Burst Properties and Adhesion Strength of Oxidized Methacrylated Alginate Lung Sealants

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Statement of Purpose: Lung diseases, cancers, and trauma can result in pleural disruption and leak of air or fluid from the lung.[1] The resulting lung collapse can be immediately life threatening and/or can cause chronic leaking, also known as a bronchopleural fistula. Currently there are only limited means of sealing significant injuries to stop the air or liquid leak and allow appropriate healing to occur. More effective sealants are desperately needed. We have devised a new technique based on methacrylated alginate (Alg-MA) hydrogels utilizing an easily applied formulation. The effect of oxidation on the burst pressure strength and material properties of the Alg-MA hydrogels was determined.

Methods: Alg-MA was synthesized through a reaction between sodium alginate (Manugel, FMC Biopolymer) in H_2O and a 20 molar excess of methacrylic anhydride (Sigma Aldrich) for 24 hours.[2] Alg-MA (degree of methacrylation = 54%) was oxidized in sodium periodate solutions of varying concentrations to obtain oxidized Alg-MA (Alg-MA-Ox) with theoretical degrees of oxidation of 10, 30, and 50%. Sodium alginate, Alg-MA and Alg-MA-Ox were dissolved in deuterium oxide at 0.5% (w/v) and analyzed ^{1}H NMR spectrometer to determine degrees of methacrylation and oxidation.[3] 3% (w/v) Alg-MA and Alg-MA-Ox aqueous solutions were mixed with photoinitiators until the following concentrations were achieved: 1 mM Eosin Y (photosensitizer), 125 mM triethanolamine (initiator), 20 mM 1-vinyl-2-pyrrolidinone (catalyst).[4] Test substrates were prepared by punching 3mm holes in the centers of 3cm x 3cm rehydrated collagen squares, which were then laid flat on glass plates. 1.5 cm diameter Teflon molds were centered on the 3mm holes and clamped to the glass plates. 0.5 mL of sealant solutions were then deposited in the molds and crosslinked for 10 minutes under a 523 nm green LED. Burst pressure was measured on a custom-designed and built device following ASTM F2392-04R10 and utilizing a pressure transducer. All burst pressure tests were conducted at room temperature and an infusion rate of 75 mL/hr (Harvard Apparatus PHD 2000 Infusion). Failure mechanism (adhesive or material failure) was visually assessed after failure.

Results: The oxidation of Alg-MA was successful and allowed for varying degrees of oxidation. While oxidation decreased the likelihood of adhesive failure, the reaction also reduced the degree of methacrylation, resulting in degradation of the material due to shortening of the polysaccharide chains and a decrease in methacrylate groups available for crosslinking. However, the burst pressure test results suggest that blending oxidized and non-oxidized materials can produce stronger and more reliable sealants by combining the adhesive properties of the Alg-MA-Ox and the material strength of the non-oxidized Alg-MA. Compared with normal human peak inspiratory pressures of 25-30 cm H_2O (9.8-11.8 in H_2O), the burst pressures for both the Alg-MA and Alg-MA-Ox blend materials show promising burst pressures.[5]

Conclusions: Controlling both the degree of methacrylation and oxidation allows for a highly tunable bioadhesive which can be adapted for a range of applications. Cytocompatibility assays with primary human pluripotent stem cells will be performed to determine toxicity of the MA and OMA and all photocrosslinking agents. In vivo testing and survival studies will be conducted to prove the efficacy of Alg-MA-Ox as a lung sealant.

Table 1. Material properties of alginate based hydrogels. DOM = degree of methacrylation, DOO = degree of oxidation.

Material	Burst Pressure (in H_2O)	DOM (%)	DOO (%)
Alg-MA	21.98±12.36	77	N/A
10 Alg-MA-Ox	14.20±8.03	70	10
30 Alg-MA-Ox	1.25±0.34	64	25
10 Alg-MA-Ox Alg-MA Blend	23.36±2.33	73.5	5
30 Alg-MA-Ox Alg-MA Blend	19.25±1.46	70.5	12.5
50 Alg-MA-Ox Alg-MA Blend	13.26±3.14	54	19.8

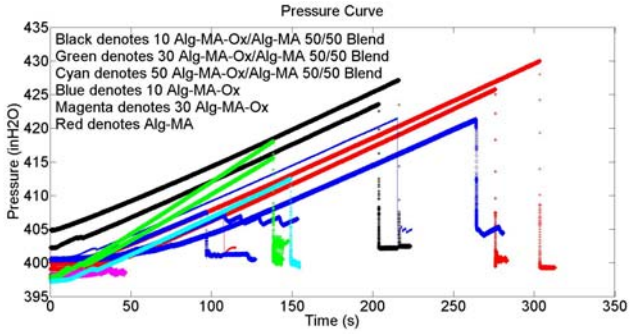

Figure 1. Pressure curves for material testing; burst pressure (in H_20) versus time. Red denotes Alg-MA, blue denotes 10 Alg-MA-Ox, magenta denotes 30 Alg-MA-Ox, and black, green, and cyan denote a 50/50 blend of the 10, 30, and 50 Alg-MA-Ox and Alg-MA material.

References: 1. Schraufnagel DE et al. *Breathing in America: diseases, progress, and hope*. American Thoracic Society, 2010. 2. Smeds *et al.* J. Macromol. Sci. (1999). 3. Park *et al.* Biomaterials. (2003) 4. Jeon, Oju, et al. *Biomaterials* (2012). 5. Wheeless, C. R. "Wheeless' textbook of orthopaedics." (1996).