In vitro and in vivo Hemocompatibility Assessment of Thin Film Sulfobetaine and Carboxybetaine Zwitterionic Coatings

Z. Iqbal[1], S. Kim[2], W. Moses[3], E. J. Kim[1], J. Park[1], W. H. Fissell[4], S. Roy[1]
[1]*Department of Bioengineering and Therapeutic Sciences, UCSF*
[2]*Department of Nephrology, UCSF*
[3]*Department of Surgery, UCSF*
[4]*Division of Nephrology and Hypertension, Vanderbilt University*

Background:

Silicon nanopore membranes (SNM) for use in renal replacement, islet therapy, and membrane oxygenation applications require blood contacting surfaces that are non-activating and non-fouling. Polyethylene glycol (PEG) is widely used as a surface coating to improve hemocompatibility, but its degradation characteristics over time limit performance. Zwitterionic polymers such as poly(sulfobateine methacrylate) (pSBMA) and poly(carboxybetaine methacrylate) (pCBMA) have shown promise for long-term reduction of protein and cell adhesion. This study examines the performance of sub-5nm thickness pSBMA and pCBMA coatings on silicon surfaces.

Methods:

Atom transfer radical polymerization was used to graft pSBMA and pCBMA on silicon substrates. Surface modification was verified using contact angle (n = 6) and x-ray photoelectron spectroscopy (XPS) (n = 3). Coating thickness (n = 6) was measured via ellipsometry. Protein adsorption was measured by incubating surfaces (n = 2) in 1 mg/ml fibrinogen and quantifying adsorption using enzyme-linked immunosorbent assay. Cell adhesion was evaluated by exposing surfaces to blood for 6 hours in an extracorporeal porcine circuit. Scanning electron microscopy (SEM) and immunohistochemistry (IHC) was then conducted on the substrates to examine adhesion of cells.

Results:

The XPS, contact angle and coating thickness data is shown in Table 1 and indicate that the coating process for pSBMA and pCBMA was successful. Fibrinogen adsorption decreased to 50.4% with PEG and 13.5% with pSBMA, while there was no significant change with pCBMA compared to uncoated silicon substrates. SEM and IHC results following blood exposure demonstrate that pSBMA performance is comparable to PEG. Therefore, modification with pSBMA may be a viable option for application on SNM. In contrast, pCBMA underperformed in both in vitro and extracorporeal studies compared to pSBMA, which may be due to a lower degree of polymerization. Further studies optimizing polymerization conditions for pCBMA need to be performed.

Table 1: Surface modification characterization

		No Coating	PEG-Silicon	pSBMA-Silicon	pCBMA-Silicon
Contact Angle (H_2O)		52.8 ± 2.6°	43.8 ± 1.0°	8.5 ± 2.4°	39.3 ± 5.5°
Thickness (nm)		--	0.8 ± 0.2	3.46 ± 0.64	1.7 ± 0.11
Elemental Composition (%)	Si, 2p	56.8 ± 0.8	52.1 ± 3.1	20.6 ± .4	31.5 ± 1.8
	O, 1s	28.5 ± 1.8	32.2 ± 0.4	27.6 ± 0.5	30.0 ± 0.4
	C, 1s	14.0 ± 2.2	15.6 ± 2.8	44.9 ± 0.6	35.6 ± 1.9
	N, 1s	0.4 ± 0.1	0.2 ± 0.1	3.9 ± 0.1	2.5 ± 0.1
	Br, 3d			0.2 ± 0.1	0.5 ± 0.1
	S, 2p			2.8 ± 0.1	