Decreased Infection of Nanomodified Endotracheal Tubes in a Bench Top Airway Model

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Statement of Purpose: Ventilator associated pneumonia (VAP) is a serious and costly clinical problem. Specifically, receiving mechanical ventilation over a 24 hour time period increases the risk of VAP and is associated with high morbidity, mortality and medical costs. Diagnosis is especially difficult in children because of non-specific clinical signs and diagnostic methods that are not applicable to these patients because of their size. Cost effective endotracheal tubes (ETTs) that are resistant to bacterial infection would be essential tools in the prevention of VAP. The objective of this study was twofold, first to develop strategies to decrease bacterial adhesion on ETT and secondly to develop better methods to assess *in vitro* bacterial adhesion and biofilm formation on ETT.

Methods: Nanomodified tubes were created using a chemical etching process where the tubes were enzymatically degraded by a 0.1% mass solution of one of two bacterial lipases, *Candida cilindracea* (Nano-C) or *Rhisopusarrhisus* (Nano-R). These tubes were then evaluated in two different ways, static studies and a bench top airway model that simulated the dynamic airway conditions found *in vivo*.

Static studies were performed to analyze two bacteria commonly found in VAP, *Pseudomonas aeruginosa* (ATCC #25668) and *Staphylococcus aureus* (ATCC #25923). These two bacterial strains were inoculated into trypticase soy broth TSB media and an artificial saliva media composed of K_2HPO_4 Na_2HPO_4, $KHCO_3$, NaCl, $MgCl_2$, citric acid and $CaCl_2$. Polyvinyl chloride (PVC) was then immersed into the one of the inoculated media and into a control containing media without bacteria. Bacterial growth on the surface of the PVC was assessed at 4, 12, 24, and 72 hour time points for TSB media and 4, 12, 24 and 48 hour time points for saliva. The bacteria found on these samples were quantified using optical density after crystal violet stain. Additionally, this study sought to evaluate the bacterial resistance of these ETTs more comprehensively by testing these tubes in a bench top airway model that simulated mechanical ventilation and continuous contamination which ETTs are exposed to *in vivo*. The airway model designed for this purpose contains two polymethylmethacrylate chambers representing the oropharynx and the lungs connected by a tube representing the trachea. An intricate pumping system was added to provide a continuous flow of an artificial normal oral flora solution to the oropharynx. A sensor system consisting of temperature, humidity, and pressure sensors was also constructed to yield real time data and to control variability. In no less than three separate trials in the airway chamber, the antimicrobial properties of nanomodifed ETTs were evaluated. Sampling from both lung and oropharynx chambers during continuous operation measured bacterial proliferation. Moreover, pieces of the ETT were collected during each trial. Bacterial concentration in both chambers and on the ETT was again characterized using a crystal violet assay.

Results: Results showed that nanomodified PVC ETTs were effective at reducing bacterial colonization in both TSB media and artificial saliva media. Specifically, *Pseudomonas aeruginosa* was significantly reduced in both media and saliva at the 24 hour time point (Figures 1 and 2). *Staphylococcus aureus* was reduced on the nanomodified ETTs at all time points in the TSB media

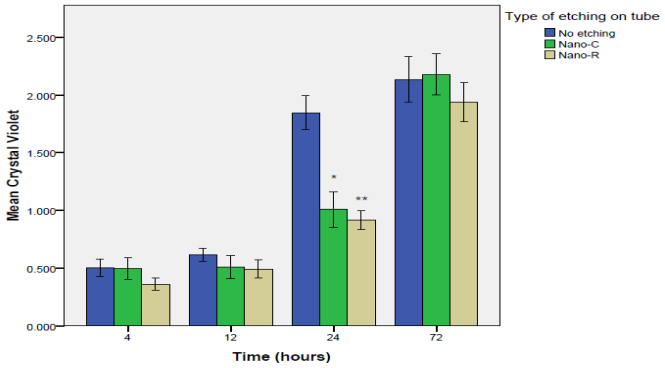

Figure 1: *Pseudomonas aeruginosa* in TSB N=3 Error bars +/- 1 SE, $*P < 0.05$ $**P< 0.05$ compared to controls

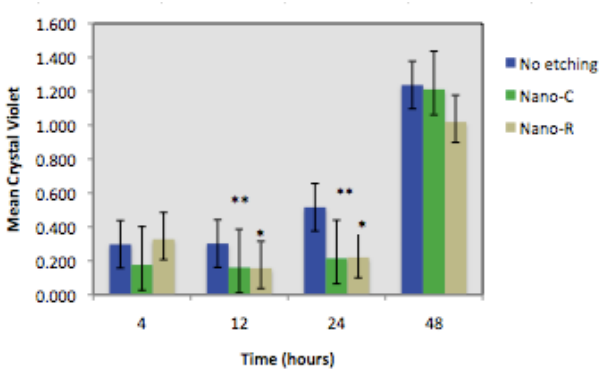

Figure 2: *Pseudomonas aeruginosa* in Saliva N=3 Error bars +/- 1 SE, $*P < 0.05$ $**P< 0.05$ compared to controls

Conclusions: Chemical etching techniques can create nano-rough surface features on PVC that inhibits *P. aeruginosa* growth in TSB at the 24 hour point and *S. aureus* was inhibited at all time points. Additionally, *P. aeruginosa* growth was inhibited in artificial saliva at the 24 hour point. Work will also be presented which examines bacteria function on the nanomodified ETTs using the Plexiglas lung model taking into account effects such as dual gas exchange and long term immersion. These results will also be compared to ETTs taken from patients to provide further evidence to determine if nanomodifiedETTs are a valid solution to VAP.

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