Evaluations of epithelial sealing and peri-implant epithelial down-growth around “step-type” implants

Key words: dental implant, down-growth, epithelial attachment

Abstract

Objective: Implant designs that can stimulate and integrate with an epithelial wound-healing process may significantly enhance the efficacy of dental implants. Here, we evaluated the potential of “step-type” implant systems to improve the sealing between the peri-implant epithelium (PIE) and the implant surface, and investigated the effect of implant structure on PIE down-growth.

Materials and methods: Right maxillary first molars were extirpated from rats and implanted with either a straight-type or a step-type implant varying in step height and/or width (Ws): 0.8 mm height, 0.2 mm width; 0.4 mm height, 0.1 mm width). Maxillae were harvested at various time points over 16 weeks to evaluate laminin-5 distribution as an indicator of wound healing and PIE formation, horse-radish peroxidase (HRP) penetration as a measurement of epithelial sealing, and PIE down-growth formation.

Results: In all implant models, the PIE formed from the oral sulcular epithelium and spread apically along the implant surface. In the Ws group, HRP penetration was detected only in the coronal region of the PIE at 4 weeks, whereas in the straight-type, it was observed in the apical region and the connective tissue. At 16 weeks, the Ws implants exhibited markedly less PIE down-growth than the Con, Nh, or Hs implants, and were equivalent to that observed in natural teeth.

Conclusion: The step-type implant system may have the potential for improving epithelial sealing at the tissue–implant interface, as well as reducing apical PIE down-growth, thus enhancing dental implant efficacy.

Dental implant treatment has emerged as one of the most important prosthetic therapy options for completely and partially edentulous patients. However, because the oral mucosa is penetrated by the implant, the peri-implant tissue has a risk of peri-implantitis [Albrektsson et al. 2000].

Peri-implantitis includes not only the mucosa but also the bone tissue and may compromise osseointegration between the bone and the implant surface (Lindhe et al. 1992; Marinello et al. 1995). Therefore, implant designs that can stimulate and integrate with an efficient epithelial wound-healing process may significantly enhance the efficacy of dental implants.

In order to improve epithelial sealing and thus minimize the risk of peri-implantitis, it is necessary to understand the histopathology and the mucosal-healing process surrounding adjacent teeth and the implant. The epithelial attachment structures around natural teeth at the interface consist of the junctional epithelium (JE). The JE is connected to the enamel via an internal basal lamina (IBL). This contains hemidesmosomes (HD), which are epithelial adhesion plaques that adhere to the extracellular matrix in the plasma membrane of the epithelial cells (Listgarten 1975; Stern 1981). The external basement lamina (EBL) links the JE to the connective tissue at the JE–connective junction. At the JE of a natural tooth [NT], the HDs of these basement membranes (BM) form mechanical closures as a defense mechanism against the exotic factor (Jones & Clemmons 1995; Borradori & Sonnenberg 1996). There is ultrastructural evidence that HDs localize at the IBL between the peri-implant epithelium [PIE] and the implant (Ikeda et al. 2000). The aforementioned finding suggests that epithelium cells adhere to the implant surface via these attachment structures. However, a previous study, which investigated experimentally the adherence at both the dento-JE and the implant–PIE interface at the light and electron microscopic levels, reported that the PIE adheres to implants poorly, primarily due to the inferior...
quality and quantity of the attachment structures [Ikeda et al. 2000]. We have reported that the BBL and HDs form only in the lower region of a PIE–titanium implant interface [Atsuta et al. 2005a, 2005b]. In contrast, in natural teeth, these structures are formed throughout the dento–JE interface [Ikeda et al. 2002].

Laminin-5 (Ln-5) is the major adhesive ligand for integrins in the mature, cutaneous BM (Carter et al. 1990; Rousselle et al. 1991). Ln-5 localizes to anchoring filaments that connect to HDs directly and promotes this assembly in epithelial cells [Green & Jones 1996]. Furthermore, this protein has significant roles in cell migration, cell adhesion, proliferation and differentiation. After injury, Ln-5 is deposited into the wound bed by epithelial cells at the leading edge of the epithelium [Nguyen et al. 2000]. In mucosal wounds, the deposition of Ln-5 occurs before the deposition of the other BM components, such as type 4 and 7 collagens (Larjava et al. 1993). The deposited Ln-5 is required to repair the BM and to re-establish epithelial anchorage to the BM via integrin α6β4 in HDs [Carter et al. 1990]. Therefore, Ln-5 is important for the wound healing of the epithelium, including PIE formation and stability after implantation.

