Kinetics of Phenotype Modification Therapy with VISTA: A Retrospective Case Series Using 3D Digital Analysis

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Phenotype modification therapy has emerged as one of the main treatment objectives of periodontal plastic surgery. However, long-term data on the stability of gingival thickness gains are not
available. This study examined the kinetics of mucosal thickness gain as a measure of phenotype modification therapy following treatment of multiple gingival recession defects with vestibular incision subperiosteal tunnel access (VISTA). Six patients with 14 recession type (RT) II teeth were treated using VISTA and subepithelial connective tissue grafts (SCTG). Scanned images of study casts at pre- and postoperative periods (6 to 66 months) were digitally superimposed for quantitative evaluation of soft tissue dimensional changes. Mucosal thickness gains ranged from 1.0 ± 0.7 mm (1 mm apical to cement-enamel junction [CEJ]) to 1.4 ± 0.4 mm (5 mm apical to CEJ). The gingival thickness gains remained relatively stable, with thickness gains at 66 months of 0.5 ± 0.8, 0.9 ± 0.6, 1.1 ± 0.6, 1.0 ± 0.4, and 1.2 ± 0.6 mm at 1, 2, 3, 4 and 5 mm apical to the CEJ, respectively. Treatment of multiple gingival recession defects with VISTA and SCTG led to stable gingival thickness gains and shows promise as a strategy for phenotype modification therapy. *Int J Periodontics Restorative Dent* 2022. doi: 10.11607/prd.5621

**Introduction**

A systematic review and meta-analysis demonstrated that untreated gingival recession has a likelihood of progression of approximately 80% (Chambrone & Tatakis 2016). An array of gingival recession therapeutic options have been reported by many clinicians (Cohen DW & Ross SE. 1968, Bernimoulin et al. 1975, Langer & Langer 1985, Allen 1994, Zadeh, 2011). A series of different graft materials has been investigated (Harris 2000, McGuire & Scheyer 2010, Tonetti et al. 2018). Several outcome measures have been reported, including flap thickness (Huang LH 2005, Cairo et al. 2016, Garces- McIntyre et al. 2017), flap tension (Pini Prato et al. 2010) and surgical position of the gingival margin (Pini Prato et al. 2005). Although root coverage has been used as the main outcome measure in periodontal plastic surgery, mucosal phenotype modification therapy has emerged as a key measure (Lin et al, 2020, Kao, et al. 2020). It may be argued that phenotype modification therapy should be
considered as a primary objective of periodontal soft tissue augmentation. Connective tissue graft has been considered a gold standard for periodontal root coverage (Rasperini et al. 2018, Cairo et al. 2020).

However, there is often significant volume loss with autologous graft during tissue remodeling (Ward 1974). The increase in gingival thickness gain using coronally advanced flap has been shown to be approximately 0.4 to 0.5 mm (Silva et al. 2004, Woodyard et al. 2004, Zucchelli et al. 2010). In contrast, thickness gain with VISTA has been shown to be between 0.8 and 1.1 mm (Gil et al. 2019). Previously, mucosal thickness changes have been examined using a customized acrylic stent with a periodontal probe (Rotenberg & Tatakis 2014) or caliper (Huang et al. 2005, Garces- McIntyre et al. 2017). A small number of studies have employed digital tools for analysis of the outcome of periodontal procedures (Zuhr et al. 2014, Rebele et al. 2014, Gil et al. 2018, 2019). To the best of our knowledge, only a few clinical studies have used 3D volumetric analysis following root coverage procedures (Rebele et al. 2014, Gil et al. 2018, Gil et al. 2019). Moreover, data on long-term stability of mucosal thickness changes are limited. The aim of this study was to investigate the long-term outcomes of the treatment of multiple gingival recession defects (recession type II) with VISTA using 3D digital analytical tools.

