Laser-Assisted Esthetic Crown Lengthening: Open-Flap Versus Flapless

This study compares the clinical outcomes of Er,Cr:YSGG (2,780 nm) laser-assisted open-flap (OF) and flapless (FL) esthetic crown lengthening (ECL) for the treatment of altered passive eruption. Thirty-six healthy patients requiring ECL were randomly divided into two groups: OF and FL. Gingivectomy and ostectomy were performed with an Er,Cr:YSGG laser in both groups. The periodontal condition and gingival margin level (GML) were assessed at baseline, immediately postsurgery, and at 1, 3, and 9 months postsurgery. The effect of periodontal phenotype and tooth location on GML and supracrestal gingival tissue dimension were evaluated. A significant difference was detected in the mean of GML at all time points, except between 3 and 9 months. The main tissue rebound after 9 months was 0.25 ± 0.3 mm in the OF group and 0.26 ± 0.3 mm in the FL group (no significant difference) and was significantly higher in thick periodontal phenotypes. Er,Cr:YSGG laser-assisted ECL is a predictable technique that achieved similar outcomes using flap and flapless approaches, providing esthetic and restorative opportunities for clinicians.


Excessive gingival display, also referred to as “gummy smile,” can play an important role in oral health–related quality of life and can have an adverse effect on the patient’s perception of attractiveness, friendliness, trustworthiness, intelligence, and self-confidence.2

The correction of excessive gingival display improves both the esthetics and confidence of the patient.3

Altered passive eruption (APE) is a causal factor of excessive gingival display.4 Coslet et al classified altered passive eruption into two types and classified two subgroups.5 Esthetic crown lengthening (ECL) surgery could be considered a suitable protocol to manage APE and achieve more harmonious and symmetrical smiles.6

Ribeiro et al suggested a minimally invasive flapless procedure for the treatment of APE; that split-mouth, randomized controlled trial found that ECL with and without flap elevation had similar and stable clinical results for up to 12 months.7 Flapless procedures have to meet precise indications in order to achieve an adequate width of attached keratinized tissue after ECL.

The literature suggests that a variety of instruments can be used in ECL to obtain a more physiologic gingival contour, including scalpel, electrosurgery, or laser.3 Clinical application of lasers in periodontal...
surgery has continued to expand in the last decade, and the concept of minimally invasive dentistry can be achieved by choosing laser treatment.\textsuperscript{5} Er\textsubscript{3}Cr:YSGG (erbium, chromium:yttrium-scandium-gallium-garnet; 2,780 nm) laser ablate both hard and soft tissues with excellent surgical precision and minimal collateral effects. This ability creates the opportunity for a minimally invasive flap and flapless ECL, resulting in decreased tissue damage, minimized bleeding, and less inflammation and postoperative discomfort, thus enhancing healing.\textsuperscript{10} Clinical case reports suggest that laser-assisted flapless ECL might allow faster uneventful wound healing and eliminate irregular tissue positioning, in addition to the overall positive experience for the patient.\textsuperscript{11,12}

This study aims to compare the clinical outcomes of laser-assisted open-flap (OF) and flapless (FL) ECL for the treatment of APE over a 9-month healing period. The positional changes of the gingival margin level (GML) and the supracrestal gingival tissue dimension (SGT) following ECL were evaluated between groups.

**Materials and Methods**

**Study Sample**

Thirty-six healthy patients (14 men, 22 women; aged 22 to 45 years) were enrolled in the study from August 2014 until March 2019. Patients required ECL in the six maxillary anterior teeth due to APE.

**Inclusion and Exclusion Criteria**

The inclusion criteria were as follows: excessive gingival display \( \geq 3 \) mm; a gingival overlap of over 19% of the anatomical crown height\textsuperscript{13}; > 22 years old; having at least 20 teeth, with 6 maxillary anterior teeth indicated for ECL; full-mouth Plaque Index (PI) and bleeding on probing index (BOP) scores < 15%.

The exclusion criteria were as follows: treatment sites with a probing depth (PD) \( \geq 3 \) mm; cases where the restorative procedure changes the incisal edge in an apical direction; pregnancy and lactation; history of smoking; patients requiring antibiotics prior to dental procedures; previous mucogingival surgery; systemic conditions that could affect tissue healing; and undergoing active orthodontic therapy.

