Enhanced Strength Retention of Bioresorbable Implants Sterilized by Ethylene Oxide (ETO)

Anastasia J. McManus, Rodney C. Moser, Rhiannon B. Dabkowski, Kevin A. Thomas
MacroPore Biosurgery, a Cytori Therapeutics Company, 6740 Top Gun Street, San Diego CA 92121

Statement of Purpose

Following a successful clinical history in cranio-maxillofacial surgery, the application of bioresorbable polymer materials to spinal fusion applications has emerged. Advantages of bioresorbable devices versus metallic implants include radiolucency, an elastic modulus comparable to cortical bone (minimizing stress shielding), and gradual load transfer to host bone as resorption occurs and the implant is replaced with remodeled bone. As an alternative to structural bone grafts, resorbable implants obviate autograft related donor site morbidity, and eliminate allograft related issues such as possible disease transmission and limited supply. Radiation sterilization is known to affect various properties of bioresorbable polymers. The purpose of this study was to compare the strength retention and polymer characteristics of bioresorbable implants following standard sterilization using electron-beam (e-beam) irradiation and ethylene oxide (ETO).

Methods

Commercially available 70:30 poly(L-lactide-co-D,L-lactide) material was fabricated into various designs using standard thermoforming and machining processes. The samples evaluated included sheets (1.0 mm thick, type V dog bones [1]), screws (nominal 2.7 mm Ø), cylinders (13 mm outer Ø, 2 mm wall), and rectangular (14 W x 26 L x 12 H, 2-4 mm wall) forms. Samples of identical devices were sterilized by either e-beam or ETO using qualified processes. All samples were subjected to in vitro ageing in phosphate buffered saline at 37 °C per ASTM F1635 [2]. For comparison, nonsterile samples were also evaluated (at time 0 only). Samples were subjected to mechanical testing after 0, 12, 26, 39 and 52 weeks of real time ageing, following standard methods [1,3]. Polymer analysis of all samples included determination of thermal properties (differential scanning calorimetry), inherent viscosity (IV, by dilute solution viscometry), and molecular weight (Mw, by gel permeation chromatography).

Results / Discussion

Following sterilization (prior to ageing) significant differences in IV and Mw were observed. The IV and Mw of the rectangular devices after ETO were nearly identical to nonsterile (approximately 4.3 dl/g), versus approximately 1.6 dl/g for e-beam. Following ageing, each of ETO devices maintained an IV greater than the initial value for corresponding e-beam devices for a minimum of 39 weeks. No devices, regardless of sterilization, exhibited a change in glass transition temperature (Tg) over the 52 week ageing period, and no crystallinity was detected in any sample at any time point.

At time zero (prior to ageing) there were no differences in strength for ETO versus e-beam for any of the forms. Initial strength in tension, shear and compression were approximately 60 MPa, 44 MPa, and 84 MPa, respectively.

Following ageing, the strength retention of ETO devices was equivalent or superior to e-beam at all time points. Enhanced strength retention was observed with ETO sterilization in all devices. In tension and shear, strength retention of the ETO devices at 52 weeks was equivalent to the e-beam at only 26 weeks. In compression the ETO samples retained 95% to 100% of initial compressive strength through 52 weeks.

The results are summarized in the table below.

Device Shape	Polymer and Mechanical Results
1.0 mm Sheet	IV, Mw ETO at 52 wks > E-beam at 0 weeks Tensile Strength (% of 0 weeks) ETO 68% at 52 wks, E-beam 70% at 26 wks
2.7 mm Screws	IV, Mw ETO at 39 wks > E-beam at 0 weeks Shear Strength (% of 0 weeks) ETO 85% at 52 wks, E-beam 80% at 26 wks
Cylinders	IV, Mw ETO at 52 wks > E-beam at 0 weeks Compression Strength (% of 0 weeks) ETO 100% at 52 wks, E-beam 44% at 39 wks
Rectangles	IV, Mw ETO at 39 wks > E-beam at 0 weeks Compression Strength (% of 0 weeks) ETO 95% at 52 wks, E-beam 60% at 26 wks

Conclusions

Sterilization by ethylene oxide had a nearly negligible effect on the molecular weight and inherent viscosity of the polymer. The immediate decrease in IV or Mw observed with e-beam sterilization required approximately 39 weeks of ageing following ETO sterilization. At all time points, the strength retention of ETO devices equaled or exceeded that of the e-beam. The essential effect of the ETO sterilization was to decrease the molecular degradation and corresponding mechanical strength loss typically observed with this material when sterilized by e-beam. These results indicate that bioresorbable 70:30 poly(L-lactide-co-D,L-lactide) implants sterilized by ETO can maintain substantially more strength than if sterilized by e-beam, for periods exceeding that typically required for bony healing or fusion, with no difference in the biocompatibility or crystallinity of the polymer.

References

[1] ASTM D638, *Standard Test Method for Tensile Properties of Plastics*.
[2] ASTM F1635, *Standard Test Method for In Vitro Degradation Testing of Poly(L-lactic Acid) Resin and Fabricated Form for Surgical Implants*.
[3] ASTM D695, *Standard Test Method for Compressive Properties of Rigid Plastics.*