Materials & Methods

Study design

This study was designed as a retrospective case series. Following approval by the Institutional Review Board (IRB) of the University of Southern California (USC), patients had received root coverage procedure by the same post-doctoral periodontology resident (S.M.) at the USC Periodontology Clinic. In total, fourteen teeth with multiple recession type (RT) II gingival recessions in six patients were included in this study. All patients had received VISTA with subepithelial connective tissue graft (SCTG) harvested from either the lateral palate or maxillary tuberosity.

Outcome variables
The primary outcome variable was the change in mucosal thickness at 1, 2, 3, 4 and 5 mm relative to the cement-enamel junction (CEJ) following VISTA plus SCTG. The secondary outcome variable was root coverage (%).

Surgical procedures

The periodontal root coverage procedure was performed by means of VISTA (Zadeh, 2011) plus SCTG. In brief, after administering local anesthesia through infiltration and/or block anesthesia, the exposed root surface was cleaned by scaling and root planning. To allow access to the surgical area, a vertical vestibular incision of adequate length was made in an appropriate location (Figure 1B). A subperiosteal full thickness tunnel was created according to the extent of the sites requiring root coverage, separating tissue from vestibular to gingival margin as well as the papillae area in a minimally invasive approach using a series of periosteal elevators (VISTA ABC Elevators Kit, Regeneimmune, Woodland Hills, CA, USA). Donor tissue was then harvested from either the lateral palate or tuberosity (Figure 1C). The donor tissue was inserted inside the tunnel and stabilized to the overlying mucosa by placement of 6.0 polypropylene mesio-distal sutures (Klosure 6-0 Polypropylene sutures, Regeneimmune). The vertical incision and donor site were adapted by continuous interlocking suture and crisscross suture, respectively, using 4-0 PTFE monofilament suture (Klosure 4-0 PTFE sutures, Regeneimmune). Subsequently, a coronally advancement of the gingival margins at least 2 mm above the CEJ was achieved (Figures 1D) by means of a suture bonding technique using 6-0 polypropylene monofilament suture (C3 needle), as well as flowable composite resin to attach the suture to the tooth surface (Figure 1D). The sutures were removed 3 weeks after surgery. Antibiotics (amoxicillin or clindamycin), naproxen sodium (550 mg every 12 hours when needed) and chlorhexidine rinse (0.12% twice a day for three weeks) were prescribed to the patients. Follow-up examinations were scheduled at 6, 12, 18, 24, 30, 36, 42, 60, and 66 months post-operatively. Alginate impressions were obtained of sites prior to the root coverage procedure (baseline) and following recession therapy at every follow-up appointment. The mean follow-up period for monitoring the
mucosal dimensional alterations was 40.0 ± 13.5 months. Five and one-half year follow-up data were recorded from only one patient. Study casts were made and scanned by a desktop optical scanner (3Shape, D850; Copenhagen, Denmark) for image acquisition. The obtained stereolithographic (STL) files were imported into a reverse engineering software program (Geomagic control, 3D system, Cary, NC, USA). STL files from baseline and different post-operative time points were superimposed by manually adjusting for optimal superimposition of the repeatable anatomical landmark sites to evaluate the kinetics of volumetric mucosal alterations at treated sites following VISTA. Data evaluation

One calibrated examiner (Y.W.) performed all measurements. Ten percent of sites were randomly selected for repeated measurement and the second measurement differed less than 5% from the first measurement. The following mucosal dimensional changes were assessed: 1) mucosal thickness change at different locations (1, 2, 3, 4, and 5 mm below CEJ) relative to baseline (mm); and 2) amount of root coverage (%).

Statistical analysis

Descriptive statistics were calculated for all variables of interest. Continuous measures were summarized using means and standard deviations whereas categorical measures were summarized using counts and percentages. The correlation between mucosal thickness gain and root coverage was assessed using Pearson correlation coefficients. A linear mixed model, adjusting for the correlation among observations taken on the same patient, was run to model the relationship between mucosal thickness and potential predictors of interest (tooth type, location, time, NCCL, and recession depth). Prior to analysis, the predictors were assessed for the presence of multicollinearity (tolerance statistic <0.4). If multicollinearity was found to exist, only one member of a correlated set of variables would be retained for the final model. No evidence of multicollinearity was found and therefore all variables were considered suitable for inclusion into the multivariable model. All analyses were carried out using SAS Version 9.4 (SAS Institute, Cary, NC, USA).
Results

