Coating Morphology and Corticosteroid Delivery Impact Upper Airway Microbiome in Intubated Injured Swine

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Statement of Purpose: Injuries caused by prolonged intubation are observed in the larynx, including in the vocal fold and subglottic area [1] and are especially worrisome as cases of prolonged intubation rose during the respiratory pandemic. While targeted immunomodulation is necessary to promote effective wound healing, infection is a crucial yet often overlooked factor which is affected by an imbalance in the native microbiome and the overall microbial load [2]. In this study, we aimed to analyze the impact of a novel endotracheal tube coated with dexamethasone loaded polycaprolactone electrospun fibers in swine models of upper airway epithelial injury.

Methods: Injured swine models were developed through mechanical abrasion of the mucosal epithelium of the larynx (n=3 per each group and time point). Next, endotracheal tubes with and without dexamethasone loaded Polycaprolactone (PCL) electrospun fibers were placed in the trachea. Animals were sacrificed after 72 hours and 14 days and microbiome samples were collected from the tubes and the epithelium using sterile swabs. Microbiome Sequencing (Illumina MiSeq platform) was conducted following the isolation of bacterial DNA and the 16S rRNA dataset was processed in R. Biofilm formation and surface coating stability on the tubes was evaluated using Scanning Electron Microscopy (SEM) and 3D models of the tubes, mucus, and bio-inclusions were created from Micro Computed tomography (μCT) scans using contrast enhancement to identify inclusions. Statistical analysis was conducted using two-way ANOVA (treatment and side) with Tukey's post hoc test. Figure 1 shows the vocal fold (before and after the injury) and also after the ETT placement.

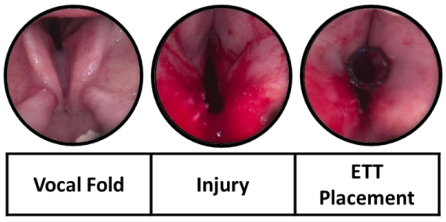
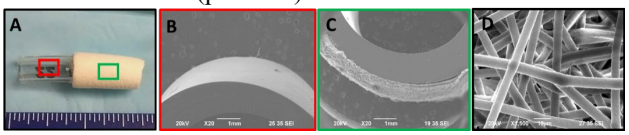


Figure 1. Surgical Procedure of injury development and ETT placement in the swine larynx.

Results: Electrospun coating loaded with dexamethasone was observed to form a homogenous coating on the endotracheal tube. Biofilm formation identified through mucosal inclusions was observed on both tested groups (Figure 2). SEM micrographs of the tested groups show adherent films on both groups; however, the structure of biofilm was different between groups. This distribution was also observed in μCT composites as a thicker layer of biofilm was formed on coated, drug-loaded ETTs.

19 phylum-level taxonomic categories were identified which 7 top classifications are presented in Figure 3. After 72h, the fusobacterial prevalence as a percentage of the microbiome was significantly higher in the swine exposed to dexamethasone compared to the use of the native endotracheal tube (p=0.049).



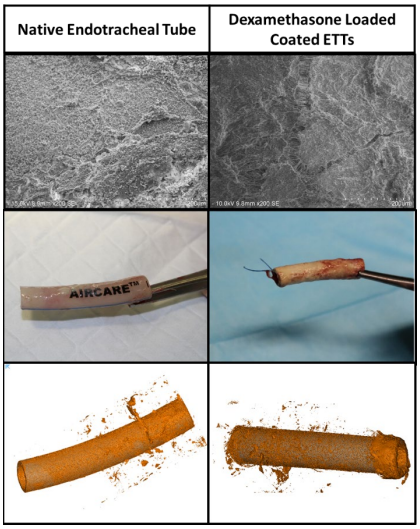


Figure 3. Endotracheal tube and modified ETT after 14 days of placement in swine models. (A) SEM micrographs of the surface of tubes after the study. (B) ETT and modified ETT removed from the larynx. (C) 3D μCT graphs indicating the biofilm formation around the tubes.

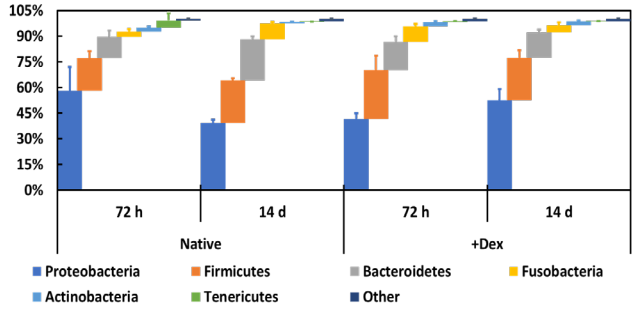


Figure 3. Top Phylum Classification. 7 major categories of bacterial abundance in tested groups after 72 hours and 14 days.

Conclusions: The microbiome of the upper airway is a sensitive environment and biomaterials in contact with this environment, especially when releasing immunomodulatory drugs have a significant impact on the bacterial abundance and makeup over time. Biofilm formation during prolonged intubation was distinctly affected by surface chemistry and morphology of the endotracheal tube and associated endothelial abrasion.

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References: [1] Dorris, Emma R., et al. Eur Respir 30.159 (2021). [2] Shilts, Meghan H., et al. Scientific Reports 10.1 (2020): 1-11.