Adaptive randomization was used as a method of changing the allocation probability according to the progress and position of the study to minimize the imbalance between treatment groups. Keeping at least 2 mm of attached keratinized gingiva (AKG) width after gingivectomy on all six maxillary anterior teeth, according to the aesthetic treatment plan, was the absolute condition to enroll the patient into the FL group. The first subject was allocated through simple randomization (coin toss), and the subsequent patients were divided randomly based on the response of previous subjects into one of two groups: OF and FL (\( n = 18 \) patients each). In other words, the information of the subjects who already participated in the study was used to allocate the newly recruited subjects.

The OF group was treated by surgical crown lengthening using an apically positioned flap and osseous recontouring. The FL group was treated with a flapless technique, which includes gingivectomy and osseous recontouring without raising a flap. All of the patients were selected according to the study inclusion and exclusion criteria. Patients were informed of the nature and potential risks of the proposed surgical procedures, and they reviewed and signed an informed consent form. This study was approved by the human subjects ethics board of Health Research Governance Department – Ministry of Public Health in Qatar and was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2000.

**Clinical Indices**

**Measurement procedure**

At baseline, patients received a comprehensive periodontal examination, including PI, Gingival Index (GI), BOP, and PD for all teeth. The measurements were performed using a UNC 15 periodontal probe (Develmed) based on differences of 0.5-mm increments at six points around the teeth. AKG width was recorded on the maxillary anterior teeth. Dental smile design (DSD) was done to analyze the dentolabial gingival relationship. An individual stent (mock-up) was used as a surgical stent and reference for the clinical measurements during the treatment and follow-ups.
The clinical measurements were assessed on the midbuccal aspect of each tooth involved in the study at baseline, immediately postsurgery, and at 1, 3, and 9 months postsurgery. For each tooth, the reference point for these measurements was the incisal edges of the stent (Fig 1).

Cone beam computed tomography
The height of the alveolar bone and the outline of the bone crest was examined by CBCT at baseline and 9 months postsurgery. The crown-to-root ratios on the treated teeth were respected, and the periodontal bone support appeared to be adequate. The thickness of the buccal bone and gingiva at a distance of 2 mm apical to the bone crest was measured with CBCT (CRANEX 3d, Soredex) to check the periodontal phenotype, which was classified as follows: ≥ 2 mm as thick, < 2 mm as thin.

Gingivectomy
The surgical template was used to mark the gingival contour prior to gingivectomy using a 4-mm–diameter tip (MT4 tip Biolase), with the following laser parameters: 1-W average power, 50-Hz frequency, 700-µs pulse duration, 43-J/cm² energy density, W10 water, A10 air. With the MZ6 cylindrical tip (Biolase) almost parallel to the root surface, the soft tissue was cut in a sweeping motion from the mesial to the distal level, just coronal to the desired points, using the following parameters: 0.6-mm diameter, 3-W average power, 50-Hz frequency, 700-µs pulse duration, 57-J/cm² energy density, W40 water, A20 air. The total estimated duration of exposure for each tooth was approximately 2 minutes.

Flap incision (OF group)
An intrasulcular internal bevel incision was performed on the treated tooth’s buccal aspect with an MT4 laser tip (2.5 W, 50 Hz, 60 µs, 106 J/cm², W20, A20) in contact mode. A variable-thickness flap was elevated, made to be split-thickness at the surgical papillae and full-thickness at the buccal aspect of the incision. The periosteal separation was carried out to facilitate apical positioning of the flap and to permit suturing of the flap to the periosteum.

Ostectomy
The flap margin was used as a reference instead of the cementoenamel junction (CEJ), and osseous resection was performed such that there was at least 3 mm between the osseous crest and the newly created free gingival margin. For the FL group, the intracellular soft tissue was ablated down to the bone crest to form a pouch, and the bone was ablated using an MC3 tip (4 W, 20 Hz, 60 µs, 148 J/cm², W80, A20) that was
Fig 2 (a) Example patient in the open flap group with an altered passive eruption (class A, subgroup 2). (b) The individual stent (mock-up) was put in place and used as a surgical stent, and the incisal edge of the anterior teeth was used as a reference for periodontal measurements. (c) Because the GML was already determined, a surgical template was used to mark the gingival contour of the treated area using a laser, perpendicular to the gingival tissue and following the margins of the surgical template. (d) The ostectomy and recontouring of the alveolar bone crest were performed after raising the flap, using a laser chisel tip, holding the tip adjacent to the tooth, and “walking” the tip across the treated area. (e) After the ostectomy, there was a distance of 3 mm between the osseous crest and the newly created free gingival margin. (f) The surgical sites in the open flap group were closed with interrupted sutures, keeping the gingival margins 3 mm away from the bone crest. (g) Clinical view of the periodontal condition after 9 months.

