Decreased Functional Biological Activity of Polyethylene Wear Debris From Revised HXLPE Liners

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Rational of Study

• Highly crosslinked UHMWPE (HXLPE) is known clinically to reduce osteolysis.

• In vitro cell culture studies, on the other hand, predict that submicron wear debris from these materials might show comparable osteolytic potential to conventional PE over time.

References:

Advances in Bearing Technology

Highly Crosslinked Polyethylene

• Annealed HXLPE
  Electron beam or γ-Irradiation
  Thermally treated below crystalline melt transition
  *Residual free radicals*

• Remelted HXLPE
  Electron beam or γ-Irradiation
  Thermally treated above crystalline melt transition
  *Decreased crystallinity and reduced mechanical properties*
Frequency of Hip Osteolysis for Conventional and HXLPE Liners

<table>
<thead>
<tr>
<th>Study name</th>
<th>Odds ratio</th>
<th>p-Value</th>
<th>Odds ratio and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bitsch 2008</td>
<td>0.002</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>D’Antonio 2005</td>
<td>0.103</td>
<td>0.004</td>
<td></td>
</tr>
<tr>
<td>Engh 2006</td>
<td>0.230</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>Fukui 2010</td>
<td>0.081</td>
<td>0.111</td>
<td></td>
</tr>
<tr>
<td>Leung 2007</td>
<td>0.240</td>
<td>0.041</td>
<td></td>
</tr>
<tr>
<td>Mall 2011</td>
<td>0.067</td>
<td>0.011</td>
<td></td>
</tr>
<tr>
<td>Olyslaegers 2008</td>
<td>0.310</td>
<td>0.214</td>
<td></td>
</tr>
<tr>
<td>Rajadhyaaksha 2009</td>
<td>0.050</td>
<td>0.044</td>
<td></td>
</tr>
<tr>
<td>Rohr 2007</td>
<td>0.167</td>
<td>0.119</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>0.131</strong></td>
<td><strong>0.000</strong></td>
<td></td>
</tr>
</tbody>
</table>

Odds ratio for osteolysis of conventional vs HXLPE liners was 0.131 (nine studies). Consensus that HXLPE reduces wear and osteolysis in total hip arthroplasty during the first 5-10 years after implantation.

Aseptic Loosening & Osteolysis

Complex Etiology

✓ Poor initial fixation - loosening
✓ Stress shielding - loosening
✓ Intracapsular fluid pressure - loosening
✓ Endotoxin - loosening
✓ Polyethylene wear debris - osteolysis
Wear Particle Generation

- Level of polymer cross-linking
- Surface roughness
- Implant conformity
- Complexity of wear path
- Usage & Applied load

- *In vitro* simulator testing shows increased submicron wear debris generation due to multidirectional friction, PE oxidation, & increased PE cross-linking.
In Vivo Studies of HXLPE Wear Debris

• Previous *in vivo* studies have been limited to two single case reports of cemented HXLPE liners, and only one looked for submicron wear (>0.5μm).

• For first-generation HXLPE liners it remains unknown whether the decreased incidence of osteolysis can be attributed to a reduction in the biological activity (*size, shape and number*) of polyethylene wear particles generated *in vivo*.

**In vivo References:**
Objectives

• Determine the size, shape and number of polyethylene wear debris in tissues from primary THA revisions of CPE, remelted and annealed HXLPE liners.

• Assess how these differences affect the predicted biological, pro-inflammatory activity of particles that initiate osteolysis and implant loosening.
## Tissue Cohorts

<table>
<thead>
<tr>
<th>CPE cohort</th>
<th>Remelted Cohort</th>
<th>Annealed Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=4</td>
<td>N=5</td>
<td>N=5</td>
</tr>
<tr>
<td>revised after 6.4 yr (2.3-9.3yr)</td>
<td>revised after 3.3yr (1.7-6.6)</td>
<td>revised after 4.2 yr (2.0-5.2yr)</td>
</tr>
<tr>
<td>Howmedica Omnifit, Biomet Ringloc, Zimmer Trilogy</td>
<td>Zimmer Trilogy</td>
<td>Stryker Trident</td>
</tr>
<tr>
<td>wear, loosening &amp; osteolysis (3 of 4)</td>
<td>loosening or malposition (1)</td>
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</tr>
<tr>
<td>female</td>
<td>4 female, 1 male</td>
<td>3 female, 2 male</td>
</tr>
<tr>
<td>68 ± 5 yr</td>
<td>61 ± 4 yr</td>
<td>61 ± 6 yr</td>
</tr>
</tbody>
</table>
Approach

- Tissue (0.025g) digested with concentrated HNO$_3$
- Sequential filtration of digest through a 1.0µm & 0.05µm membrane
  - ~98% particle recovery
- Membranes are prepared for ESEM
- Imaged at 1,000, 5,000 & 12,000X
- Image Analysis of ≥1,000 particles per cohort using NIH ImageJ to determine particle area and dimension.
Representative Images of Polyethylene Wear Debris

CPE

Remelted HXLPE

Annealed HXLPE

>90% of particles were granular or ellipsoidal for all three groups, with the remainder being composed of fibrillar wear debris.
Particle Characteristics

- **Equivalent Circular Diameter**
  
  \[ ECD = \sqrt{\frac{4 \cdot A_p}{\pi}} \]
  
  Size (circle diameter) particle area

- **Aspect Ratio**
  
  \[ AR = \frac{L_p}{W_p} \]
  
  Ratio of particle length to breadth

- **Roundness**
  
  \[ R = \frac{4 \cdot A_p}{\pi \cdot (L_p)^2} \]
  
  Measure of circularity based on particle length

- **Form Factor**
  
  \[ FF = \frac{4 \cdot \pi \cdot A_p}{(\text{perimeter})^2} \]
  