Inflammatory cells are often associated with implant–PIE interfaces and with microbial adhesion, a prerequisite for infection. Thus, implant designs that can inhibit or limit bacterial adhesion may prevent infection and increase implant longevity. Porous and grooved biomaterials also have the potential to promote soft tissue ingrowth, with pore and groove size being critical to their success. However, transcutaneous devices composed of porous materials are associated with a high risk of infection [Shin & Akae 1997].

Epithelial down-growth around the implants occurs on the soft tissue–implant interface, providing a route for invasion of external pathogens and ultimately leading to implant failure. Pocket formation provides a moist, warm environment for bacterial assembly, which is protected from mechanical cleaning. While the epidermis can migrate through damaged collagenous tissue, migration is halted by confrontation with a healthy collagenous matrix [Winter 1974]. Furthermore, the supporting bone around the implant may decrease in response to the approaching epithelium. As a result, the unsecure implant may begin to move in the alveolar bone. It is critical to prevent epithelial down-growth by designing implants that can promote epithelial cell adherence and stabilize the epithelial soft tissue seal.

In this study, we evaluated the potential of a new step-type implant to increase and maintain epithelial adherence to the implant surface. We want to clarify that the step that contained the step-type implants is below the middle region of the implant with attachment structures and that the step width is enough to support a long epithelial layer attachment. And from the results, we speculated that it is important to lengthen the horizontal distance of the interface between the PIE and the implant surface at an appropriate position. By facilitating and increasing the area of dermal attachment to the implant, we hypothesized that epithelial downgrowth would be reduced.

Materials and methods

Implants

Three variations of a screw-type titanium alloy implant with or without a step at the same level (‘‘step-type’’ [Stp]) were investigated in this study (Sky blue, Fukuoka, Japan). Each implant body was 4.5 mm in length and 2 mm in diameter. The level of step on the normal step-type (N) implant was at half the height of the PIE, whereas the high step-type (H) implant contained a step at three quarters the PIE. The Ns and Hs implants had the same width of step (0.1 mm), and the Ws implant had a slightly wider step (0.2 mm). A ‘‘straight-type’’ implant (control group [Con]) body was 4 mm in length and 2 mm in diameter (Sky blue), a similar design to those described in our previous reports [Atsuta et al. 2005a, 2005b]. All implants were compared with a Nt as an additional control. The designs of the experimental implants are shown in Fig. 1. Before use, the implants were treated with 100% acetone and distilled water, and subsequently disinfected by autoclaving.

Oral implantation

Rats were treated according to the guidelines for animal care established by Kyushu University. The details of surgical implantation in the rat oral cavity are described in our previous studies [Ikeda et al. 2000; Atsuta et al. 2005a, 2005b]. Briefly, 6-week-old Wistar rats (20 males, 120–150 g) were used in each implant model. Under sodium pentobarbital anesthesia (50 mg/kg intraperitoneal injection, Nembutal, Abbott Laboratory, North Chicago, IL, USA), the maxillary right first molar was extracted and the cavity was drilled immediately with a K-Reamer (#20–120; Torpan, Maillefer, Switzerland) to prepare for implantation. The implant body was screwed into the cavity. After the operation, all the animals were treated with buprenorphine (0.05 mg/kg intracaudal injection, Lepetan, Otsuka Pharmaceutical, Tokyo, Japan) for analgesia. The animals were housed and given water and a powdered diet until euthanasia at 3 days, 1, 2, 4 weeks (n = 10, each group) or 16 weeks (n = 6, each group) following implantation.

Tissue preparation for immunohistochemistry

Tissues were prepared following the methods described in our previous report [Ikeda et al. 2000]. After each experimental period, the rats were anesthetized and perfused intracardially with heparinized saline, pH 7.4, followed by 4% paraformaldehyde and 0.3% picric acid in 0.1 M phosphate buffer (PB), pH 7.4, for 4 days at 4°C. The maxillae were dissected and immersed in the same fixative for 3 h at 4°C, then demineralized in 5% tetrasodium ethylenediaminetetraacetate (EDTA), 4% sucrose in 0.01 M PB, pH 7.4, for 4 days at 4°C. The oral mucosa surrounding the implant site was carefully removed from the bone or implant as described previously [Ikeda et al. 2000; Atsuta et al. 2005a, 2005b]. The gingiva around the right first molar was also removed from the tooth. All specimens were immersed in 20% sucrose in 0.1 M PB at 4°C overnight for cryoprotection and then embedded in O.C.T. compound (Sakura, Tokyo, Japan). All samples were quickly frozen in dry ice/isopentane, before cutting 10 μm bucco-palatal sections with a cryostat at −20°C. The cryosections were mounted on gelatin-coated glass slides.

