tr>
<td><strong>Vitamin E</strong></td>
<td>100 kGy</td>
<td>Vitamin E doping with subsequent annealing</td>
<td>Gamma in argon</td>
<td>130 kGy</td>
</tr>
</tbody>
</table>

Vitamin E doping with subsequent annealing
The purpose of this multicenter study was to assess the oxidative, mechanical behavior, wear, and reasons for revision of 1st and 2nd generation highly crosslinked polyethylene.
Drexel University Implant Repository
• 10 Surgical Centers
• 2 Retrieval Laboratories
### Cohorts (n = 431)

<table>
<thead>
<tr>
<th>Cohort</th>
<th>n</th>
<th>Manufacturer</th>
<th>Polyethylene Trade name</th>
<th>Terminal Sterilization</th>
<th>Total Irradiation Dose (kGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gas Sterilization</td>
<td>27</td>
<td>Depuy S&amp;N</td>
<td>N/A</td>
<td>Gas Plasma</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>EtO</td>
<td></td>
</tr>
<tr>
<td>Gamma Inert</td>
<td>47</td>
<td>Depuy Zimmer</td>
<td>N/A</td>
<td>Gamma in inert environment</td>
<td>~35</td>
</tr>
<tr>
<td>Remelted</td>
<td>218</td>
<td>Wright Medical</td>
<td>A-Class</td>
<td>Gas Plasma or EtO</td>
<td>50 – 100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Zimmer</td>
<td>Durasul</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Zimmer</td>
<td>Longevity</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Depuy</td>
<td>Marathon</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Smith &amp; Nephew</td>
<td>XLPE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annealed</td>
<td>84</td>
<td>Stryker</td>
<td>Crossfire</td>
<td>Gamma in Nitrogen</td>
<td>105</td>
</tr>
<tr>
<td>Sequentially Annealed</td>
<td>52</td>
<td>Stryker</td>
<td>X3</td>
<td>Gas Plasma</td>
<td>95</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>3</td>
<td>Biomet</td>
<td>E1</td>
<td>Gamma in Argon</td>
<td>130</td>
</tr>
</tbody>
</table>
## Patient Demographics

<table>
<thead>
<tr>
<th>Cohort</th>
<th>n</th>
<th>Age (years)</th>
<th>Gender (%F)</th>
<th>BMI (kg/m²)</th>
<th>Implantation Time (y)</th>
<th>Max UCLA Score (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gas Sterilization</td>
<td>27</td>
<td>49 ± 17</td>
<td>56%</td>
<td>32.4 ± 6.9</td>
<td>8.4 ± 3.7</td>
<td>7 (2 – 10)</td>
</tr>
<tr>
<td>Gamma Inert</td>
<td>47</td>
<td>59 ± 15</td>
<td>55%</td>
<td>29.4 ± 7.1</td>
<td>6.2 ± 3.8</td>
<td>6 (1 – 9)</td>
</tr>
<tr>
<td>Remelted</td>
<td>218</td>
<td>61 ± 13</td>
<td>54%</td>
<td>29.3 ± 7.2</td>
<td>1.9 ± 2.3</td>
<td>5 (1 – 10)</td>
</tr>
<tr>
<td>Annealed</td>
<td>84</td>
<td>62 ± 12</td>
<td>54%</td>
<td>28.4 ± 6.2</td>
<td>3.8 ± 2.9</td>
<td>5 (2 – 10)</td>
</tr>
<tr>
<td>Sequentially Annealed</td>
<td>52</td>
<td>58 ± 15</td>
<td>53%</td>
<td>31.7 ± 6.5</td>
<td>1.2 ± 0.9</td>
<td>5 (1 – 8)</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>3</td>
<td>48 ± 25</td>
<td>0%</td>
<td>31.8 ± 2.8</td>
<td>1.2 ± 0.7</td>
<td>4 (3 – 5)</td>
</tr>
</tbody>
</table>
Reasons for Revision

- Gas Sterilization
- Gamma Inert
- Remelted
- Annealed
- Sequentially Annealed
- Vitamin E Stabilized

Revision Reasons:
- Loosening
- Instability
- Infection
- Malalignment
- Periprosthetic Fracture
- PE Wear
- Other

Percentages shown in the chart represent the proportion of each revision reason across different categories of materials or processes.
Methods
Penetration Measurement