  Measure of circularity based on particle perimeter

- **Number/gram wt. of tissue**
  
  \[ N_p = N_i \cdot \left( \frac{A_f}{A_t} \right) / W_T \]
Particle Size

Non-parametric Wilcoxon Mann-Whitney. Boxed ranges of the 25th to 75th percentile & whiskers showing the 10th and 90th percentile.

\[
ECD = \sqrt{\frac{4 \cdot A_p}{\pi}}
\]

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<tr>
<td>Mean ± Std. Dev. (Median)</td>
<td>0.32 ± 0.37 μm (0.20)</td>
<td>0.31 ± 0.39 μm (0.20)</td>
<td>0.43 ± 0.53 μm (0.26)</td>
</tr>
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Particle Morphology

\[ AR = \frac{L_p}{W_p} \]

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<tr>
<td><strong>Aspect Ratio</strong></td>
<td>2.00 ± 1.06 (1.66)</td>
<td>2.01 ± 1.07 (1.70)</td>
<td>2.15 ± 1.13 (1.80)</td>
</tr>
<tr>
<td><strong>Roundness</strong></td>
<td>0.59 ± 0.19 (0.60)</td>
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<td>0.55 ± 0.19 (0.56)</td>
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<td><strong>Form Factor</strong></td>
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\[ R = \frac{4 \cdot A_p}{\pi \cdot (L_p)^2} \]

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\[ \text{FF} = \frac{4 \cdot \pi \cdot A_p}{(\text{perimeter})^2} \]

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# Particle Number

![Bar chart comparing HXLPEs and Conventional Polyethylene](chart.png)

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<th>Conventional Polyethylene</th>
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<tbody>
<tr>
<td>Number (x10^8/gram of tissue)</td>
<td>1.34 ± 0.48 (1.11)</td>
<td>5.14 ± 3.37 (3.78)</td>
</tr>
<tr>
<td>Submicron Number %</td>
<td>94.83 ± 1.75 (95.08)</td>
<td>90.50 ± 3.60 (91.00)</td>
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Submicron Number Percentage

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Biological Activity

Original Model by Fisher et al. 2001

Specific Biological Activity (SBA)
- relative biological activity per unit volume,
where $C(r)$ is the % volumetric concentration
of wear debris as a function of particle size $(r)$

$\text{SBA} = \int_{0.1}^{100} C(r)B(r) \, dr$

The product of the volumetric
wear rate (mm$^3$/10$^6$ cycles) X SBA

$\text{FBA} = V \times \text{SBA}$

B(r) is the biological activity as a function of particle size

The product of the particle volume
(mm$^3$)/gm of tissue X SBA

$\text{FBA} = \text{SBA} \cdot \sum V_p$
Cumulative Particle Volume

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<tr>
<td>Total Estimated volume (mm³)/gram tissue (x10⁻³)</td>
<td>0.36 ± 0.05 (0.35)</td>
<td>6.47 ± 4.83 (5.73)</td>
</tr>
<tr>
<td>Functional Biological Activity (x10⁻³)</td>
<td>0.14 ± 0.09 (0.10)</td>
<td>1.51 ± 0.93 (1.49)</td>
</tr>
</tbody>
</table>

Malposition
Functional Biological Activity

\[ \text{FBA} = \text{SBA} \cdot \sum V_p \]
Summary of Findings

- Submicron particle number is increased for HXLPE vs CPE liners
- Wear particle volume % is significantly decreased for HXLPE vs CPE liners
- Resulting in a wear particle FBA that is significantly less for HXLPE vs CPE
Conclusion

Based on the current findings the pro-inflammatory, osteolytic potential of HXLPE wear debris is out-weighted by a significant improvement in wear resistance and decrease in particle generation.
Funding

U.S. Department of Health and Human Services

Supported by the

National Institutes of Health

NIAMS
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Questions?

Drexel University Implant Repository
- 10 Surgical Centers
- 2 Retrieval Laboratories

- University of Texas Science Center at San Antonio
- Jewish Hospital
- Tennessee Orthopaedic Clinics
- Sinai Hospital of Baltimore
- Lancaster General Hospital
- Case Western Reserve University and University Hospitals Case Medical Center
- Lutheran Hospital
- Hackensack University Medical Center
- Drexel University
- University of Pennsylvania
- Rothman Institute
Shape Validation

Validation: Shape

- NIST Traceable UHMWPE Wear Debris
  - R2 - Round
    - Diff: 1.3 ± 0.4 %
  - E1 - Elongated
    - Diff: 2.9 ± 0.8 %

![Graph showing fraction vs aspect ratio]

![Image of wear debris particles]
Polyethylene Validation

• Fourier Transform Infrared (FTIR) Analysis
Homogeneity

Validation: Homogeneity

\[ N_p = N_1 \cdot \left( \frac{A_F}{A_1} \right) / W_T \]

\[ R^2 = 0.9167 \]

Shapiro-Wilk Goodness of Fit P < 0.09
References:


Modes of Wear & Wear Particle Generation

Intended  Unintended  Abrasive  Impingement

- Usage
- Surface roughness
- Implant conformity
- Level of polymer cross-linking
- Complexity of wear path
- Applied load
Questions?

Clinical Centers

Ohio Centers
- Cleveland Clinic
- Case Western Reserve University Hospital

Case Western University

Implants Cleaned and Triaged

NJ, TX, KY, MD, TN Centers
- Hackensack University Medical Center
- University of Texas Hospital San Antonio

- Jewish Hospital
- Sinai Hospital of Baltimore

University of Tennessee

Drexel University Implant Research Center

Pennsylvania Centers
- Rothman Institute
- University of Pennsylvania
- Lancaster General