An Alginate-Based Pulmonary Patch for Repairing Pleural Injuries

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Introduction: Injury to the connective tissue that lines the lung, the pleura, or to the lung itself can occur from many causes including trauma, as well as underlying lung diseases or lung cancers. Bronchopleural fistulas, malignant pleural effusions, and traumatic or ventilator-induced pleural injuries are a continuing source of morbidity, mortality, and increased health care expenditures. There are currently only limited means of patching significant injuries to stop the air or fluid leak and allow appropriate healing to occur. New approaches are desperately needed. We have devised a new technique based on methacrylated alginate hydrogels utilizing an easily applied patch formulation.

Materials and Methods: Methacrylated alginate (AA-MA) was synthesized through a reaction between 1% w/v sodium alginate (Manugel, FMC Biopolymer) in H2O and a 20 molar excess of methacrylic anhydride (Sigma Aldrich) for 24 hours.1 A 3% w/v AA-MA in water solution was mixed until fully in solution. Using only red light for illumination and mixing syringes, visible green light activated photoinitiators are added until the following concentrations are achieved: 1 mM Eosin Y (photosensitizer), 125 mM triethanolamine (initiator), 20 mM 1-vinyl-2-pyrrolidinone (catalyst).2 Using a spin-coater, glass slides spinning at 1500 rpm were coated in the AA-MA and photoinitiator solution for 5-10 seconds. The coated slides were flash frozen in liquid nitrogen and subsequently lyophilized, ensuring the material remains in complete darkness throughout the procedure. The films were then removed from the slides and stored in sealed light proof packaging until use. Lungs were excised from mice, cannulated, and placed in a PBS solution. Baseline pressure and volume measurements were performed on the excised mouse lungs (max pressure 30 cm H2O) prior to introduction of a small puncture. Similar pressure and volume measurements were repeated after the puncture for comparison with the artificially sealed lungs. The AA-MA films were cut into separate pieces of approximately 1 cm² and applied to the incision on the moistened lungs in their dry form with the use of forceps, layering 2 pieces of patch at 45°, relative to each other. The patched lungs were then exposed to green light (530 nm) for 10 minutes, photo-crosslinking the AA-MA patches over the incision. The now-sealed lungs were then subjected to breath hold testing at pressures of 15, 20, and 30 cm H2O using a FlexiVent device to assess the effect of patching on restoration of lung mechanics.

Results and Discussion: A novel approach was developed that utilizes spin-coated AA-MA which can be cross-linked in the presence of appropriate photoinitiators by brief exposure to visible light to form a non-toxic, flexible pleural seal that provides tensile strength and durability, ideal for pulmonary applications. In proof of concept testing, use of the patch restored lung volumes and pressures following experimental injury of up to 20 cm H2O pressure (Figure 1).

Conclusions: The use of AA-MA to overcome the limitations of current approaches in treating pleural leaks has not been previously evaluated or utilized in any context. A novel approach was developed to provide an easy-to-apply hydrogel sealant patch which can rapidly repair pleural leaks.