



Bio-inspired enhancement of friction and adhesion at the polydimethylsiloxane-intestine interface and biocompatibility characterization



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ABSTRACT

An active navigation of self-propelled miniaturized robot along the intestinal tract without injuring the soft tissue remains a challenge as yet. Particularly in this case an effective control of the interfacial friction and adhesion between the material used and the soft tissue is crucial. In the present study, we investigated the frictional and adhesive properties between polydimethylsiloxane (PDMS, microscopically patterned with micro-pillar arrays and non-patterned with a flat surface) and rabbit small intestinal tract using a universal material tester. The friction coefficient-time plot and adhesive force-time plot were recorded during the friction test (sliding speed: 0.25 mm/s; normal loading: 0.4 N) and adhesion test (preloading: 0.5 N; hoisting speed: 2.5×10^{-3} mm/s). In addition, biocompatibility of the PDMS samples was characterized in terms of cell morphology (scanning electron microscope) and cell cytotoxicity (alarmarBlue assay) using human vascular endothelial cells (HUVECs). The results demonstrated that the interfacial friction (0.27 vs 0.19) and adhesion (34.9 mN vs 26.7 mN) were greatly increased using microscopically patterned PDMS, in comparison with non-patterned PDMS. HUVECs adhered to and proliferated on non-patterned/microscopically patterned PDMS very well, with a relative cell viability of about 90% following seeding at 1 d, 3 d, and 5 d. The favorable enhancement of the frictional and adhesive properties, along with the excellent biocompatibility of the microscopically patterned PDMS, makes it a propitious choice for clinical application of self-propelled miniaturized robots.

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1. Introduction

The development of self-propelled miniaturized robots presents a promising avenue towards the diagnosis and treatment of intestinal tract disorders by active locomotion, and offers many advantages over wireless capsule endoscopy [1]. Effective frictional and adhesive control between surfaces is crucial for the application of robotic devices in a biological system. In order to improve a robot's traction over the slippery intestinal surface and facilitate movement, hooks or spikes are commonly used as an actuator. However, the intestinal tract is prone to be injured by these sharp appendages as a result of direct contact [2]. Adhesion is another important factor often required for devices to stop at suspicious sites to perform prolonged diagnosis or therapeutic treatment, for example, biopsy and drug delivery [3].

In the past few years, there has been an increased focus on strengthening the interaction between robots and the intestinal tract through various methods [4,5]. Among these adhesive film and micro-patterns represent promising strategies in this field [6,7]. Although an improvement in frictional and adhesive forces has been reported in previous studies [8,9], it is indicated that the experiments are performed utilizing custom-built tribo-tester. As such no sufficient attention has been paid to accurately simulating the physiological conditions of the intestine. In addition, most of these studies did not examine the biocompatibility of the micro-patterns, which is deemed as an essential evaluation prior to clinical application [10]. A deeper understanding of the friction and adhesion mechanism between the micro-patterns and the intestinal tract as well as the interfacial cell response is imperative to optimization of a self-propelled miniaturized robot. Consequently, in the present study we investigated the frictional and adhesive properties at the micro-patterned polydimethylsiloxane (PDMS, with the presence of micro-pillar arrays)-intestinal tract interface; this was done together with cell morphology and cell cytotoxicity studies, using the non-patterned PDMS as a comparison.

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2. Materials and methods

2.1. Micro-pillar array fabrication

PDMS (Dow Corning Corp., MI, USA), a flexible polymer, was used to fabricate micro-pillar arrays by soft lithography. Firstly, a negative photoresist SU-8 mould with micro-holes was prepared consecutively by silicon spin-coating (600 r/min, 30 s; 2400 r/min, 60 s), ultraviolet exposure (1440 s), development (300 s), and then drying with compressed air. PDMS was then spin-coated on the SU-8 mould (100 r/min, 30 s; 200 r/min, 60 s), and peeled off to generate the micro-pillar arrays using trimethylchlorosilane as the demoulding agent.

2.2. Friction & adhesion tests and characterization

The friction and adhesion tests were performed in order to verify the micro-patterned PDMS samples could enhance the frictional and adhesive properties at the PDMS-intestinal tract interface, compared with the non-patterned PDMS samples.

2.2.1. Friction & adhesion tests

Non-patterned and micro-patterned PDMS disk samples with a flat surface or micro-pillar arrays (diameter: 100 μm) were manufactured to the following size: diameter: 6 mm; thickness: 1.5 mm. Rabbit small intestinal tract (with the presence of mucus layer) was obtained from Center of Biomedical Analysis, Tsinghua University, and preserved in 0.9% saline solution before use.

The PDMS sample and intestinal tract were used as the upper and the lower specimens respectively in the friction and adhesion tests, which were performed using a universal material tester (UMT-III, Center for Tribology Inc., CA, USA). A schematic graph depicting the friction and adhesion tests is shown in Fig. 1. The PDMS sample was attached firmly to a stainless steel holder, and the intestinal tract was fixated on a reciprocating linear stage, held at a temperature of $37 \pm 1^\circ\text{C}$. The sliding speed and normal loading in the friction test were 0.25 mm/s and 0.4 N, respectively. In the adhesion test, the PDMS sample was placed into contact with the intestinal tract under a preloading of 0.5 N (dwell time: 30 s), and then detached from the intestinal tract at a speed of 2.5×10^{-3} mm/s. The friction coefficient-time plot and adhesion force-time plot were recorded during the tests, and all the tests were repeated at least three times.

