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# Generation of functionalized polymer nanolayer on implant surface via initiated chemical vapor deposition (iCVD)

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ABSTRACT

Initiated chemical vapor deposition (iCVD) was utilized to generate a 200 nm thick, uniform, functionalized polymer nanolayer comprised of glycidyl methacrylate (GMA) on the surface of titanium implants as a means to improve cellular attachment. Dot-patterned GMA-coated specimens were prepared as well as fully coated specimens. *In vitro* cellular responses, including cell morphology, protein adsorption, cell proliferation assays, alkaline phosphate activity (ALP) assays, and calcium deposition assays were studied using adipose derived stem cells. The mechanical stability of the thin film was investigated by XPS and FE-SEM analysis of the GMA-coated implant after implantation to an extracted bone from a pig. The GMA-coated specimens displayed increased protein adsorption, higher alkaline phosphatase activities, and higher calcium deposition as compared to control sample with no cytotoxicity. Additionally, no defect was observed in the test of mechanical stability. Notably, dot-patterned GMA-coated samples displayed higher alkaline phosphatase activities than others. Functionalized polymer nanolayer deposition via iCVD is a flexible and robust technique capable of mass production of biocompatible layers. These properties make this technique very suitable for implant applications in a variety of ways.



## 1. Introduction

Titanium has been widely used as a biomaterial, especially in dental and orthopedic implants, due to its mechanical properties, resistance to corrosion, and excellent biocompatibility [1,2]. The surface properties of these implants, such as roughness, wettability, and surface charge, play a critical role in cell adhesion and ultimately osseointegration. This is crucial for the ultimate success of an implant. For increasing surface roughness, various methods such as grit-blasting, acid-etching, and anodization have been investigated [3,4]. Furthermore, various surface treatments for introducing hydrophilicity, antibacterial activity, and osteoconductivity have been studied [5–7].

Initiated chemical vapor deposition (iCVD), as reported by Gleason [8,9], is a facile method to deposit a variety of functional polymer nanolayers even on rough surfaces such as fabrics and surfaces with 7 μm trenches [7,10]. iCVD is a solvent-less and low-temperature radical polymerization technique, which can be utilized to make uniform nanolayers with high conformation [11], to synthesize copolymers [12], and to make stable and rigid cross-linked polymers by adding crosslinkers [13].

In this study, anodized titanium implants were deposited with a functional polymer nanolayer via iCVD technique. As shown in Fig. 1, this treatment created a three-layered structure, which is composed of a layer of poly(glycidyl methacrylate) (pGMA) on top of an anodized oxide layer with the base layer being Ti metal. To increase surface area and roughness, a rough titanium oxide layer was introduced by anodization with $H_2SO_4$. GMA was polymerized on the anodized Ti surface using *tert*-butyl peroxide (TBPO) as the initiator. This results in the formation of a pGMA nanolayer. GMA, containing an epoxy ring, provides a good binding site and allows for various functionalities to be incorporated through a ring-opening reaction of the glycidyl moiety [14–16]. In anticipation of increasing cell attachment with chemical

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interaction, ~200 nm of pGMA was introduced onto the rough oxide surface. These were then evaluated *in vitro* with adipose derived stem cells (ADSCs). ADSCs are easily accessible and abundant. Also ADSCs are similar to bone marrow stem cells in their differentiation potencies and have been widely applied in the tissue engineering field [17,18].

## 2. Materials and methods

### 2.1. Materials

Titanium disks (diameter: 12 mm, thickness: 1 mm) and fixtures (diameter: 4 mm, length: 10 mm) were supplied by Biotem Co., Ltd. (Busan, Korea). Glycidyl Methacrylate (97%) and tert-butyl peroxide (98%) for iCVD were purchased from Sigma–Aldrich. Bradford assay solution was purchased from Bio-Rad (Hercules, CA, USA). StemPro® Human ADSCs (adipose derived stem cells) and MesenPRO RS™ medium (MPRO medium) were obtained from Invitrogen (Carlsbad, CA, USA). Fetal bovine serum (FBS), penicillin, and streptomycin were purchased from GIBCO (Gran Island, NY). The other chemicals were purchased from Sigma–Aldrich.

### 2.2. Methods

#### 2.2.1. Sample preparation

For the *in vitro* experimentation, three kinds of specimens were prepared (Fig. 1). For a control, a commercially used surface consisting of anodized Ti (**ANOD**) [19] was included. The test samples included fully pGMA coated (**GMA-full**) specimens and dot-patterned pGMA coated (**GMA-dot**) specimens.