Experimental population

Six patients (2 female, 4 male) were included in this study (Table 1). The mean age was 58.8 ± 17.8 years old. In total, fourteen gingival recession defects greater than 2.0 mm were present that were classified as RT II (N=14). The numbers of sites treated in the maxillae and mandible were six and eight, respectively. A mean of 2.3 ± 1.5 teeth with recession defects were treated per patient. The mean initial recession depth was 2.8 ± 0.8 mm.

Quantitative analysis of post-augmentation mucosal thickness changes

A representative treated clinical case is shown to illustrate the VISTA and SCTG procedure (Figure 1). All composite restorations (Figure 1A) were removed from the roots (Figure 1B). An important step of the protocol is coronal advancement at least 2 mm coronal to the CEJ using coronal anchoring with sutures that were bonded to facial surfaces of the teeth (Figure 1D). A representative treatment site is shown with follow-up at various post-operative intervals up to 66 months (Figure 2). The clinical photographs (Figure 2A) and images of scanned models (Figure 2B) show stability of the root coverage. The superimposed orthogonal slices of scanned models taken at pre-operative and various post-operative intervals show the thickness gain (Figure 2C). The quantitative data of mucosal thickness changes at 1, 2, 3, 4 and 5 mm apical to the preoperative CEJ at various post-operative intervals up to 66 months are shown in Figure 3. Results demonstrated that at 6 months, the thickness gain ranged from 1.0 ± 0.7 mm (1 mm apical to CEJ) to 1.4 ± 0.4 mm (5 mm apical to CEJ). The thickness gains at 6 months were relatively stable during the observation period of this study, so that by 66 months, the thickness gain ranged from 0.5 ± 0.8 mm (1 mm apical to CEJ) to 1.2 ± 0.6 mm (5 mm apical to CEJ).

Quantitative analysis of root coverage changes

The mean percentage of root coverage for all sites at 6 months was 91.7 ± 31.9%, and was lower between 24 and 42 months (Figure 4). The percentage root coverage outcome for all sites at 66 months
was 98.6 ± 23.8%. Root coverage outcomes in maxilla and mandible were 107.0 ± 28.8% and 80.2 ± 30.7%, respectively, at 6 months (P = 0.12) and 99.3 ± 24.8% and 60.9 ± 34.6%, respectively, at 36 months (P = 0.08). Multivariate analysis of parameters affecting mucosal thickness gain Tooth type had a significant effect, in that incisors had lower thickness gains than premolars at 1 mm (p=0.03), 2 mm (p=0.01) and 3 mm (p=0.009) apical to the CEJ (Table 2). At the 3-mm level, both incisors and canines had lower thickness gains compared with premolars (p=0.009). Time was also a significant factor, such that for every one month post-augmentation, the mucosal thickness decreased by 0.01 mm at 1 mm (p=0.0001) and 2 mm (p<0.0001) apical to the CEJ (Table 2). The mucosal thickness loss was 0.007 mm for every one month post-augmentation at 3 mm (p=0.0003). At 4 mm there was a 0.005 mm decrease in thickness every post-augmentation month (p=0.0252). At 5-mm apical to the CEJ, the thickness changes over time were not significant (p=0.0542). Recession depth had a significant effect at 1 mm (p<0.0001), 2 mm (p<0.0001), 3 mm (p<0.0001) and 4 mm (p=0.0007) apical to the CEJ (Table 2). For every mm of increased recession depth, there were decreases in mucosal thickness gains of 0.53 mm (at 1 mm), 0.55 mm (at 2 mm), 0.58 mm (at 3 mm) and 0.22 mm (at 4 mm). Multivariate analysis of parameters affecting root coverage Tooth type had a significant effect (p=0.05), in that canines had greater root coverage than incisors; incisors had less root coverage than premolars. Time also had a significant effect (p=0.0058), such that for every post-augmentation month there was a 0.005 mm decrease in root coverage. Thickness gains (mm) were significant at 1 mm (p<0.0001), 2 mm (p<0.0001), 3 mm (p=0.0186), 4 mm (p<0.0001) and 5 mm (p<0.0001) (Table 3). Thickness gain was significantly correlated with root coverage outcome.