2.2.2. Material characterization

The PDMS samples were sputter-coated with a gold-palladium layer and examined using a Quanta 200 FEG scanning electron microscope (SEM, FEI, Eindhoven, Netherlands) before and after testing. Surface wettability of the PDMS samples was evaluated using an OCA-20 contact angle system (Dataphysics Instruments, Filderstadt, Germany) based on sessile drop method. The average water contact angle was

calculated from eight random measurements on the surface. Additionally, the rheological property of the small intestinal tract mucus was evaluated using a MCR 301 rheometer (Anton Paar, Austria) with a cone-and-plate geometry (diameter: 49.955 mm; cone angle: 0.988°).

2.3. Cell morphology and cell cytotoxicity

The cell morphology and cell cytotoxicity experiments were performed in order to verify the micro-patterned PDMS samples could potentially be applied in vivo, with an ample cell biocompatibility.

2.3.1. Cell culture

Unless otherwise noted, the reagents used in the following experiments were purchased from Sigma-Aldrich, St Louis, USA. Human vascular endothelial cells (HUVECs) were cultured in DMEM/F12 medium with 10% fetal bovine serum (FBS) and 1% penicillin/streptomycin in an atmosphere of 5% CO_2 at 37°C . HUVECs were subcultured using 0.25% trypsin-1 mM EDTA at 80% confluency, and the cells at passage 3 to 6 were used in the following tests.

2.3.2. Cell morphology

Non-patterned and microscopically patterned PDMS samples were prepared with a size fitting the well of 24-well culture plate, and then sterilized using an ultraviolet lamp for at least 6 h. Subsequently, HUVECs were seeded on the PDMS samples with a density of 1×10^4 /well, and the culture plate were transferred to a CO_2 incubator (Forma 311, Thermo scientific, Marietta, USA) to allow for cultivation of HUVECs.

After culturing for 1 d, 3 d, and 5 d, the PDMS samples were taken out and rinsed thoroughly with phosphate-buffered saline solution (PBS) to remove the unattached cells. HUVECs were fixed in 2.5% glutaraldehyde at 4°C for at least 6 h, and then dehydrated progressively with a graded series of ethanol (30%, 50%, 70%, 80%, 90%, 95%, and 100%), each for 5 min. The PDMS samples were vacuum dried or freeze dried for at least one day before use, and then sputter-coated with a gold-palladium layer for cell morphology observation using the SEM.

2.3.3. Cell cytotoxicity

The seeding of HUVECs on the non-patterned and microscopically patterned PDMS samples was the same as above, and the wells without PDMS samples (namely tissue culture plate, TCP) were set as negative control. After culturing for 1 d, 3 d, and 5 d, an alamarBlue assay (Invitrogen, Carlsbad, USA) was performed based on previous work [11,12]. A microplate reader (Molecular Devices, Sunnyvale, USA) was used to measure the absorbance of the alamarBlue solution at 570 nm (excitation) and 600 nm (emission). At each time point, at least three duplicate PDMS samples or negative control were included. The relative cell viability for the non-patterned and microscopically patterned PDMS samples was normalized to TCP, with the results shown as mean value \pm standard deviation.

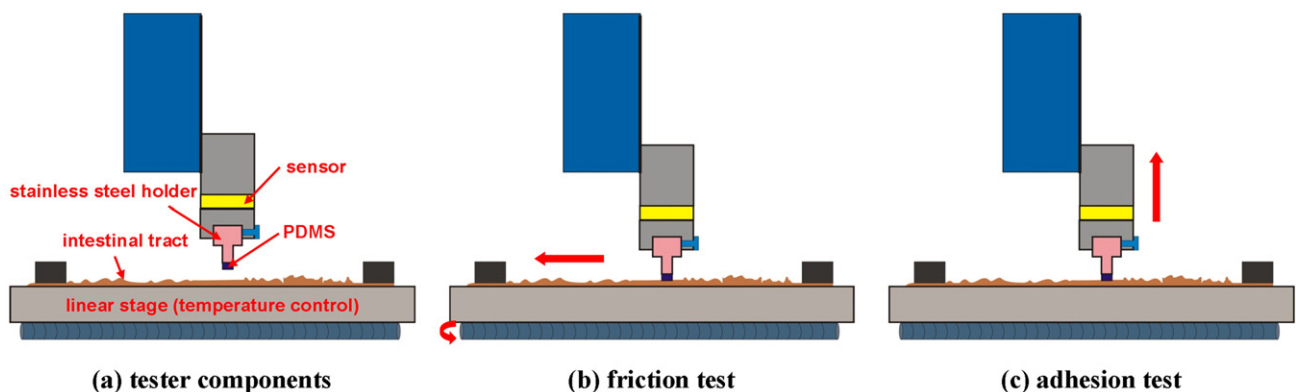


Fig. 1. The schematic graph depicting friction and adhesion experimental setup between PDMS and small intestinal tract: (a) test components; (b) friction test; (c) adhesion test.

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