Immunohistochemistry

Immunohistochemistry using the avidin-biotinylated peroxidase complex (ABC) kit (Vector Laboratories, Burlingame, CA, USA) was performed as described previously [Atsuta et al. 2005a, 2005b]. Briefly, after sections were washed in 0.01 M phosphate-buffered saline (PBS), pH 7.2, the sections were treated with 0.3% H2O2 and 0.1% NaN3 in PBS, pH 7.2, for 60 min to inhibit endogenous peroxidase activity, and blocked for 30 min with 10% normal goat serum in PBS. The tissue sections were then incubated overnight at 4°C with affinity-purified polyclonal rabbit IgG antibody to the rat γ1 chain of Ln-5 in PBS (1:100), kindly provided by Drs Koshikawa and Quantra (Scrpps Research Institute, CA, USA). The sections were then rinsed and incubated for 45 min with biotinylated goat anti-rabbit IgG in PBS (1:200), followed by a 60-min incubation with ABC dissolved in PBS (1:100). Immunopositive staining was visualized by treatment for 5 min in 0.02% diaminobenzidine (DAB)-tetrahydrochloride (Dojin Laboratories, Kumamoto, Japan) and 0.006% H2O2 in 0.05 M Tris buffer, pH 7.6, and counterstained lightly with hematoxylin. For negative immunohistochemical controls, some sections were incubated with either non-immune rabbit IgG or PBS alone instead of the primary antibody. All sections were observed and photographed with a light microscope.

Topical application of horse-radish peroxidase (HRP)

Fifty milligram per milliliter of HRP (type 1, molecular weight 40,000 Da; Sigma, St. Louis,
MO, USA) was applied topically to 50 rats (10 rats for each implant model), 4 weeks after implantation. The procedure for topical application of HRP was similar to that reported previously (Ikeda et al. 2000). Under systemic anesthesia (100 mg/kg; Nembutal), cotton floss was immersed in HRP dissolved in isotonic saline (50 mg/ml), and then laid on the gingival margin around the implant body without imposing any mechanical stress. Then, the same solution was dripped onto the floss every 10 min for 60 min. This procedure was also performed in the gingiva around the maxillary left first molar in the same animal for comparison with the permeability of HRP in the gingiva surrounding the implant. As a control for HRP, isotonic saline alone was applied around implants and teeth using the same method in four rats (two animals for each model, Nt and Con).

Tissue preparation for HRP histochemistry
Under deep ether anesthesia, the animals were euthanized 60 min after topical application of HRP, and the maxillae containing either the implant or the maxillary left first molar with the surrounding gingiva were dissected en bloc.

The tissue blocks were quickly immersed in a fixative consisting of 2.5% glutaraldehyde and 2% paraformaldehyde in 0.1 M PB, pH 7.4, for 2 h at 4°C and decalcified with 5% tetrascarodium EDTA and 4% sucrose in 0.01 M PB, pH 7.4, for 3–4 days at 4°C.

Cryosections were prepared and mounted on gelatin-coated glass slides as described for the immunohistochemistry tissues.

HRP histochemistry
The protocol for HRP histochemistry using the DAB method was similar to those described in previous studies (Yamaza et al. 1997).

Several 10-μm-thick sections were washed with 0.01 M PBS and incubated in DAB medium containing 0.02% 3, 3′-DAB-4HCl (Dojin Laboratories, Kumamoto, Japan) and 0.006% H2O2 in 0.05 M Tris-HCl buffer, pH 7.6, for 5 min at room temperature. For histochemical controls, additional sections were treated with DAB medium without H2O2.

As in immunohistochemistry, all sections were observed and photographed with a light microscope.

Quantification of HRP penetration and down-growth
All sections were observed using an Axiotech Microscope (Carl Zeiss Co. Ltd, Göttingen, Germany) and an Axiocam digital camera (Carl Zeiss Co. Ltd). The data were imported and measured with Axio Vision 3.0 (Carl Zeiss Co. Ltd). The frozen sections were selected for five sections from only the PIE buccal-side of each rat and used for the linear measurements, and the landmarks to measure these were the top and bottom of the PIE. This vertical distance between the landmarks was determined in a direction parallel to the long axis of the implant. A one-way analysis of variance with a Fisher’s least significant difference test was performed for the data. Values of *P* < 0.05 were considered to be statistically significant.

