Evaluation of Next-Generation Silicon Nanopore Membranes Optimized for Diffusive Clearance

Steven Kim[1,2], Charlie Blaha[2], Zohora Iqbal[2], Clarence Chow[2], Rishi Kant[2], Ben Chui[3], Ken Goldman[4], Jaehyun Park[2], Eun Jung Kim[2] William Fissell[5], Shuvo Roy[2]
[1] Nephrology, UCSF
[2]Bioengineering, UCSF
[3]Ben Chui Consulting
[4]H-Cubed
[5]Nephrology, Vanderbilt University

Background:

Silicon nanopore membranes (HF-SNM) designed for hemofiltration have demonstrated remarkable permeability and selectivity. However, diffusive clearance was hindered by their thickness. Here we report hemodialysis-SNM (HD-SNM) with enhanced diffusive clearance.

Methods:

A new MEMS (microelectromechanical systems) fabrication protocol utilizing nested etch-back techniques was used to decrease the effective SNM thickness (HD-SNM 100um vs. HF-SNM 400 um). Diffusive clearances of polyethylene glycol coated HD-SNM and HF-SNM with sub-10 nm pore sizes were tested in a parallel plate flow cell. PBS with Cr 10 mg/dL, BUN 90 mg/dL, and albumin 3 g/dL was recirculated (45ml), while dialysate (160 mEq NaCl) was recirculated in a counter-current fashion. At $Q_d=Q_b=10$ ml/min and zero transmembrane pressure (TMP) clearance was independent of flow rate. Solute clearance (K) was calculated by fitting concentrations measured at 0, 2, 4 hrs (n=3) to an exponential decay function: $C(t)=C_i e^{-Kt/V}$. C(t): conc at time t ,C_i: initial conc, V: volume. Filtration was tested in water and fetal bovine serum at various TMP (1, 2, 4psi) using cross flow velocities at 0.1, 0.5 and 3ml/min. Platelet adhesion and activation were evaluated by immunohistochemistry (IHC) and scanning electron microscopy (SEM) after flowing human blood for 2 hrs at 2ml/min.

Results:

HD-SNM had a ~2.5 fold improvement in K, consistent with mathematical models. Creatinine, BUN and phosphorus clearances were 232.5±17.2, 314.6±15.6, 191.4±6.3ml/min/m^2(HD-SNM) and 85.5±10.6, 135.3±22.9, 75.5±12.8ml/min/m^2(HF-SNM), respectively. HD-SNM maintained mechanical integrity at over 200mmHg. The HD-SNM also showed comparable filtration rates (71.5 ± 21.3ml/hr/mmHg/m^2) and selectivity to HF-SNM. IHC for CD62 and SEM images showed similar levels of platelet activation and adhesion.

Conclusion:

These preliminary studies demonstrate significant improvement in diffusive clearance with the HD-SNM while still maintaining mechanical robustness, selectivity, permeability and hemocompatibility.