Discussion
Gingival thickness has been considered a strong predictor of achieving complete root coverage (Huang et al. 2005). Several studies demonstrated that coronally advanced flap (CAF) with either CTG or collagen matrix yielded better root coverage compared with CAF alone (Woodyard, et al 2004, Ahmedbeyli et al 2014, Cairo et al 2016, Garces- McIntyre et al 2017). Thus, mucosa phenotype modification has been recommended to achieve the best outcome of root coverage as well as to prevent further soft tissue deficiency (Lin et al, 2020, Kao, et al. 2020). There is a need to understand whether a change of mucosa phenotype has occurred and which areas benefit from this increased thickness for future tissue stability. In the present study, thickness gains of 1.0-1.4 mm were observed at 6 months post-operatively and were stable thereafter. A multivariate model demonstrated that tooth type, time, and recession depth were factors influencing thickness changes following VISTA with SCTG. Premolar sites showed better thickness gains compared with incisor and canine sites. Deeper recessions negatively correlated with thickness gains. An important finding of this study was the relative stability of the thickness gains, because the gingival thickness decreased by only 0.005-0.03 mm every 6 months. Thus, mucosa thickness following VISTA plus SCTG was very stable over time. Mean percentage of root coverage was relatively stable over the observation period.

Recently, Pini Prato et al reported the 20 years outcomes of root coverage for Miller class III recession defects using CAF + SCTG. Compared with those data, the VISTA + SCTG showed greater root coverage outcomes. It was speculated that VISTA enables to minimize surgical trauma by locating the access incision which is remote from the therapeutic area. Percentage root coverage outcome in maxilla and mandible were 107.0% and 80%, respectively, at 6 months and 94% and 53%, respectively, at 42 months. It is important to note that at latter time points, the number of sites under observation declined and some of the changes in the percentage root coverage may be attributed to the fewer mandibular teeth that were included. There were five treated sites in mandible in two patients lost to 42 months follow up and all treated sites in mandibular lost to 60 months follow up. To the best of our knowledge, this is the first study that has digitally assessed the kinetics over time of post-

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operative mucosal thickness alterations after soft tissue augmentation. The root coverage outcome following soft tissue augmentation with VISTA plus SCTG after 66 months showed 98.6% root coverage. It is noteworthy that the thickness gain achieved was positively correlated with root coverage. Because of its significance, the thickness gain as a predictor of periodontal root coverage merits further investigation. The advantage of using VISTA is that the coronally advanced gingival margin is stabilized with bonded sutures, creating a stable protected space which likely contributes to the thickness gain achieved. The present study has some limitations, including small sample size and retrospective design. This study was intended as an exploratory investigation in order to establish the protocol and feasibility of mucosal thickness assessment over time. Although only a limited number of patients were included, establishing a protocol to superimpose 3D volumes over time and developing the technique to quantify mucosal thickness changes over time made this project complex. The significant observations made from the present data warrant conducting a prospective randomized controlled clinical trial to assess the significance of thickness gain on the stability of the root coverage procedure.

Acknowledgments

The authors declare no conflicts of interest.

References:


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Figure Legends

Figure 1. Treatment of a representative clinical case that used the VISTA and SCTG procedure. The initial condition with multiple gingival recession defects and thin mucosal phenotype was previously treated with class V restorations (A). The composite restorations were removed from roots apical to the CEJ (B). Odontoplasty was conducted to reduce root prominences. A vertical vestibular incision was made in the midline frenum, starting from the vestibular fornix to the base of the midline papilla.

