Anti-microbial coatings for urological applications

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Nosocomial infections, which account for 600 000 cases annually, are the fourth leading cause of mortality in the US. Urinary tract infection (UTI) due to indwelling urethral catheterization remains the most common nosocomial infection and is associated with a significant increase in costs, morbidity and even mortality. Bacterial adhesion to the inner or outer surface of the urethral catheter is the key event in the pathogenesis of catheter associated UTI (CAUTI). In a few hours, adherent bacteria can aggregate, multiply and form a biofilm which, once surrounded by dense glycocalyx, may become resistant to anti-microbial agents and constitute a reservoir of viable micro-organisms. When the biofilm becomes firmly established, bacteria migrate to the bladder ascending the surface of the catheter in a rapidly expanding coherent biofilm. Migration may occur either intraluminally, from the collection bag or the catheter-drainage tube junction, or extraluminally, in the space between the catheter and the urethral mucosa. The development of a biomaterial that inhibits bacterial adherence and does not allow upstream colonization of bacteria would preclude both of these major pathways of bacterial ascent and would therefore have a significant influence in decreasing the rate of CAUTI. While numerous attempts have been made to make urethral catheters more resistant to bacterial adhesion, there remains a need for anti-microbial coatings. The present study was designed to develop an anti-microbial coating for Foley catheters since Foley catheters account for 85% of CAUTI.

The bacterial infection of catheters was studied on two levels; the implant-anatomical level and the surface-biomaterial level. The resulting technology combines a silver-based anti-microbial agent with a lubricious hydrophilic coating. Lubricious hydrophilic coatings have shown to reduce the damage to the mucosal lining caused by the insertion/removal of urological catheters. Mucosal lining damage is recognised as an initial nidus of infection. A lubricious coating also results in greater comfort to the patient and ease of administration by the health care workers. Moreover, lubricious hydrophilic coatings can reduce bacterial adhesion to the surface of hydrophobic materials. Lubricious coatings reduce the adhesion of bacteria due to the surface bound water that contributes to the smooth and slippery surface. Silver is the anti-microbial compound of choice, due to its multi-modal action. Silver ions exhibit biocidal activity toward the broad spectrum of bacteria and fungi found in CAUTI. Other advantages are its low toxicity to mammalian cells and in contrast with antibiotics, silver does not easily provoke microbial resistance.

A dual coating consisting of a primer layer and a topcoat is developed. Both layers are applied to the inner and outer surface of the urethral catheter by a dip coating procedure involving UV radiation curing. The topcoat is PVP based and contains a cross-linker and silver.

Friction tests show that this coating is lubricious, exhibits good wear resistance and is characterised by a dry-out time of about 10 min. Moreover, the coating is uniform and the coating process is reproducible as revealed by optical microscopy. *In vitro* testing of the anti-microbial activity of the coatings is going on. Coated catheters are challenged with laboratory strains of *E. coli* and *S. aureus* as well as with clinical isolates of *P. aeruginosa*, *E. coli*, *E. faecalis* and *C. albicans*. Preliminary results of anti-microbial activity tests under various conditions confirm that the DSM lubricious silver coating reduces the adhesion of bacteria and is bactericidal for several weeks.