Results
After implantation, there was no remarkable mucosal inflammation surrounding the implants of each model (Fig. 2A). In the decalcified section of the Con and Stp implants, the gingival epithelium consisted of oral epithelium (OE), peri-implant sulcular epithelium (PISE) and PIE. The PISE resembled the oral sulcular epithelium.
OSE), as both continued to the adjacent connective tissue and exhibited a keratinized stratum corneum, similar to the OE (Fig. 2B).

**Light microscopic evaluations of Ln-5 deposition in the JE and in the PIE around the tooth, the straight- and step-type implants**

In normal gingiva, immunohistochemical staining of Ln-5 showed an immunoreactive band along the dento-JE interface (Fig. 3; Nt). Additionally, positive Ln-5 staining was detected along the JE–connective tissue interface. The staining intensity of Ln-5 along the dento-JE interface was stronger than that along the JE–connective tissue interface. No Ln-5 was noted in the BM underlying either the OSE or the OE.

At the interface between the straight-type implant after 4 weeks and PIE, the Ln-5 deposition pattern exhibited considerable differences from that in the JE of the Nt (Fig. 3; Con). As defined in a previous study, the implant–PIE interface of the oral mucosa around a dental implant can be divided into three areas: the coronal (upper), middle and apical (lower) portions (Atsuta et al. 2005a, 2005b). In the oral mucosa around the Con implant, Ln-5-positive staining was apparent as a band along the implant–PIE interface, but the majority of the upper portion of the interface did not exhibit Ln-5 detection.

In the step-type implant groups after 4 weeks, the majority of Ln-5 immunoreaction was located around the lower portion, below the step (Fig. 3; Stp). The upper portion exhibited minimal Ln-5. The strongest Ln-5 immunoreaction was detected as a band along the implant–PIE interface on the upper and apical portions of the step (black arrow in Fig. 3d). Furthermore, Ln-5 appeared as an immunoreactive line along the PIE–connective tissue interface. Ln-5 was also demonstrated along the PISE–connective tissue and OE–connective tissue interfaces of the oral mucosa. The positive staining pattern for Ln-5 was noted in the BM underlying both the OSE and the OE. At 4 weeks, the light microscopic morphological findings in the step-type implants were very similar to the epithelial structures around the Con implant, and this result was observed in most of the experimental specimens.

There was no immunoreactivity of Ln-5 in the immunohistochemical negative controls in either the natural gingiva or in the oral mucosa (not shown).

**Immunohistochemical deposition of Ln-5 during the formation of the peri-implant oral mucosa around the step-type implant**

During formation of the PIE, Ln-5 deposition around the step-type implant was similar to the straight-type implant (Fig. 4A).

After 3 days, the OSE had begun to extend over the surface of the implant. Ln-5 was distributed along the BM under the OSE and OE. The leading cells of the new epithelium strongly expressed Ln-5, while the innermost cells adjacent to the implant did not.

After 1 week, the thin epithelium extending from the OSE had spread further along the implant. It resembled the PIE, because the epithelium consisted of stratified squamous cells without keratinization. The OSE facing the upper portion of the implant also consisted of stratified squamous cells with poor keratinization and resembled the PISE. Ln-5 was widely distributed.
in the connective tissue under the PIE, but was not detected on the PIE adjacent to the body of the implant. Ln-5 was also strongly detected at the BM under the PISE and OE.

After 2 weeks, the PIE had migrated more deeply on the implant surface. As seen after 1 week, Ln-5 was strongly distributed in the apical portion of the connective tissue adjoining the PIE. Ln-5 was also detected in the PIE adjacent to the implant and distributed weakly at the BM under the PISE and OE.

Four weeks after implantation, the PIE had extended further apically along the implant surface over the step. A thin band of strong Ln-5 immunostaining was observed along the implant–PIE interface. However, little Ln-5 was detected at the upper portion of the implant–PIE interface and was deposited in the CT. Ln-5 was scarcely expressed along the upper portion of the implant–PIE interface and was deposited in the CT.

The patterns of Ln-5 distribution during formation of the peri-implant mucosa after implantation are shown schematically in Fig. 4B.