Fig 3 (a) Preoperative anterior view of an example patient in the flapless group with an altered passive eruption (class A, subgroup 2) with short clinical crowns and gingival margin discrepancies. (b) With the tip almost parallel to the root surface, the soft tissue was cut in a sweeping motion from the mesial to the distal level, just coronal to the desired points. The soft tissue was then beveled to the marked points immediately after completion of gingivectomy. (c) An Er,Cr:YSGG laser performed the ostectomy (chisel tip) on the alveolar crest, through the gingival sulcus, without flap elevation. The tip was applied parallel with the long axis of the tooth, and the long exit surface of the chisel tip was used in the mesiodistal direction and advanced apically to its full 3-mm marked length, satisfying supracrestal gingival tissue requirements. (d) After completion of the ostectomy, a probe showed that a distance of 3 mm from the gingival margin to the alveolar crest was achieved. (d and e) Clinical views at the 3-month and (f) 9-month postoperative follow-ups.
applied parallel with the long axis of the tooth. The tip was advanced apically to its full 3-mm marked length to satisfy biologic width requirements (Fig 4). The total estimated duration of exposure for each tooth was approximately 1 minute. Following the ostectomy, the bone crest was recontoured and smoothed with a sweeping motion with the MZ6 cylindrical tip in a sweeping motion, moving laterally from the mesial to the distal aspect, following the CEJ contours through the sulcus to a depth of 3 mm from new free gingival margin. Bone troughs and irregularities were minimized using the bone file. Root planing was performed using Gracey curettes.

Postoperative Instructions

Verbal and written postoperative instructions were given to the patients, which included chlorhexidine gluconate (0.12%) rinses twice daily and 400 mg ibuprofen as needed. Patients were scheduled to return after 1, 3, and 9 months.

Statistical Analyses

Statistical analysis was performed using SPSS computer software (version 26.0, IBM). The level of significance was set at .05 for all analyses. Repeated-measures analysis of variance and least significant difference test were used to detect differences within GML among time points, methods (OF vs FL), and teeth location. The general linear model test, independent sample t test, and Wilks’ lambda test were used to detect differences in SGT and tissue rebound among periodontal phenotype, teeth, and methods. Mann-Whitney U test was used to evaluate PI, GI, and BOP indices.

Results

At the beginning of the study, 44 patients were included. Eight patients could not complete the study
(3 patients did not show at the 3-month visit, 3 patients did not show at the 9-month visit, and 2 patients were omitted from the sample to maintain balance between the two groups). Statistical analysis was performed for a total of 36 patients and 216 teeth (108 teeth per group). The treated teeth included central incisors, lateral incisors, and canines.

When comparing the OF and FL groups at baseline, no statistically significant differences were observed in PI, GI, BOP, or PD ($P > .05$). Throughout the study, all patients maintained an accepted level of plaque control (PI < 15%). There was no significant difference in GI between OF and FL groups at 3 and 9 months ($P = .85$ and $P = .67$, respectively). However, GI scores were significantly higher at 1 month in the OF group ($P = .16$). At the 1-month follow-up, the mean percentage of BOP was significantly higher for the OF group than for FL ($P = .01$), though this difference was absent at 3 and 9 months ($P = .78$ and $P = .72$, respectively). In both groups, no significant difference was detected in the mean PDs at any site between baseline and 3 and 9 months ($P > .05$).

**Gingival Margin Level**

The mean GML and SGT values of 216 treated teeth are presented in Table 1. Comparing the OF and FL groups at baseline, no statistically significant difference was detected in the mean GML height ($P > .05$). At all sites and in both groups, there was a significant difference in mean GML when comparing baseline values to those immediately postsurgery and at the 1-, 3-, and 9-month follow-ups ($P < .05$). On the other hand, no statistically significant difference was detected ($P > .05$) when comparing the new GML of the OF and FL groups immediately after surgery.

