High-Precision Surface Modification of Three-Dimensional Geometries Using Photodefinable Ultra-Thin Polymer Coatings

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INTRODUCTION

Future biomedical implant devices will use advanced surface engineering technologies to actively modulate tissue integration. Towards this goal, vapor-based polymer coatings have been interesting candidates for the coating of implant devices, because of their advanced processibility and their excellent intrinsic biocompatibility. For instance, a specific vapor-deposited polymer (poly(p-xylylene) or parylene) is already used in FDA approved drug-eluting stents. The commercially available coatings lack however, anchor groups for further modification and therefore do not allow for immobilization of biomolecules or the implementation of protein-resistance.

Functionalized poly(p-xylylenes) can be deposited via chemical vapor deposition (CVD) polymerization to generate ultra thin (20-100nm) films as conformal coatings and, due to the pre-defined chemical functionalities, provide a flexible solution to surface engineering challenges as they decouple surface design from bulk properties. Hence, the technology comprises essentially a one-step coating procedure to generate functionalized surfaces without requiring any kind of post-treatment once the films are deposited. The CVD-based polymer films can be generically applied to a wide variety of substrates and establish a reactive interface that allows for further modification. The simplicity in providing a wide range of functional groups, the excellent adhesion to various substrates, and its applicability to devices with three-dimensional geometries are key advantages when compared to polymers deposited by solvent-based methods. In principle, these polymers are well suited as a platform for biomedical applications.

EXPERIMENTAL

Ultra-thin Polymer Coatings by CVD polymerization. Benzoyl[2.2]paracyclophane was synthesized via a chemical vapor deposition (CVD) polymerizations in three-steps. The starting material was sublimed under vacuum and converted by pyrolysis into reactive species, which polymerize upon condensation (Scheme 1). A constant argon flow of 20 sccm was used as carrier. Sublimation temperatures were kept at 110-130 °C followed by pyrolysis at 800 °C. Subsequently, polymerization occurred on a rotating, cooled sample holder placed inside a stainless steel chamber with a wall temperature of 120 °C. The coating pressure was 0.12 Torr. The exit of the chamber was connected via a cooling trap to a mechanical pump. X-ray photoelectron spectroscopy, (Perkin Elmer/PHI 5400), and FTIR spectroscopy (Nicolet 6700) were used for characterizing the resulting polymers, and the results have been reported elsewhere.

Bio-Inert Modification of Surfaces. After surface modification via CVD polymerization, the coated stents were immersed in an aqueous solution of 4-arm star polyethylene glycol (star-PEO, 10.000 g/mol, 1 weight-%). For patterning, a digital micromirror device (DDM, Texas Instruments) was used as a dynamic mask. The UV radiation of about 365-400 nm wavelength was modulated by the dynamic mask. The corresponding patterns were then transferred onto the stents. Di-water was used to separate excess PEO. For protein immobilization studies, samples were incubated with protein (Alexa Fluor 546-conjugated fibrinogen, Molecular Probes Inc.) solutions for 5 min. After incubation of, phosphate buffered saline (PBS) and Di-water were used to rinse off excess adsorbed proteins. The resulting samples were then examined by fluorescence microscopy (TE 200, Nikon).

RESULTS AND DISCUSSION

Stents were first coated with the photodefinable coating via CVD polymerization followed by the incubation with an aqueous solution of PEO. For this purpose, samples (stents) were immersed in the PEO solution. And the photopatterning reaction was conducted by directing the UV light using DMD system onto the resulting sample surface. After UV exposure, the non-bound PEO was removed and the entire stents was incubated with the protein solution. Figure 1 shows fluorescence micrographs of a stent where the protein absorbed onto the PEO-free area (bright region) establishing a well-defined non-fouling environment (bio-inert) on the stent surfaces. Images are shown in high (a) and low (b) magnification. High definition patterns and precise control of protein adsorption was demonstrated on the complex three-dimensional geometry (stent) compared to the reduced contrast when using a contact mask.

In order to demonstrate the chemical and biological activity (bio-active) of the corresponding binding patterns, we conducted a series of immobilization studies. The microchannels were coated with photodefinable polymers prior to immobilization. PEO-amine-derived biotin ligand was chosen because it undergoes nearly quantitative conversion with ketones, respectively. Moreover, the interactions between biotin and streptavidin result in tight confinement of streptavidin on the biotin-modified surface, which can be exploited for visualization of ligand binding. To examine the immobilization of biotin...
ligands within the microchannels, we allowed rhodamine (TRITC) conjugated streptavidin to bind to the biotin-modified surfaces. After thorough rinsing with buffer, the surfaces were visualized by fluorescence microscopy. Figure 2 shows microchannels that were coated with photodefinable polymer and then subjected to the biotin/strepavidin protocol. Homogenous pattern distribution throughout the entire microchannel was observed, indicating that binding groups were available and well defined. Different channel geometries were shown in (a) with meandering channels and in (b) with channel network. The ability to deposit polymer coating with well defined reactive binding sides throughout the microchannel will be a critical feature when using reactive coatings to tailor surface properties of microchannels towards the needs of specific biological applications.

![Figure 2.](image_url)

**Figure 2.** Fluorescence micrographs of PDMS microchannels coated with photodefinable CVD polymer, and the resulting modification of bio-active surface in well defined areas. (a) Meandering channels. (b) Channel network. Patterns are 50µm x 50µm squares.

**CONCLUSIONS**

We have demonstrated the feasibility of using these reactive polymers to control non-specific protein adsorption on stent surfaces generating well defined bio-inert environments on complex 3-D geometries. Similarly, well defined bio-active patterns were created homogeneously on PDMS microchannels. This generic surface engineering protocol is widely applicable to a wide range of materials and even hybrid structures, and we will be able to (1) prepare well defined biofunctional patterns in micron scale range; (2) selectively initiate the binding sides on-demand; (3) precisely modify the surface properties on almost any kind of substrates (2-D, 3-D) without rendering the spatial resolution. With the precise control and the programmable flexibility of this protocol, we foresee the technology to be useful for cell-based screening and diagnostic bioassays.

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