#### 2.2.2. Anodization of Ti disk

Ti disks and fixtures were washed 2 times and cleaned in an ultra-sonicator for 15 min using hexane, acetone, ethanol and distilled water sequentially prior to use.

Anodization of the Ti disks and fixtures was performed in 2.0 M $H_2SO_4$ aqueous solution in a glass chamber with a magnetic stirrer in an ice bath. The applied voltage was 150 V for 2 min with a direct current power supply system (EX750H, Takasago Ltd., Japan). Titanium plates were used as both a cathode and an anode. After anodization, Ti samples were washed with water 3 times and then sonicated for 20 min followed by drying at 60 °C [20].

#### 2.2.3. Polymer nanolayer deposition by iCVD

Glycidyl Methacrylate (GMA) and tert-butyl peroxide (TBPO) initiator were purchased and used without further purification. The polymerization took place in a custom-built iCVD reactor described previously [21] (Daeki Hi-Tech Co., Ltd). To deposit the iCVD pGMA films, the GMA monomer was heated to a temperature of 35 °C and vapor was fed into the reactor at a flow rate of 1.9 sccm. TBPO vapors (room temperature) were fed into the reactor via metering valves at a flow rate of 0.8 sccm. For the pure pGMA film, only GMA and TBPO were fed into the reactor concurrently with a reactor pressure of 200 mTorr. The substrate was kept at a temperature of 25 °C to promote monomer adsorption, and the filament temperature was maintained at 200 °C. For a dot-patterned deposition, a dot-patterned stainless steel mask (diameter:

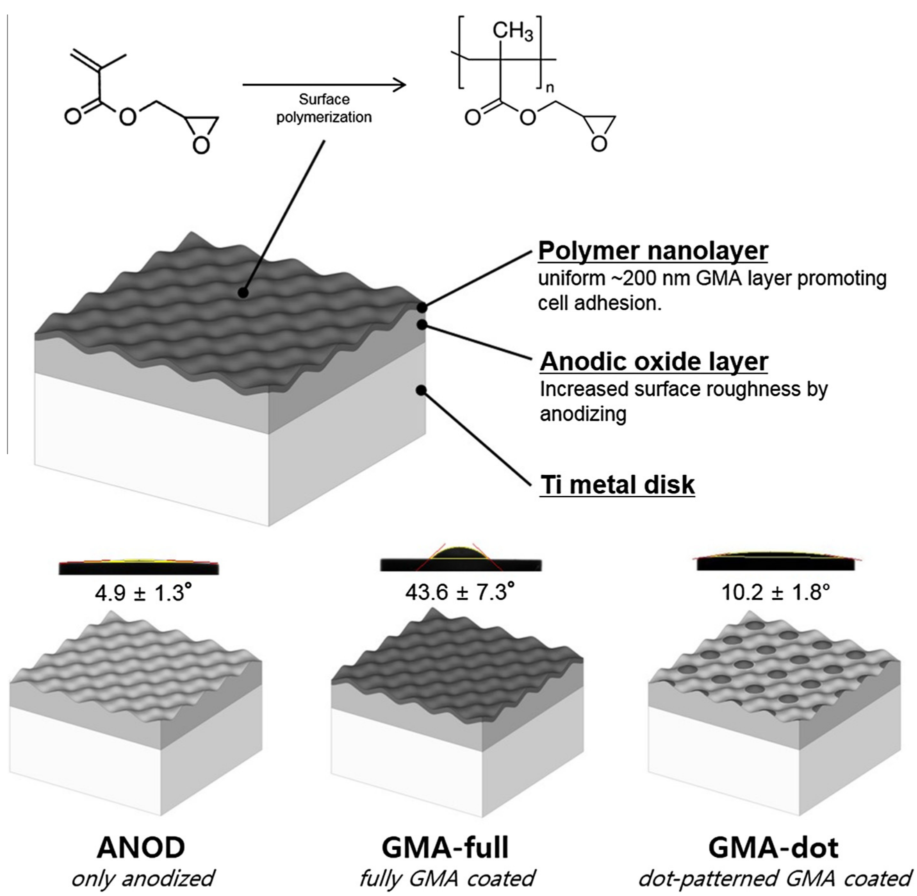


**Fig. 1.** Three-layered structure (upper) composed of a titanium metal base, an anodic oxide layer and a functional polymer nanolayer. Glycidyl methacrylate is polymerized on the surface of the oxide layer. **ANOD** is covered only with an anodized surface, **GMA-full** is coated with GMA fully and **GMA-dot** is coated with dot-patterned GMA over the anodized surface.