• Designate superior and inferior sides
• Measure thickness of superior and inferior regions
  – Point-tipped micrometer
    • Accuracy (0.001)

Inferior Thickness – Superior Thickness
Implantation Time

Linear Penetration Rate
Results
Penetration Rates

Fractured Ceramic Head

* p ≤ 0.02
Methods
Oxidation Analysis

• 200 µm sections taken:
  – From superior to inferior cross-section
• Boiled for 6h in heptane to avoid interference of absorbed lipids
• Scanned at 0.1 mm increments
  – 32 repeat scans per location
• Maximum Oxidation Index in accordance with ASTM F2102-01

\[ OI = \frac{A_{1850-1650}}{A_{1396-1330}} \]
Results
Oxidation (All Liners)

*p ≤ 0.001; Kruskal – Wallis with post-hoc Dunn Test
Results

Oxidation (*in vivo* ≤ 3.4y)

*p* ≤ 0.05; Kruskal – Wallis with post-hoc Dunn Test
Methods
Hydroperoxide Analysis

• Expose UHMWPE to nitric oxide (NO) gas in the absence of oxygen
  – Hydroperoxides → nitrates
  – Alcohols → nitrites
• Hydroperoxide index measured using FTIR
  – Represents oxidation potential for PE

\[ HI = \frac{A_{1670-1600}}{A_{1396-1330}} \]
Results

Hydroperoxides (All Liners)

*p ≤ 0.05; Kruskal – Wallis with post-hoc Dunn Test
Results
Hydroperoxides (≤ 3.4y)

* p ≤ 0.05; Kruskal – Wallis with post-hoc Dunn Test
Methods
Small Punch Test

- Cores taken from Inferior and Superior portions of the liner
- Miniature Disks machined from cores (Surface and subsurface specimens)
  - 6.4mm in diameter
  - 0.5mm in thickness
- Testing conducted in accordance with ASTM F2183
  - 4 Metrics Calculated
    - Peak Load
    - Ultimate Load
    - Ultimate Displacement
    - Work to Failure
Results

Ultimate Load (All Liners)
Results
Ultimate Load (Liners ≤ 3.4y)

[Box plot showing the distribution of ultimate load for different sterilization methods: Gas Sterilization, Gamma Inert, Remelted, Annealed, Sequentially Annealed, and Vitamin E Stabilized.]
Results
Ultimate Load

Graph showing the relationship between implantation time (y) and superior surface ultimate load (N), with different symbols representing various sterilization methods.
Results

Ultimate Load

Gas Sterilization (Spearman's Rho = -0.37; p = 0.09)
Results
Ultimate Load

Gamma Inert (Spearman’s Rho = -0.31; p = 0.04)
Results
Ultimate Load

![Graph showing the relationship between implantation time and superior surface ultimate load, with a note that Remelted (Spearman's Rho = 0.09; p = 0.27).]
Results
Ultimate Load

Annealed (Spearman's Rho = -0.31; p = 0.04)
Results
Ultimate Load

Sequentially Annealed (Spearman’s Rho = -0.30; p = 0.06)
Case Study
Sequentially Annealed

- Male, 59y
  - Black
  - BMI : 28
- Implanted 2006
  - DJD
- Revised 2010
  - Max UCLA Score: 6
  - Revised for Femoral Loosening

*In vivo 3.4 y*
Inferior Rim

$O_{I_{\text{Max}}} = 0.1$

Superior Backside

$O_{I_{\text{Max}}} = 0.1$

$O_{I_{\text{Max}}} = 0.2$

$O_{I_{\text{Max}}} = 0.3$

$O_{I_{\text{Max}}} = 0.3$

$O_{I_{\text{Max}}} = 0.1$
Case Study
Vitamin E Stabilized

- Male, 21y
  - BMI : 34
- Implanted 2009
- Revised 2010
  - Max UCLA Score: 3
  - Revised for Malalignment and Instability

In vivo 0.8 y
Discussion

- All HXLPE materials in this study effectively reduced wear as compared to control.

- Oxidative stability is formulation dependent
  - Sequential annealing (X3™) reduces oxidation as compared with 1st generation annealing
  - Vitamin E (E1™) oxidation levels were low and uniform
    - Short implantation time
Discussion

• Mechanical properties also formulation dependent
  – Only Gamma Inert and Sequentially Annealed groups negatively correlated with implantation time

• Additional Vitamin E retrievals necessary to fully characterize their *in vivo* behavior.