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Characteristics of Microphase Segmented Polyurethane Biomaterials During Hydration: Phase Restructuring, Protein Adsorption and Platelet Adhesion

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Statement of Purpose: It is well accepted that the microphase separated structure of polyurethane biomaterials contribute to the improved success of the polymers in blood-contacting medical device application. Recent studies have suggested that the structure at polymer surface in hydration is quite different than that in ambient conditions, affecting the interactions with the elements of biological environment[1,2]. Here we study the characteristics of a series of PU biomaterials with different soft segments chemistries and different percentages of hard segments under hydrated conditions. AFM was used to characterize the microphase structure and mechanical properties of PUs during hydration, and to identify fibrinogen (Fg) adsorption so that relationships between biomaterial surface chemistry, Fg adsorption, and platelet adhesion could be addressed.

Methods: PUs with different soft segment chemistries were used: poly(tetramethyleneoxide) (PTMO), poly carbonate (PC) and poly(dimethylsiloxane) (PDMS). The PDMS-based PUs have hard segment contents from 30% to 52%. The microphase structure of polymers was observed by AFM tapping mode in air and under PBS buffer. Force imaging was used to collect 32 × 32 arrays of force curves at a scan size of 500×500 nm and to produce modulus maps of surfaces at different indentation depths using a Hertzian model. The amounts and activity of fibrinogen adsorbed on surfaces were detected through antibody recognition measurements using AFM probes modified either with a polyclonal anti-fibrinogen antibody or a monoclonal antibody recognizing γ392-411. Platelet adhesion was measured optically from bovine platelet rich plasma.

Results / Discussion:

Microphase restructuring of polyurethane in aqueous environments. The separated microphase structures of all polymers were observed from phase images in air and PBS buffer. A significant microphase structure change was observed on the PU surfaces after hydration in PBS. Modulus maps including a z-depth profile were used to illustrate the 3-dimensional arrangement of micromechanical properties of polymer, showing the hard domains to be enriched on the surface due to affinity of hydrophilic hard domains for water (Fig. 1).

Platelet adhesion. Platelet adhesion was found to increase with hard segment content over the range of 35% to 52% HS contnet for PDMS-based polymers. Fewer platelets were observed on PC-PU40 and PTMO-PU40 surfaces (Fig. 2a), suggesting the platelet adhesion is related to both hard and soft domain chemistry.

Protein adsorption on PU surfaces. Fibrinogen (Fg) adsorption on surfaces was recognized by a polyclonal antibody and found to be roughly correlated to platelet adhesion on the PDMS-PUs, however, more Fg was measured on PC-PU and PTMO-PU surfaces despite the fact that fewer platelets were observed (Fig. 2b). The activity of Fg was further identified by mAb γchain (392-411). The trend of activity of Fg is generally consistent with platelet adhesion, and results suggest that the platelet adhesion appears better correlated with availability of the platelet binding site in the Fg γ-chain dodecapeptide than amount of Fg alone. The combination of dynamic hard domain enrichment on PU surfaces, protein adsorption and platelet adhesion as related to hydration time, as summarized in Fig 3.

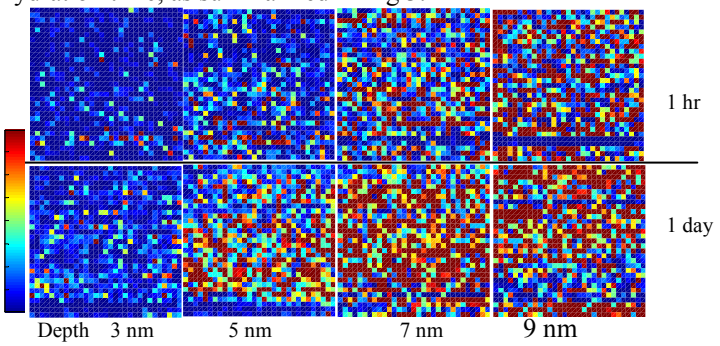

Fig. 1 Modulus maps of PDMS-PU40 at depth of 3, 5, 7, and 9 nm in PBS buffer for 1 hr and 1day (size: 500×500 nm^2).

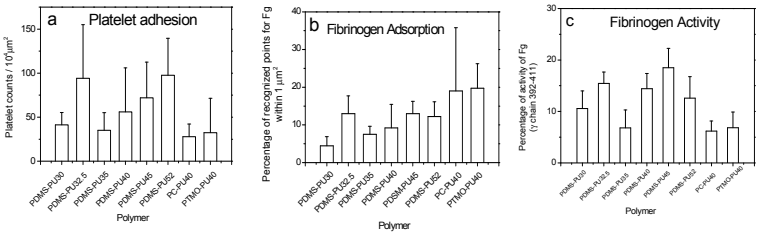

Fig. 2 (a) Platelet adhesion, (b) fibrinogen adsorption and (c) activity of fibrinogen adsorbed on a variety of PU surfaces.

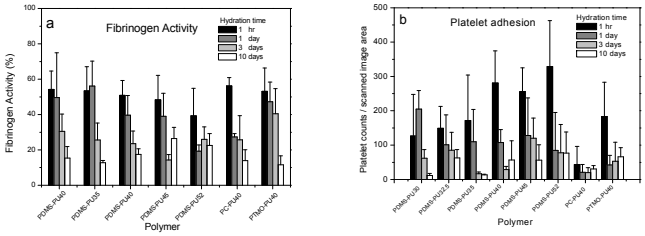

Fig. 3 Dynamic changes in (a) activity of Fg and (b) platelet adhesion were observed on PU surfaces with increasing hydration time. Results suggest that the enrichment of hard domains changes the local surface physical and chemical properties, and influences conformational changes of Fg, resulting in different availabilities of platelet binding site in the Fg γchain dodecapeptide, which is related to platelet adhesion.

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Reference:

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