Subperiosteal tunnel was elevated at least one tooth beyond the teeth being treated. Autogenous mucosal tissues were harvested from the lateral palate (*), as well as from the tuberosity (#) and overlaid on mucosa to demonstrate their eventual position within the tunnel (C). Coronal advancement of the gingival margins was performed and the gingival margin of each tooth was coronally positioned and anchored to the tooth surface, using flowable composite resin (D). Post-operative clinical image of the patient after 24 months shows stable gingival margin and mucosal thickness gain (E). CEJ, cement-enamel junction; SCTG, subepithelial connective tissue graft; VISTA, Vestibular Incision Subperiosteal Tunnel Access.

Figure 2. Representative clinical and 3D volumetric data of an included site treated with VISTA and SCTG. The clinical photographs (A) as well as facial (B) and orthogonal slices (C) of scanned
models were taken at pre-operative and various post-operative intervals. CEJ, cement-enamel junction; SCTG, subepithelial connective tissue graft; VISTA, Vestibular Incision Subperiosteal Tunnel Access.

Figure 3. Mucosal thickness change (mm) at different locations (1, 2, 3, 4, 5 mm) relative to the CEJ, measured at various time points up to 66 months. CEJ, cement-enamel junction.

Figure 4. Percentage root coverage at different sites at various follow-up times. Man, mandible; Max, maxilla
Figures and Figure Legends

Table 1. Clinical characteristics of included subjects and teeth.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Total N=6 Male (N=4) Female (N=2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>58.8 ± 17.8</td>
</tr>
<tr>
<td>Mean follow-up (months)</td>
<td>40.0 ± 13.5</td>
</tr>
<tr>
<td>Mean number of recessions/patient</td>
<td>2.3 ± 1.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tooth type</th>
<th>Maxilla (N=6) Incisor (N=3) Canine (N=0) Premolar (N=2) Molar (N=1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mandible (N=8) Incisor (N=2) Canine (N=4) Premolar (N=2) Molar (N=0)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recession Type</th>
<th>RT II (N=14)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Anatomical factor</th>
<th>NCCL (N=8) No NCCL (6)</th>
</tr>
</thead>
</table>

| Mean initial recession depth (mm) | 2.8 ± 0.8 |

NCCL, non-caries cervical lesion.

Table 2. Multivariate analysis of effects of various parameters on mucosal thickness gains at various locations.

<table>
<thead>
<tr>
<th>Apical distance from CEJ</th>
<th>Parameter</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 mm</td>
</tr>
<tr>
<td></td>
<td>F-value</td>
</tr>
<tr>
<td></td>
<td>Pr&gt;F</td>
</tr>
<tr>
<td>Tooth Type</td>
<td>14.54</td>
</tr>
<tr>
<td>Location</td>
<td>0.32</td>
</tr>
<tr>
<td>Time</td>
<td>16.04</td>
</tr>
<tr>
<td>NCCL</td>
<td>7.67</td>
</tr>
<tr>
<td>Recession depth</td>
<td>61.10</td>
</tr>
</tbody>
</table>

CEJ, cement-enamel junction; NCCL, non-caries cervical lesion.

Table 3. Correlation between mucosal thickness gain and root coverage at various locations of analysis (1, 2, 3, 4, 5mm apical to CEJ).

<table>
<thead>
<tr>
<th>Effect</th>
<th>1-mm* Correlation p-value coefficient</th>
<th>2-mm Correlation p-value coefficient</th>
<th>3-mm Correlation p-value coefficient</th>
<th>4-mm Correlation p-value coefficient</th>
<th>5-mm Correlation coefficient Pr&gt;(t)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Root coverage</td>
<td>0.71 p&lt;0.0001</td>
<td>0.60 p&lt;0.0001</td>
<td>0.56 p&lt;0.0001</td>
<td>0.36 p=0.0003</td>
<td>0.13 P=- .19</td>
</tr>
</tbody>
</table>

*Apical distance from cement-enamel junction (CEJ).
Figures

Figure 1A.

Fig 1a

Figure 1B.

Fig 1b
Fig 1c

Fig 1d
Figure 1E.