Gingival tissue rebound represents the GML reduction relative to the margin level immediately after ECL. There was a significant difference between the OF and FL groups for GML reduction at 1 and 3 months, whereas these differences disappeared at 9 months (Table 2). In addition, the GML reduction

### Table 1 Mean GML and SGT of Both Groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Tooth</th>
<th>Baseline</th>
<th>Immediately postsurgery</th>
<th>1 mo</th>
<th>3 mo</th>
<th>9 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>GML, mm</td>
<td>OF Central incisors</td>
<td>7.81 ± 0.8</td>
<td>10.18 ± 0.54</td>
<td>10.15 ± 0.48</td>
<td>9.97 ± 0.48</td>
<td>9.9 ± 0.49</td>
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<tr>
<td></td>
<td>OF Lateral incisors</td>
<td>7.18 ± 0.74</td>
<td>9.19 ± 0.54</td>
<td>9.1 ± 0.58</td>
<td>9.06 ± 0.39</td>
<td>9.03 ± 0.4</td>
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<tr>
<td></td>
<td>OF Canines</td>
<td>8.13 ± 0.69</td>
<td>10.61 ± 0.32</td>
<td>10.46 ± 0.44</td>
<td>10.35 ± 0.29</td>
<td>10.31 ± 0.34</td>
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<tr>
<td></td>
<td>FL Central incisors</td>
<td>8.0 ± 0.70</td>
<td>10.28 ± 0.39</td>
<td>10 ± 0.48</td>
<td>9.9 ± 0.33</td>
<td>10.01 ± 0.41</td>
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<tr>
<td></td>
<td>FL Lateral incisors</td>
<td>7.44 ± 0.56</td>
<td>9.33 ± 0.41</td>
<td>9.04 ± 0.53</td>
<td>8.99 ± 0.42</td>
<td>9.03 ± 0.41</td>
</tr>
<tr>
<td></td>
<td>FL Canines</td>
<td>8.36 ± 0.58</td>
<td>10.5 ± 0.41</td>
<td>10.29 ± 0.74</td>
<td>10.28 ± 0.3</td>
<td>10.28 ± 0.3</td>
</tr>
</tbody>
</table>

| SGT, mm   | OF Central incisors | 3.43 ± 0.66 | 2.93 ± 0.27 | – | – | 3.17 ± 0.34 |
|           | OF Lateral incisors | 3.79 ± 0.76 | 3 ± 0.0 | – | – | 3.19 ± 0.29 |
|           | OF Canines     | 3.69 ± 0.68 | 3.08 ± 0.19 | – | – | 3.22 ± 0.31 |
|           | FL Central incisors | 3.32 ± 0.55 | 2.98 ± 0.5 | – | – | 3.2 ± 0.3 |
|           | FL Lateral incisors | 3.65 ± 0.53 | 3 ± 0.0 | – | – | 3.27 ± 0.28 |
|           | FL Canines     | 3.53 ± 0.49 | 3.03 ± 0.12 | – | – | 3.28 ± 0.28 |

GML = gingival margin level; SGT = supracrestal gingival tissue dimension; OF = open-flap treatment group; FL = flapless treatment group.

A total of 216 teeth were treated and evaluated at all time points.
did not differ significantly when comparing 3- and 9-month values among all subjects \((P > .05)\), while a significant difference was detected when comparing the 1-month values to the 3- and 9-month values. The mean GML difference between time points for the total subjects is presented in Table 3.

The mean GML was significantly affected at certain time points by the treatment method \((F = 58.96, P = .002)\), whereas the tooth location had no such effect \((F = 0.475, P = .83)\). The mean tissue rebound values in the total subjects after 3 and 9 months were significantly higher in patients with thick phenotypes \((0.3 \pm 0.35 \text{ mm and } 0.32 \pm 0.32 \text{ mm, respectively; } F = 3.6, P = .05)\) than those with thin phenotypes \((0.22 \pm 0.28 \text{ mm and } 0.19 \pm 0.28 \text{ mm, respectively; } F = 10.79, P = .001)\).