**Light microscopy of topical HRP in the JE around a Nt**

In the control cases, in which only saline without HRP was applied to the gingiva around the implants or teeth, no DAB-positive products were found in the JE, except for leukocytes containing endogenous peroxidase (data not shown).

A strong HRP reaction was seen in the coronal portion of the JE (Fig. 5; Nt) on the tooth surface. However, the intensity of the HRP reaction gradually decreased from the middle to the apical region of the JE. Ln-5 also appeared as a linear band along the EBL under the PIE, along the BM under the PISE and OE and in the connective tissue close to the apical portion of the PIE.

**Light microscopy of topical HRP in the PIE around the implants**

In the coronal PIE region of the implantation groups (Con, Ns, Ws, Hs), HRP was found not only in the surface of the PIE, but also in the intercellular spaces of the PIE cells (Fig. 5a). In the middle PIE region of the Con group, deep layers of PIE cells exhibited the strongest HRP reaction, while the HRP reaction in the intercellular spaces of the PIE was weak. Interestingly, this weak HRP reaction became stronger close to the PIE–connective tissue junction. We could not identify penetration of HRP into the connective tissue under the PIE of the Stp groups by light microscopy. However, the PIE showed a positive HRP reaction strongly.

In the apical portion of the PIE of the Hs group, a strong penetration of HRP into the deeper portions of the connective tissue was found. In the Ns and Ws groups, the positive HRP reactions around the apical portions disappeared by the end of the PIE, and we could not observe these reactions in the connective tissue of the PIE.

As shown in Fig. 5b, the Ns and Ws groups exhibited a significant improvement in the blocking of HRP penetration, and this capacity was
equally effective to that demonstrated by the Nt group.

**Light microscopy of PIE down-growth around the implants after 16 weeks**

In Fig. 6, deposition of Ln-5 around the apical edge of the PIE was observed at 16 weeks after implantation for each group. Light microscopic images (Fig. 6a) and a schematic (Fig. 6b) of Ln-5 distribution patterns in the down-growth of the peri-implant mucosa after implantation in the Nt and implant groups are shown. The median distance of down-growth data is presented in Fig. 6c. In the Nt group, we did not observe apical migration of the JE. Most of the implants in this study exhibited apical down-growth at 16 weeks (Fig. 6a). Additionally, the keratinized stratum corneum and the OE moved into the space surrounding most implants, creating a deep pocket. Specifically, Hs implants showed a similar pattern of down-growth as that observed in the Con group. Ns had minimal down-growth as compared with Con. In contrast, down-growth was the least in the Ws group compared with the other implant models. Interestingly, of all the implants, only the Ws was able to inhibit the down-growth of PIE below the level induced by Nt at 16 weeks.

**Discussion**

Clinical and radiographic observations suggest that a biological dimension of hard and soft tissues exists around dental implants and extends apically from the implant–abutment interface. Following the apical migration of the PIE, some changes in the vertical level of the peri-implant crestal bone height have been reported (Berglundh & Lindhe 1996; Cochran et al. 1997). This change has been shown to negatively impact long-term implant success (Marinello et al. 1995). Furthermore, pocket formation by weak sealing, as well as down-growth of the PIE, are known to make the implantitis worse (Berglundh et al. 1992).

In order to improve the efficacy of dental implants and to reduce the risk of associated infections, it is necessary to improve epithelial sealing between the implant and the PIE, as well as to prevent down-growth of the PIE. Here, we investigated the potential of a new implant design, the step-type implant, to enhance PIE sealing around the implant and to deter apical PIE migration in comparison with the straight-type implant, a conventional dental implant design.

Ln-5 is an important protein for wound healing of the epithelium, including PIE formation and...
epithelial stability after implantation. It is known that Ln-5 induces the migration of epithelial cells at the leading edge of the regenerating oral mucosa (Ryan et al. 1994; Kainulainen et al. 1998). As such, Ln-5 deposition can be an indication of the wound-healing process and an index of epithelial attachment at the implant–epithelial interface. We detected intracellular Ln-5 in JE cells, in the leading cells of the epithelium covering the wound and in PIE cells. Extracellular Ln-5 was observed at both the dento-JE and JE–connective tissue interfaces, and at the implant–PIE and PIE–connective tissue interfaces.

