The Impact of Surface Modification in Endotracheal Tubes on the Tracheal Damage

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WeARE Research Area

The use of endotracheal tubes, or ETTs with large diameters, puts adults at risk for long-term breathing, voice, and swallowing complications. This results in acute laryngeal . There are current treatment options to prevent tracheal stenosis, but is limited to minimizing the duration of intubation, or using the smallest ETT possible, therefore limiting the access to proper clinical care. In this study, an electrospun fiber-coated ETT will be developed that will be capable of delivering therapeutics to the local environment.

Motivation or Background

The prolonged use of endotracheal intubation with large diameter ETTs puts adults at the risk of several respiratory complications. This results in acute laryngeal injury and includes tracheal or posterior glottic stenosis. Current treatment options to prevent posterior glottic, subglottic, or tracheal stenosis are limited to minimizing the duration of intubation and utilizing the smallest ETT possible. Therefore, this significantly limits clinical care. In this study, we developed a novel composite coating based on polycaprolactone (PCL) electrospun fibers that are embedded in a 4 arm poly-ethylene glycol acrylate matrix (4APEGA) to transform the ETT from a functional, mechanical device to a dual-purpose device that is capable of delivering therapeutics to the local microenvironment. Furthermore, the composite coating system is capable of controlled delivery of anti-inflammatory steroids.

Objectives

1. Develop a novel composite coating based on electrospun PCL fibers embedded in a 4APEGA to transform the ETT from a functional, mechanical device to a dual-purpose device that is capable of delivering therapeutics locally. 2. The composite coating system (PCL-4APEGA) is capable of controlled delivery of anti-inflammatory steroids demonstrated through the controlled release of dexamethasone over a sustained period.

Methodology

Fabrication: To fabricate dexamethasone loaded PCL electrospun fibers, the PCL pellets were first dissolved in chloroform and ethanol, and dexamethasone. Final solutions were then loaded into a syringe and a syringe pump and was then used to electrospun fibers at various diameters.

Simulation of Potential mucosal damage during intubation: Fresh Porcine trachea was harvested and the inner lining of the trachea, to mimic friction between the coated ETTs and the epithelial mucosa, a mechanoculture MCT6 loading system was programmed to apply cyclic strain of 10% at a frequency of 0.2 Hz in a sinusoidal waveform to mimic physiological breathing in the human lung. MUC5b and MUC5AC proteins were quantified using ELISA. Tissue segments were stained with Alcian Blue and Fast Red Nucleus to visualize the mucus layer.

In-vitro dexamethasone release kinetics: Release of dexamethasone from the PCL fibers was assessed and quantified over a period of 24 days. Samples (n=6 samples per group) were maintained in PBS buffer at 37° C and the released dexamethasone was collected every day and the absorbance of the collected dexamethasone in the PBS buffer was measured using a plate reader.

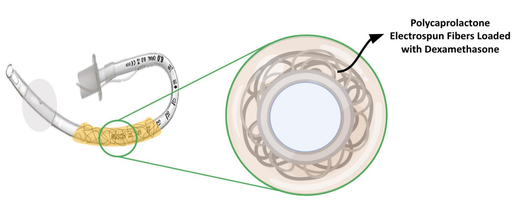

Fig. 1 Lubricating drug-eluting composites for ETTs

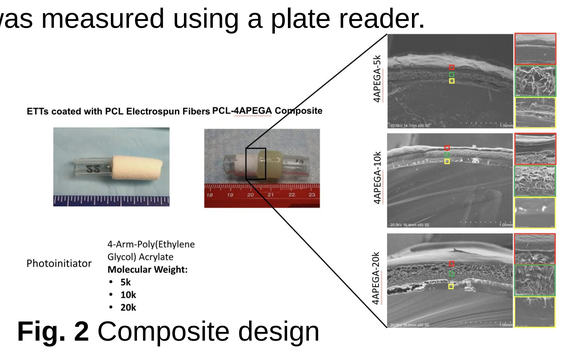

Fig. 2 Composite design

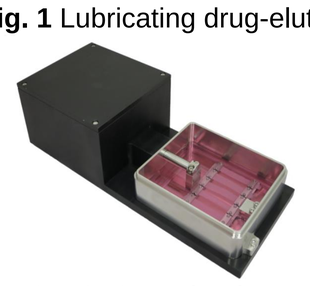

Fig. 3 MCT6 mechanical stimulator

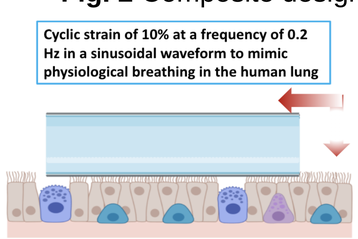

Fig. 4 Tracheal inner lining

Results

The results obtained from this study showed that when there is an increase in the surface lubrication of the ETT's surface and the reduction of the surface stiffness due to the hydrogel-based composite had a direct impact on maintaining epithelial mucus production, while reducing epithelial adhesion, and epithelial layer abrasion.