### Supracrestal Gingival Tissue Dimensions

The baseline mean SGT dimensions were \(3.63 \pm 0.7 \text{ mm and } 3.5 \pm 0.53 \text{ mm}\) for the OF and FL groups, respectively, without a significant difference \((P > .05)\). ECL was planned to create a 3-mm SGT dimension in both treatment methods, and the mean SGTs immediately after surgery were \(3.01 \pm 0.19 \text{ mm and } 2.98 \pm 0.29 \text{ mm}\) for the OF and FL groups, respectively. At 9 months, compared to immediately after surgery, the SGT dimensions were significantly increased to \(3.2 \pm 0.31 \text{ mm and } 3.25 \pm 0.28 \text{ mm}\) for the OF and FL groups, respectively \((P < .05)\). There was a significant difference in the SGT values when comparing 9 months to immediately after surgery among all study participants \((P < .0001)\). The SGT differences between time points are presented in Table 4. The time after ECL and the tooth location have a statistically significant effect on the mean SGT \((P = .02)\). The treatment method did not show this significant effect at all time points, according to Wilks’ lambda test \((P = .06)\).

No significant relationship was detected between phenotype and SGT dimensions after 9 months in either group \((P = .19 \text{ for OF, } P = .8 \text{ for FL})\). The correlation coefficient calculated between SGT and the amount of bone resection was not statistically significant in the OF \((r = -.0113, P = .25)\) and FL \((r = .144, P = .14)\) groups.

### Discussion

To the present authors’ knowledge, this is the first randomized clinical study to compare the clinical outcomes of using an Er,Cr:YSGG laser...
in ECL with and without a flap for the treatment of APE. Despite the considerable interest in using a laser in ECL, the present authors’ knowledge is largely based on a limited amount of available data: mostly case reports or case series with small samples, one single flapless technique approach, and results based on subjective patient satisfaction.12

In the present study, both OF and FL ECL were successfully used to manage APE through the reduction of the excessive periodontal tissue throughout the immediate apical shift of GML and increasing clinical crown length. The sites healed uneventfully, as shown by the low PI, GI, and BOP scores throughout the study, with the exception of a slightly higher level of GI and BOP at 1 month in the OF group. This exception might be explained by the tissue trauma/healing in the interproximal areas due to papilla elevation and suturing, possibly causing postoperative morbidity for the patient.7 PD values tended to return to the presurgical values without significant differences between the two groups. Some studies have reported a similar observation,16,17 whereas others recorded no changes in PD values.18,19

An Er,Cr:YSGG 2,780-nm laser was chosen because it has the ability to deal with both soft and hard tissues. The laser enabled the proper crown height to be established in the FL group and the gingival contouring and split-thickness interdental flap in the OF group; this helped to avoid overreliance on flap placement at the osseous crest, which might lead to a more gingival rebound.19 Precautions were taken to ensure a safe and efficient osteotomy in both groups, such as using a prism chisel tip and enhancing the laser parameters that could help in cooling, such as a short pulse duration (60 µs), fewer pulses (20 Hz), and more water irrigation. The same laser parameters were used in both groups to minimize the variables of the study. Compared to rotary instruments, osteotomy by Er,Cr:YSGG is more precise and causes less collateral damage to the root surface and less thermal damage.10

The present study relied on the use of reference stents, as they improve the reliability and reproducibility of measurements compared to measurements taken from the CEJ.20 The esthetic reference stent was produced according to the DSD concept. Using the DSD enabled the creation of a personalized treatment plan, delivery of accurate ECL, standardization of the measurements at all time points, and previewing the results.21

Transgingival probing was used as an accurate method to determine

<table>
<thead>
<tr>
<th>Time (I)</th>
<th>Time (J)</th>
<th>Mean difference, mm (I – J)</th>
<th>P*</th>
<th>95% CI for difference</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lower</td>
</tr>
<tr>
<td>OF</td>
<td>Baseline</td>
<td>9 mo</td>
<td>0.45*</td>
<td>&lt; .0001</td>
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<td></td>
<td>Immediately postsurgery</td>
<td>9 mo</td>
<td>-0.19*</td>
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<tr>
<td>FL</td>
<td>Baseline</td>
<td>9 mo</td>
<td>0.25*</td>
<td>&lt; .0001</td>
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<tr>
<td></td>
<td>Immediately postsurgery</td>
<td>9 mo</td>
<td>-0.26*</td>
<td>&lt; .0001</td>
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<tr>
<td>Total subjects</td>
<td>Baseline</td>
<td>9 mo</td>
<td>0.35*</td>
<td>&lt; .0001</td>
</tr>
<tr>
<td></td>
<td>Immediately postsurgery</td>
<td>9 mo</td>
<td>-0.23*</td>
<td>&lt; .0001</td>
</tr>
</tbody>
</table>

SGT = supracrestal gingival tissue dimension; CI = confidence interval; OF = open-flap treatment group; FL = flapless treatment group.