We further observed that the distribution of Ln-5 changed during PIE formation. By 3 days after implantation, we detected Ln-5 in the cells at the step of an Stp and in the surrounding tissue facing the epithelium. This finding suggests that the basal cells secreted Ln-5 to the outside, permitting attachment of the epithelium to the connective tissue. By contrast, at 2 weeks following implantation, only some of the cells of the epithelium at the implant surface secreted Ln-5. By 4 weeks, Ln-5 was detected in most of the PIE cells on the implant over the step. These findings indicate that it took approximately 4 weeks to form an attachment structure at the implant–epithelial interface while formation at the epithelium–connective tissue interface occurred after just 3 days. These findings are in agreement with previous reports regarding epithelium attachment to the straight-type implant (Atsuta et al. 2005a, 2005b). The formation of the attachment structures at the implant–epithelial interface was evidently delayed. This is probably attributable to a delay in the intracellular synthesis and extracellular deposition of Ln-5 caused by the presence of the titanium implant. Furthermore, the newly formed PIE did not attach to the titanium surface sufficiently until 4 weeks after implantation.

In the formation of the PIE after implantation, the direction of the growth of the epithelium changed to apical, because the horizontal growth of the new epithelium was hindered by the presence of the implant body during the healing of the oral mucosa. The PIE continued to extend apically over the step and was nearly complete at 4 weeks.

In order to investigate the nature of epithelial sealing, HRP was topically applied to the gingival sulcus of implants or normal teeth as a tracer, and the extent of HRP penetration at the implant–PIE interface was quantified. The results are shown in Fig. 6. (a) Light micrographs of the PIE around the Nt or experimental implants at 16 weeks after implantation. The Ws implant had a similar length of PIE down-growth to the Nt implant. However, deep, apical down-growth of the PIE was observed in the Con, Ns, and Hs groups. Bar = 100 μm. (b) Schematic of the PIE down-growth after implantation. Dark blue area: keratinized layer. Orange dots: Ln-5 in the CT; Red dots: Ln-5 in the basal cells. Green line: Ln-5 in the IBL and EBL of the PIE; Red line: Ln-5 in the BM under the OSE and OE. (c) Median distance of PIE down-growth in the Nt, Con, Ns, Ws, and Hs implant groups. Each bar represents the mean ± SD of five parallel experiments. *P < 0.05 vs. Con.
junction was compared with that at the dento-JE junction within each group. We observed HRP penetration into the intercellular spaces of the JE cells around the sulcular bottom, but did not observe HRP penetration across the stratum of the JE. Not only did we observe HRP in the PIE but also in the connective tissues across the PIE. Therefore, unlike the oral PIE, these findings suggest that JE permits penetration of foreign substances from the intercellular spaces of the JE cells. It is known that the PIE attaches to implants using HDSs as attachment structures (Atsuta et al. 2005a, 2005b). However, it is questionable whether these attachment structures provide a barrier to the penetration of foreign substances.

In this study, our findings of the PIE at the Ws implant differed from those of the other implants, most likely due to the differences in the length of the implant–PIE interface and the position of the step for the epithelial sealing around the implant. Because we reported that straight-type implants were associated with the majority of attachment structures between the implant and the coronal-middle region of the PIE (Atsuta et al. 2005a, 2005b), it was important that the step-type implants contained the step in the middle region of the implant. From the results of this study, we observed that the step width is also important, because a wide step can support a long epithelial layer attachment.

Next, we investigated the possibility of long-term, PIE down-growth around the implants after treatment. Most of the experimental implant models exhibited apical down-growth and marked spreading deposition of Ln-5 around the apical edge of the PIE. Because Ln-5 induces not only adhesion, but also migration of epithelial cells, this result suggests that the PIE is not stable. It seems that the epithelial cells of the PIE have a high inclination to migrate because the cells at the apical edge of the PIE secreted Ln-5, which induces the migration of epithelial cells at the leading edge of regenerating oral mucosa to the surrounding tissues facing the epithelium.

The PIE around each implant type showed a similar pattern of down-growth to the Nt except for the epithelium surrounding the Hs implant. We speculate that a strong adherence between the PIE and the implant can block the down-growth of PIE. For the epithelial cells, adhesion and migration are contrary behaviors (Hormia et al. 1998). Additionally, the length of the implant may also influence the capacity of PIE down-growth; in this study, the Ws implant had a longer implant body than the Hs implant.

In conclusion, we have shown that if a long epithelial layer attachment is provided by the step implant, down-growth of the PIE is inhibited and the sealing around the implant is reinforced. Future studies should include investigations into how to promote the synthesis and deposition of Ln-5 at the implant–PIE interface and evaluations of step-dimensions that can optimize dental implant performance with regard to epithelial healing and integration.

References


