Increased Initiator Density using Plasma Polymerized Bromoesters for Grafting Zwitterionic Polymer Brushes

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Statement of Purpose: Surface modifications using zwitterionic polymers such as polysulfobetaine methacrylate (*pSBMA*) are frequently employed to enhance the biocompatibility of biomedical implants. A common technique is ARGET-ATRP, which involves the use of halide initiators. The immobilization of these initiators on substrates requires organic solvents, restricting applicability to compatible materials. For example, polyurethane swells when soaked in methylene chloride and shrinks upon solvent removal, substantially compromising mechanical properties. To this end, past work introduced a solvent-free method using radio frequency glow discharge (*RFGD*) plasma polymerized bromoesters as initiators for surface initiated polymerization.[1] In this work, we demonstrate the ability of this technique to yield higher initiator density relative to solvent-based methods, while maintaining the mechanical integrity of bulk material. Increased initiator density is associated with higher polymer brush density, which further improves non-fouling and lubrication properties. To illustrate this, the grafting of pSBMA brushes is studied on reinforced polyurethane (*RPU-70*) using two immobilization techniques–a solvent-free approach using methyl-3-bromopropionate (*M3BP*), and a solvent-based initiator, α-Bromoisobutyryl bromide (*BIBB*). These approaches were compared by evaluating surface composition, tensile properties, protein adsorption and lubricity of the modified surfaces.

Methods: RPU-70 discs (Carbon Inc., Redwood City, CA) were first argon-etched in a RFGD plasma chamber, followed by deposition of a methane plasma layer for adhesion. The discs were then coated with pHEMA (*solvent-based*) or M3BP (*solvent-free*) at set parameters, followed by quenching and washing to remove unreacted monomers. For solvent-based approach, the substrates were then soaked in hexane with BIBB and stored at 4°C for 24 h, after which the reaction was terminated and samples washed with hexane and dried under vacuum. The same ARGET-ATRP protocol was then used for both sets of samples, in which a predetermined amount of SBMA and L-ascorbic acid were dissolved in DI-water, and Cu(II)Br and 2,2'-Bipyridine were dissolved in methanol. The two solutions were then mixed and briefly degassed with nitrogen while stirring. This was followed by adding the reaction mixture to vials containing initiator immobilized substrates. The reaction mixture was allowed to polymerize for a set time, followed by washing. The surface composition of samples was studied using X-ray photoelectron spectroscopy (*XPS*). Protein adsorption was studied using Iodine-125 radiolabeled albumin, while friction coefficients were measured using a nanoindenter.

Results: Initiator (*solvent-based: RPU-O-Br and solvent-free: RPU-Br*) and pSBMA brush (*solvent-based: RPU-g-pSBMA and solvent-free: RPU-pSBMA*) densities were studied using XPS survey scans (Table 1). Substantially higher bromine density (29.4%) was observed on the RPU-Br surfaces relative to RPU-O-Br surfaces (3.2%), indicating potential for higher brush density in the subsequent pSBMA grafting step.

Table 1. Surface composition from XPS survey scans.

Sample	Elemental Composition (%)				
	C	O	Br	N	S
RPU	80	17	0	3	0
RPU-O-Br	69.1	27.1	**3.2**	0.6	0
RPU-Br	59.6	11.0	**29.4**	0	0
RPU-g-pSBMA	66.3	24	**0.2**	**5.3**	**4.4**
RPU-pSBMA	61.6	26.6	**0**	**5.28**	**6.56**

A comparison of the tensile properties is shown in Table 2. RPU-pSBMA samples exhibit significantly higher young's modulus (1.73 GPa *vs.* 0.38 GPa) and yield stress (39.98 MPa *vs.* 7.40 MPa) relative to RPU-g-pSBMA. This confirms the assertion that the solvent free approach retains the mechanical integrity of the material.

Table 2. Comparison of tensile properties

Sample	Young's Modulus (GPa)		Yield Stress (MPa)	
	RPU-g-pSBMA	RPU-pSBMA	RPU-g-pSBMA	RPU-pSBMA
Pristine	1.90	1.70	45.00	40.00
Coated and Sterilized (EtO)	**0.38**	**1.73**	**7.40**	**39.98**
Coated	**0.66**	**1.59**	**8.50**	**39.55**
Sterilized (EtO)	0.65	1.62	14.55	39.09

From protein adsorption studies, RPU-pSBMA surfaces exhibited an 87% reduction relative to pristine RPU (14-17 ng/cm^2 *vs.* 130 ng/cm^2). This value, while marginally smaller than the RPU-g-pSBMA case (10 ng/cm^2), is still comparable and indicates potential for further reduction upon protocol optimization, a key focus of ongoing work. The strong hydration effects that result in these superior non-fouling properties, also manifest in friction coefficient measurements. RPU-pSBMA surfaces showed a friction coefficient of 0.86 *vs.* 1.15 for RPU-g-pSBMA, indicating higher surface lubricity arising from higher overall brush density and reduced surface roughness.

Conclusions: A solvent-free initiator immobilization technique has been described that yields increased initiator density over conventional approaches. This method has been used for successful grafting of robust pSBMA brushes on an industrially relevant substrate. The method has also been demonstrated to preserve the mechanical properties of the substrate material, a significant advantage over solvent-based alternatives, making it a viable candidate for biomedical applications. Ongoing work is focused on protocol optimization and demonstrating this approach for titanium and glass substrates.

References: **1.** Mecwan, M. M., et al; *Biointerphases* **2019**, *14* (4), 041006.