Introduction: Catheters are medical devices that are inserted into the body to remove fluid, create an opening, or deliver a drug, and have become an indispensible part in almost all fields of medicine. However, nowadays catheter associated infections are the most serious and costly healthcare-associated infections. Moreover, shunt catheter obstruction most often caused by macrophages (or inflammatory cells) is also very problematic, especially in the treatment of hydrocephalus. Recent studies have suggested a sensitivity of cell and bacteria to nano-scale topographical properties as a potential tool for selectively increasing desirable cell functions while simutaneously decreasing competitive cell functions. It is the hypothesis of this study that Polydimethylsiloxane (PDMS), a commonly used polymeric catheter material, which mimics the nano-patterned topography of natural tissue, will decrease inflammation and infection while remaining non-toxic to mammalian cells. Here we present a simpe and cheap methodology to prepare a nano-pattened PDMS replica by using highly ordered nanotubular anodized titanium (Ti) as the template.

Materials and Methods: 99.5% pure titanium foils (Alfa Aesar) were cut into 2.5cm×2.5cm squares and cleaned with acetone, 70% ethanol, deionized water. The samples were etched for 1min with a solution of 1.5% nitric acid and 1.5% hydrofluoric acid (HF) to remove the thin oxidized layer. The cleaned Ti sample was used as an anode, while a platinum (Pt) mesh served as a cathode. Both were immersed in an electrolyte solution consisting of 1.5% HF. The Ti and Pt samples were connected to a DC power supply. After anodization Ti samples were rinsed with large amounts of deionized water immediately and air dried. Next, the PDMS precursor and liquid stabilizer (Sylgard 184, Dow Chemical Co.) were mixed at 10:1 and were then placed in a vacuum chamber for 1h. The mixture was cast onto the anodized Ti template and then was placed into a vacuum chamber for another 1h. The PDMS sample was cured at 60 °C for 2h followed by cooling and was gently peeled away from the Ti template.

Staphylococcus aureus (ATCC 25923) was used in this study. Sterile samples were treated with the prepared bacterial solution ($\times 10^7$) and cultured for either 24h or 48h in an incubator (37°C, 5% CO_2, humidified). Afterwards, the samples were rinsed with a 10mg/mL PBS solution twice and placed into 15 mL tubes with 4 mL PBS. These tubes were shaken at 3000 rpm for 15 minutes on a vortex mixer to release the bacteria attached on the surface into the solution. Solutions with bacteria were spread on agar plates and bacteria colonies were counted after 18 hours of incubation. Bacterial tests were conducted in triplicate and repeated three times.

Human fibroblasts (ATCC, CCL-110) and macrophages (TIB-186; ATCC) at population numbers less than seven were used for all cell experiments. Cells were seeded onto the substrates at a density of 5000 cells/cm^2 and were allowed to adhere for 4 h in a 37°C, humidified 5% CO_2 atmosphere. The medium was removed from the wells four hours later and the cells were washed twice with PBS. Sterile samples were transferred to fresh 24-well tissue culture plates, and 1 mL of fresh growth medium was added to each well. Next, 150 mL of a dye solution from the cell proliferation assay kit (3-(4, 5- dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium (MTT) (Promega) was added to each well and the plates were incubated for 4h. Afterwards, 1 mL of the Solubilization solution/Stop MixV1R (Promega) was added to each well and the plates were allowed to stand overnight. The contents of the wells were then mixed to obtain a uniformly colored solution, and then transferred to 96-well plates (200 mL per well). The absorbance at 570 nm was recorded using a microplate reader (Molecular Devices, SpectraMax® M3). The test was performed in triplicate and repeated three times.

Results and Discussion: As expected, the nano-sized tubes were distributed uniformly on the titanium surface after anodization. Moreover, nano-patterned structures were fabricated successfully on the surface of PDMS by using anodized Ti as the template. The contact angles for distilled water over plain and nanostructured PDMS surface were about 100° and 76°, respectively. These values highlighted that upon nanostructuring the PDMS surface became slightly more hydrophilic. It was found that nano-patterned PDMS templates increased fibroblast adhesion compared with plain PDMS and, thus, were non-toxic to fibroblasts. Results also showed that nano-patterned PDMS inhibited *S.aureus* growth by 70.5% and 79.2% after 24h and 48h, respectively (Fig. 1).

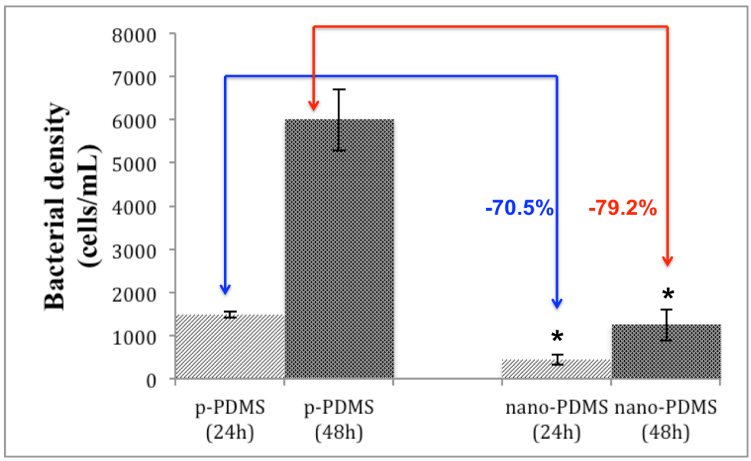


Figure 1. *S. aureus* growth on the surface of nano-patterned PDMS (nano-PDMS) and plain PDMS (p-PDMS).
Data represents mean ± SD, n=3. *p<0.05 compared with p-PDMS

Conclusions: Nano-patterned structures were successfully fabricated on the surface of PDMS through an anodized titanium template method. The direct consequence of this modification was that the nanostructured surface became slightly more hydrophilic. This increase in the hydrophilicity could in part be responsible for the little increase of the fibroblast adhesion on the nano-patterned PDMS. Further more, the nano topography on PDMS could inhibit *S.aureus* growth and also demonstrated promise to inhibit inflammatory cells potentially, and thus should strongly be considered for reducing catheter associated inflammation and infection.

Acknowledgements: The author would like to thank the Webster Nanomedicine Lab and the Department of Chemical Engineering, Northeastern University for help and funding.