Surface modification of Ti with micro/nano multi-scale roughness for the growth factor loaded implant

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Statement of Purpose: Titanium (Ti) has been widely used for implant applications because of its excellent mechanical and biological properties. In particular, various micro- and nano- scale surface modifications such as 'sandblasted with large grits and acid etched' (SLA) treatment on Ti surface have been widely introduced to improve osteointegration of Ti implants. However, further improvement on osteointegration ability and bioactivity are still required for faster recovery of defected areas [1, 2]. In this study, we have applied a selective plasma etching (SPE) process in addition to SLA treated surface (SLA-SPE) to create micro/nano multi-scale roughness and have explored the newly modified surface as a drug carrier for enhanced bioactivity and fast osteointegration ability of Ti implants.

Methods: Ti discs with three different surfaces (non-treated, SLA treated, SLA-SPE treated) were prepared. To create nanoporous structures on the SLA surface, SPE was performed using direct current sputter with a Ta target under Ar-rich ambient condition at high negative bias up to 850 V. To load the BMP-2, each sample was immersed in a BMP-2 solution (1 μg/ml, and 10 μg/ml) and dried up at room temperature. The surface morphology of Ti samples was observed by FE-SEM and the total loading amount of BMP-2 was quantified using a UV spectrophotometer after each BMP-2 loaded sample was fully dissolved in PBS under sonification for 1 h. Biological properties of each BMP-2 loaded surface were evaluated with pre-osteoblast (MC3T3-E1) cell. Initial cell attachment was observed with FE-SEM after 3 h culturing. Cell proliferation and differentiation were evaluated by MTS assay after 3 d (n=3) and ALP activity assay after 10 d (n = 3).

Results: Non-treated Ti showed the smooth surface (**Fig. 1a**) while SLA treatment created micro-roughness (**Fig. 1b**). Micro/nano dual roughness possessing nano-pores with a dimension of 100 nm (width) and 300 nm (length) was uniformly created by SLA-SPE treatment (**Fig. 1c, d**). The increased roughness of Ti surface was found to be closely related to the total loading amount of growth factors as shown in **Fig. 2**. The amount of loaded BMP-2 was significantly increased as micro and nano-scale roughness from each surface treatment were added, exhibiting the maximum loading amount on SLA-SPE treated surface. SLA-SPE treated sample was found to allows the loaded BMP-2 up to 3 times more than non-treated sample (**Fig. 2**). The *in vitro* tests to evaluate the biological properties of each sample were presented in Fig. 3. Cells were well spread on Ti with or without treatment (**Fig. 3a, b**). The cell proliferation was likely less influenced by either roughness or loaded BMP-2 amount, whereas cell differentiation was found to be improved as BMP-2 loading capacity increased.

Conclusions: The micro/nano dual roughness was uniformly formed on the Ti surface by SLA-SPE treatment. It was confirmed that the growth factor (BMP-2) loading capacity is enhanced as the roughness of Ti surface was improved, leading to improved bioactivity on SLA-SPE treated surface. The multi-scale roughness on Ti surface created by SLA-SPE treatment has great potential for the application of drug-loaded Ti implants

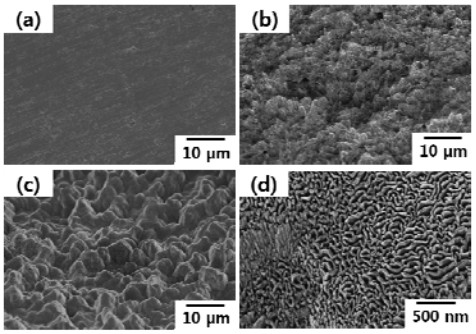


Figure 1. Surface morphology of (a) non-treated, (b) SLA treated, and (c, d) SLA-SPE treated Ti at different magnifications

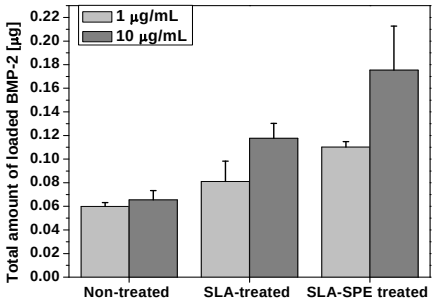
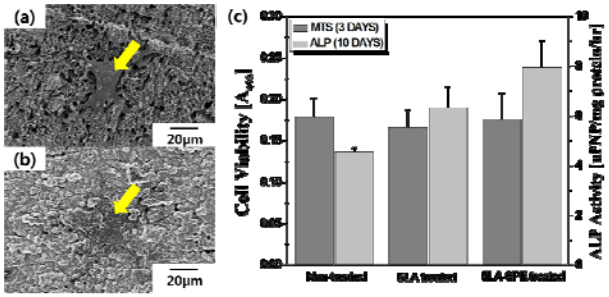


Figure 2. Total amount of loaded BMP-2 on non-treated, SLA treated and SLA-SPE treated Ti substrates using different BMP-2 solutions (1 μg/ml, and 10 μg/ml).



Fiure 3. (a, b) Cell attachment morphologies on BMP-2 loaded (a) SLA treated, and (b) SLA-SPE treated Ti, and (c) cell proliferation and differentiation on three different surfaces of Ti with BMP-2 after 3 days and 10 days, respectively.

References:

[1] S.K. Moon et al. Curr Appl Phys 2014;14:S183-S187
[2] T. Luo et al. Clin Oral Implan Res 2012;23:467-474