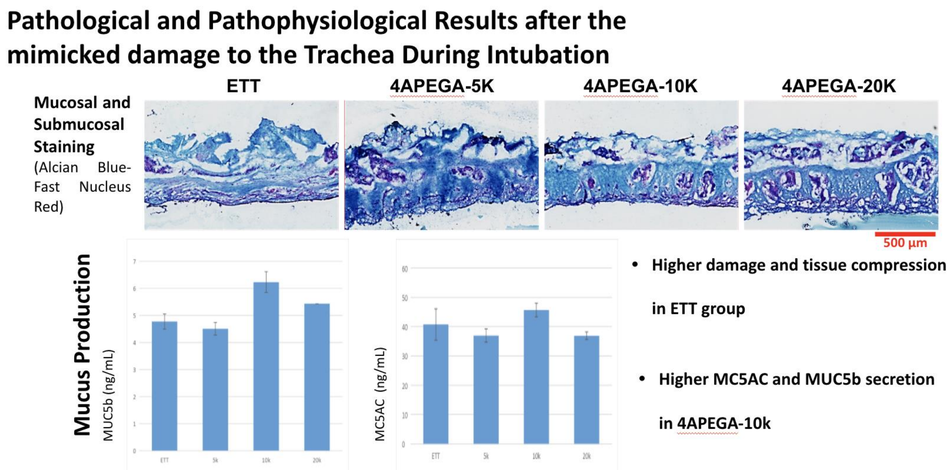

Figure 5. Pathological and Pathophysiological results after the mimicked damage to the Trachea during intubation

The results also showed that when there is an increased percentage of dexamethasone when the fiber's diameter is less, there is more drug released.

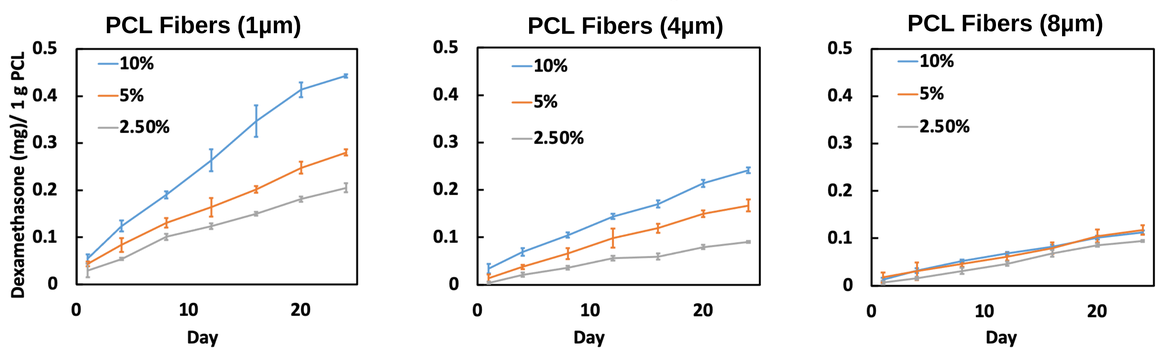

Fig 6. Dexamethasone Release Profile from PL electrospun fibers over 24 days.

Skills and Experience

In this study, I did a lot of imaging of stained epithelial tissue from the ex vivo study and quantification of them, which showed me how these tissues can be affected without the local drug release and with the local drug release. Moreover, conducting a drug release study helped show how effective the dexamethasone will be if placed in a patient.

What I Learned

I learned that tracheal stenosis is a very common problem that patients experience when they have long-term tracheal intubation. With the local release of drugs, I learned that patients would have increased stability and comfort with fewer vocal or breathing issues.

Future Plans

The next steps would be to extend the *ex vivo* experiments and try to do *in vivo* studies on porcine models to study the impacts of the composite and drug release on the prevention of tracheal stenosis.

Acknowledgments

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