**Background and Objectives**

- Bacterial adhesion and subsequent biofilm formation on urethral devices can lead to device-associated urinary tract infections (UTIs) and other co-morbidities, thereby negatively impacting patient care and health economics.
- Catheter-associated UTIs are one of the most common healthcare infections and affect ~450,000 people in the USA annually. The risk of infection increases 3 – 8 % per day of catheter placement, and all patients develop bacteriuria after one week. Intra-abdominal and urogenital tract infections associated with central venous access in ~49% of cases.
- Various methods of device modification have been investigated to reduce UTI rates, including incorporation of active antimicrobials that induce bacterial kill, as well as passive surface modification aimed at reducing bacterial adhesion to the device surface. However, successful development of these modifications in commercial products and their clinical efficacy have been limited.
- Extrinsic antimicrobials can lose potency over time as the active component becomes desorbed, loses biological activity, or is diffusion hindered due to biofilm formation on the device surface. Extrinsic antibiotics are of additional concern due to the potential for development of antimicrobial resistance.
- The objective of this study was to investigate the ability of a passive surface modification technology utilizing fluorinated surface modifying macromolecules (SMMs), which can be incorporated into a device during the manufacturing process, to reduce bacterial adhesion and biofilm formation on intraluminal surfaces. SMMs are used clinically in intravascular devices to resist platelet adhesion and thrombus formation.\(^5\)

**Methods – Bacterial Adhesion Experiments**

- **Static conditions**: RID samples (6.5 cm long) were incubated for 24 h at 33°C in PBS. Inoculum of human pooled urine (3 ml) inoculated with 10\(^9\) cfu/ml bacteria or fungi. After incubation, samples were rinsed with PBS and sonicated for 30 min to detach adhered bacteria. Semiquantified samples were diluted and spot plated to enumerate bacteria via colony counting.
- **Flow conditions**: A peristaltic pump was used to pump artificial urine inoculated with 10\(^9\) CFU/ml through test tubing at 0.5 ml/min and 37°C for 24 h to seed bacteria on the luminal surface, followed by sterile artificial urine flow for 3 days. Samples (6.5 cm long) were cut from the circuit and processed for colony counting as described above. Samples were also stained using crystal violet to visualize biofilm formation and demulsified, dried, and imaged by SEM.
- Bacterial adhesion from clinical urine was evaluated by inoculating tubing samples for 24 h at 37°C in urine collected from patients with indwelling urethral devices.
- Statistically significant differences in adhesion were assessed using student’s t-test (\(p<0.05\); \(p<0.001\)). Error bars represent standard deviations of the mean.

**Methods – Surface Modification**

- Unmodified Control and SMM-modified polyurethane rod or urethral tubing prototypes were prepared using standard melt extrusion processes at 200°C.
- SMMs were compounded into the polyurethane resin (Carbothane 84A by 3M) at a loading of 2% (by weight) and migrated to the proteoglycan surface during extrusion.
- Surface modification was modified by X-ray photoelectron spectroscopy (XPS – atomic % Fluorine detected on SMM prototypes). Both inner and outer surfaces of tubing were simultaneously modified.

**Results – Flow Experiments**

**Flow System set up for evaluating bacterial adhesion under flow conditions**

- **Control**: No SMM-modified
- **SMM-modified**: SMM-modified tubing

**Results – Static Experiments**

- **Microlbial adhesion to polyurethane rods after 24h Incubation**
  - **In Artificial or Human Pooled Urine (n = 6)**

**Results – Clinical Urine Experiments**

**Overall bacterial adhesion to polyurethane tubing after 24h Incubation in clinical urine specimens compared from patients with urethral stents (n=6)**

**Conclusions and Outlook**

- **SMM modification of polyurethane prototypes resulted in a reduction in bacterial adhesion of up to 2 log (or 99%) when treated with a variety of microbial species (gram positive bacteria, gram-negative bacteria and yeast), suggesting an overall anti-adhesive property of the modified surfaces.**
- **Reductions in bacterial adhesion were confirmed with 3 unimicroscopic and artificial human pooled urine. Furthermore, when incubated in clinical urine specimens containing mixed bacterial populations, SMM-modified samples reduced attachment compared to unmodified controls in 8 out of 9 cases.**
- **Experiments under flow conditions showed potential of the SMM-modified surfaces to resist bacterial adhesion in dynamic environments and over extended time frames, with 5 log lower in cell attachment to modified vs control tubing at both 1 and 3 days post inoculation. Corresponding reductions in biofilm formation were visible through crystal violet staining and SEM imaging.**
- **SMM modification of urethral devices may be an effective strategy to reduce bacterial adhesion and biofilm formation, which has the potential to reduce device-related UTIs and make a measurable positive impact on patient outcomes.**

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References:

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