Enhanced Bone Healing of Titanium Surface with RGD through Electrodeposited PEG

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Statement of Purpose: Enhancement in early osteoblastic cell response on implant surface such as adhesion and spreading is prerequisite for subsequent favorable cell behavior and ultimately, rapid and strong bone healing of endosseous Ti implants. A cell-adhesive peptide containing Arg-Gly-Asp (RGD) is an active peptide located in binding site of cell attachment-promoting proteins, which has been frequently used in surface modification of implants in order to improve bone healing by facilitating the integrin-mediated cellular adhesion and subsequent cell differentiation. Recently, we reported a simple and effective method for producing stable RGD-immobilized Ti surface through functional molecule (polyethylene glycol, PEG) with a long molecular chain (RGD/PEG/Ti surface) [1]. The chain length of PEG played an important role in improving in vitro osteoconductivity. The RGD/PEG/Ti surface accelerated differentiation and mineralization of osteoblastic cells [2]. In this study, we investigated whether this biofunctionalized surface further enhances the bone healing of commercial microrough oral implants in the rabbit cancellous bone by using histomorphometric method.

Methods: Moderately rough-surface commercial screw implants (cp Ti, ASTM grade 4), produced by grit-blasting with an external diameter of 3.3 mm and a length of 10 mm were used. Immobilization process of RGD is summarized in **Fig.1**. We have employed PEG with a molecular weight of *ca.* 3000. Both terminals of PEGs were terminated with functional groups: One terminal was terminated with -NH_2, and the other, with -COOH. NH_2-PEG-COOHs were dissolved in 0.5-mol L^{-1} NaCl solution with a concentration of 0.2 mass%. The pH was adjusted to pH12 with a 0.1 mol L^{-1} NaOH solution. During electrodeposition, NH_2-PEG-COOHs migrated electrically to the cathode Ti and were immobilized on it (PEG/Ti). PEG/Ti was immersed in a 0.001 mass%RGD aqueous solution which was adjusted to pH12 with NaOH at 4°C for 24 h (RGD/PEG/Ti). Each surface was characterized with an ellipsometer and a scanning probe microscope. Ti implants simply socked in a 0.001 mass%RGD aqueous solution without PEG immobilization were used as control (RGD/Ti). All implants were sterilized by γ-irradiation. Twenty-eight screw implants (14 RGD/PEG/Ti implants and 14 RGD/Ti implants) were alternatively placed in the right or left femoral condyles of 14 New Zealand White rabbits. Histomorphometric analysis was performed at 2 and 4 weeks of healing. In order to evaluate osteoconductivity of implants, the percentage of bone-to-implant contact (BIC%) was measured over all threads region, which was measured as the percentage of the length of mineralized bone in direct contact with the implant surface (7 implants per group at each healing period).

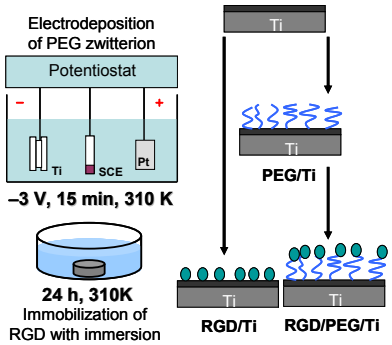

Fig.1 Specimen preparation process.

Results: All of the investigated implants had come into direct contact with the surrounding bone, with no signs of inflammation at the bone-implant interface. At both evaluation time points, the RGD/PEG/Ti implants displayed active new bone apposition on their surface, which exhibited more continuous direct bone contact compared with the RGD/Ti implants. Figure 2 shows the result of histomorphometric analysis, the RGD/PEG/Ti implants demonstrated significantly greater mean BIC% values in all threads area compared with RGD/Ti implants at 2 ($P < 0.05$) and 4 ($P < 0.01$) weeks of healing.

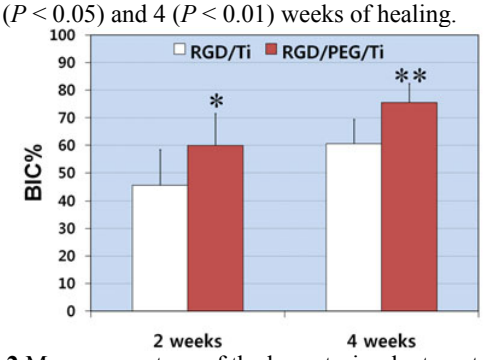

Fig. 2 Mean percentage of the bone-to-implant contact (BIC%) over all threads of implants 2 and 4 weeks after implantation (*$p < 0.05$, **$p < 0.01$).

Conclusions: The RGD/PEG/Ti surface was effective in improving implant bone healing compared with simple RGD-soaked surface, RGD/PEG/Ti surface promoted early bone apposition of commercial microrough oral implants in rabbit cancellous bone. These results indicate that this RGD/PEG/Ti surface may be an effective tool for enhancing the bone healing of rough-surfaced oral implants by increasing the degree of BIC in areas of cancellous bone, thereby enabling rapid osseointegration.

References

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[2] Oya K et al., Biomaterials 30: 1281 (2009).