Mechanical properties and in vivo performance of light-cured hydrogel/ABM/P-15 grafting materials

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Statement of Purpose: Particulate and putty bone grafts are widely used in orthopedics and dental. Allogenic or autograft blocks are utilized when space maintenance is required. The use of photopolymerization technology to create an *in situ* light-curable putty grafting material provides the advantages of better handling and performance, giving the clinician the ability to shape the graft and cure it *in situ*, thus protecting the desired area from compressive forces. Additionally, the use of a resorbable hydrogel carrier allows for bone ingrowth. While *in situ* hardening materials exist, such as calcium sulfate or calcium phosphate cements, they either lack resorption, or lack the ability to be cured on demand. We present formulation of a novel photopolymerizable, biodegradable bone graft, *in vitro* mechanical properties and *in vivo* bone formation results.

Methods: *Synthesis of photopolymerizable hydrogels:* Methacrylated sodium hyaluronate (MHy) and methacrylated hydroxyethylcellulose (MHEC) were synthesized in an aqueous solution of glycidyl methacrylate (GMA), treithylamine, tetrabutylammonium bromide, and sodium hyaluronate (Hy) or hydroxyethylcellulose (HEC), using a method similar to Leach et al.[1] The amount of derivatization was increased by increasing the GM:Hy molar ratio. MHy or MHEC gel was mixed with anorganic bone matrix (ABM) to form a putty and was polymerized by visible light (400-500nm) with Eosin Y photoinitiator.

In vitro physical property assessment: Compressive modulus of MHy/ABM materials was measured with a texture analyzer (n=4-5). The effects of cure time, particulate concentration, and MHy derivatization level were compared. Student's T-test was used for statistical analysis and $p<0.05$ was considered statistically significant.

In vivo performance: Material was tested in two animal models. Bilateral, unicortical tibial defects, 5mm in diameter, were created in four New Zealand (NZ) rabbits. Sites were grafted with light-cured putty material composed of anorganic bone matrix coated with P-15 cell binding peptide (ABM/P-15) in either MHEC or MHy. Grafts were cured *in situ* with visible light. After six weeks, histology and radiography were performed. In a second study, bone formation at four weeks with uncured and *in situ* cured MHy were compared in bilateral 2.0 mm diameter defects in the femurs of six NZ White Rabbits.

Results / Discussion: *Physical properties:* Curing for two minutes resulted in a 40-fold significant increase in compressive modulus above uncured materials. Increased particulate concentration, cure time, or methacrylate derivatization resulted in increased compressive modulus, as can be seen in Figure 1. In the absence of ABM, the compressive modulus of MHy with 120 second cure time is 0.23 ± 0.02, which is statistically significant four-fold less than MHy with 40% ABM. 55% particulate shows a significant two-fold increase in compressive modulus over 40% particulate at 60, 90, and 120s cure times. With 55% particulate, there is a significant increase in compressive modulus for a GM:Hy molar ratio of 15 vs. 10 at 60, 90, and 120s cure times.

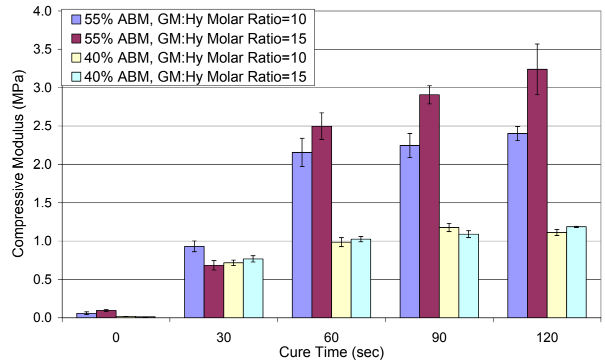

Figure 1: Compressive modulus of MHy with various ABM concentrations, GM:Hy molar ratios, and cure times.

In vivo performance: In the six-week study, histological and radiographic results showed moderate to abundant bone formation within both graft materials, in all defects. Mild to moderate inflammation was observed. Figure 2 shows a representative histological result of bone formation six weeks after implantation and *in situ* curing of light-curable hydrogel/ABM/P-15 graft material.

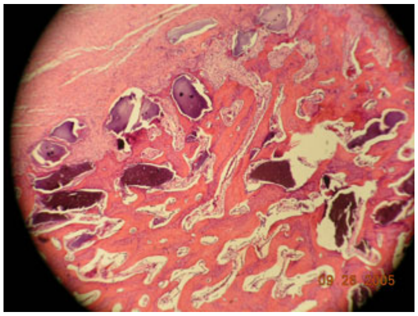

Figure 2: Histological result of six-week implantation of MHEC/ABM/P-15 material.

In the four-week rabbit study, both cured and uncured test materials were well tolerated in the bone and adjacent muscle tissue. Uncured material resulted in slightly better defect repair and osteo-integration than the cured material. Both materials were considered to be nonirritants to the muscle overlying the bone.

Conclusions: Photopolymerizable hydrogel/ABM/P-15 bone graft demonstrated enhanced physical properties over uncured materials and demonstrated good biocompatibility and osteoconductivity in two rabbit models.

References:

1. Leach, J.B., et al. Biotechnol Bioeng, 2003. **82**(5):578-89.