Based on estimated marginal means.

*Statistically significant (P < .05).

Adjustment for multiple comparisons: least significant difference (equivalent to no adjustments).

Table 4: Pairwise Comparisons of the Mean SGT Differences Between Measurements at 9 Months and Both Baseline and Immediately Postsurgery
the bone level and calculate the SGT. SGT measurements relied on the reference point in the stent rather than CEJ, because the CEJ was hidden in some teeth with restorations and can be difficult to distinguish from the buccal bone crest during probing or bone sounding, as Mele et al have noted. After 9 months, SGT dimensions were measured using CBCT, which has been suggested as a precise diagnostic tool for these dimensions.

A tendency was observed for the GML to grow coronally from the immediate postsurgical level up to 3 months following ECL in both groups, and the mean GML was affected significantly with the treatment method only up to 3 months postsurgery, but lacked significance at 9 months. The alteration of GML was not affected by tooth location.

These results are in agreement with previous investigations demonstrating that after 6 months, the marginal periodontal tissue showed a minimal tendency to grow in the coronal direction from the level defined at the surgery. In contrast to the present results and other results reported in the literature, Chen et al did not detect changes in GML after 3 months of ECL assisted by an erbium laser. In the present study, there was no significant change in the GML from 3 to 9 months, which is similar to Lanning et al, who found that the GML remains stable from 3 to 6 months.

The observed GML reduction is related to the gingival tissue rebound, which was higher in the FL group at 1 and 3 months compared to the OF group. The differences disappeared after 9 months, with a mean tissue rebound of 0.25 mm in the OF group and 0.26 mm in the FL group. These findings point to the probability that clinical differences between OF and FL appear only in the short term. Apart from using the laser as an unconventional method for ECL, the present results are a confirmation of Ribeiro-Júnior et al’s findings: Once the GML was defined, its changes were minimal up to 6 months without differences between the two methods.

In the present study, a distance of 3 mm was maintained between the gingival margins and new bone level in both groups. This might explain why the minimal tissue rebound values observed after 9 months (0.25 mm and 0.26 mm in the OF and FL groups, respectively) compare to the values registered in previous studies (0.77 mm and 2.7 mm). Multiple studies have reported that tissue rebound has an inverse correlation with the distance from the flap to the bony crest at the time of suturing.

Periodontal phenotype was measured by CBCT, which shows a high diagnostic accuracy in assessing periodontal phenotype, while visual inspection might not be considered a valid method of identification. In both groups, higher tissue rebound was seen in the subjects with a thick periodontal phenotype at 3 and 9 months. These results provide additional support to the importance of assessing periodontal phenotype before planning ECL. Other authors have demonstrated the role of periodontal phenotype on the amount of the coronal re-growth of the soft tissue margin after crown lengthening.

SGT dimensions were significantly increased at 9 months compared to immediately postsurgery but still did not reach the baseline values. It can thus be reasonably assumed that the amount of osseous resection is based on the individual’s baseline SGT, and not only on the fixed distance (3 mm) between the gingival margin and the bone crest. SGT dimensions were not affected by the treatment method, while the time after ECL and the tooth location had significant effects. This finding is consistent with the observations of other studies.

Conclusions

With the limitations of this study, Er,Cr:YSGG laser-assisted APE is a predictable technique that achieves similar outcomes using a flap or flapless approach, providing esthetic and restorative opportunities for clinicians.

Acknowledgments

The authors declare no conflicts of interest related to this study.

The contribution statement: Walid Altayeb and Georgios E. Romanos made substantial contributions to conception and design of the study. Walid Altayeb was involved in clinical procedures and data collection. Ahmed Abdulla was involved in statistical data analysis. Walid Altayeb, Arnabat-Dominguez Josep, and Georgios E. Romanos were involved in drafting the manuscript and revising it critically. All authors agreed to be accountable for all aspects of the work in en-
References


