

HYPERDILUTED RADIESSE AND BELOTERO BALANCE : A NOVEL INJECTABLE HYBRID FOR INTERDENTAL PAPILLARY REGENERATION

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ABSTRACT

Objective: The loss of interdental papilla presents both aesthetic and functional concerns, often resulting in the formation of black triangles that compromise smile harmony. This study evaluates the efficacy of hyperdiluted calcium hydroxylapatite (CaHA) combined with hyaluronic acid (HA) as a minimally invasive injectable therapy for interdental papilla regeneration, aiming to restore soft tissue volume without inducing bone loss.

Methods: A prospective clinical study was conducted on patients exhibiting interdental papillary deficiency. Hyperdiluted Radiesse (CaHA) mixed with HA was precisely injected into the deficient papillary region using an insulin syringe. Objective assessments included digital caliper measurements of papillary height and volume, while subjective evaluations comprised patient satisfaction scores. Follow-ups were scheduled at baseline, 1 month, 3 months, and 6 months post-treatment. Statistical analysis was performed to compare pre- and post-procedure outcomes.

Results: A significant increase in papillary height and volume was observed across all patients, with the most pronounced improvements recorded at 3 months and sustained results at 6 months. Patients reported high satisfaction levels, with no complications such as infection, excessive inflammation, or underlying bone loss.

Conclusion: The use of hyperdiluted CaHA combined with HA filler represents a promising, minimally invasive approach for interdental papilla reconstruction. This technique offers aesthetic enhancement and patient satisfaction while preserving bone integrity. Future studies with larger sample sizes and extended follow-ups are warranted to confirm long-term efficacy and establish standardized treatment protocols.

KEYWORDS: Soft tissue augmentation, collagen biostimulation, gingival aesthetics, papilla preservation, minimally invasive dentistry

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INTRODUCTION

The absence or reduction of interdental papilla is a frequent complication resulting from periodontal disease, aging, or post-surgical tissue recession, leading to compromised aesthetics and functional concerns such as food impaction. Traditional management strategies include surgical augmentation techniques, soft tissue grafting, and the application of hyaluronic acid fillers. However, these approaches often yield variable outcomes and require invasive procedures.¹⁻⁵

Traditional management strategies for papillary loss include surgical augmentation techniques, such as subepithelial connective tissue grafts, papillary flaps, and guided tissue regeneration. While these techniques may offer partial improvement, they are often invasive, technique-sensitive, and associated with unpredictable long-term outcomes. Soft tissue fillers, including hyaluronic acid (HA), have been explored as a non-surgical alternative, providing temporary volumization. However, HA lacks biostimulatory properties and requires repeated applications to maintain results⁶⁻⁸.

Calcium hydroxylapatite (CaHA) fillers have emerged as a promising alternative due to their dual action as a volumizing agent and a collagen stimulator. Unlike traditional fillers, hyperdiluted CaHA injections initiate a regenerative cascade by stimulating fibroblast activity and neocollagenesis, leading to enhanced soft tissue volume and structural support over time. CaHA's biocompatibility and long-lasting effects make it an ideal candidate for minimally invasive interdental papillary regeneration⁹⁻¹¹.

This study investigates the combined approach of mixing hyaluronic acid filler with hyperdiluted calcium filler due to the potential of hyperdiluted CaHA as a minimally invasive solution for interdental papillary regeneration and the hyaluronic acid filler for volumization. Up to this moment there is no single study that tested the combined effect of

both products so by assessing both subjective and objective outcomes at multiple follow-up intervals, we aim to provide clinical evidence supporting the integration of this approach into contemporary periodontal and aesthetic dentistry practices.

MATERIALS AND METHODS

This study was a prospective clinical study that included 20 patients who presented with complaints of black triangles and papillary recession in relation to a natural tooth. The papillary recession was classified as Class I and II, with no evidence of bone loss. These patients sought treatment at our private clinic. Prior to their inclusion in the study, all participants provided written informed consent before enrollment, in accordance with the Declaration of Helsinki. The diagnosis and assessment of interdental papillary deficiency were based on a combination of clinical evaluation and radiographic imaging, ensuring comprehensive analysis of soft and hard tissue conditions

Inclusion Criteria

- Patients aged 25 to 55 years with visible interdental papillary loss (black triangles) in the anterior maxilla.
- Good periodontal health, with no active periodontitis or untreated dental caries.
- Adequate oral hygiene maintenance.
- Willingness to comply with follow-up visits.

Exclusion Criteria

- History of autoimmune disorders or connective tissue diseases.
- Smoking or excessive alcohol consumption.
- Previous filler injections or surgical interventions in the interdental papilla region.
- Pregnancy or lactation.
- Active oral infections or systemic conditions affecting wound healing.

Injection Protocol

Two products were utilized in this study, the first product was Radiesse® (Merz Pharmaceuticals GmbH, Germany), a calcium hydroxylapatite (CaHA)-based biostimulatory filler, while the second product was Belotero Balance® (Merz Pharmaceuticals GmbH, Germany) a hyaluronic acid filler. To enhance its distribution and reduce viscosity, the Radiesse was hyperdiluted with saline and lidocaine at a final dilution ratio of 1:2 (CaHA to saline/lidocaine mixture) while the hyaluronic acid syringe was also diluted with 1.5 ml saline to form a mesoblend. The two final diluted products were then mixed together with Lue Locker to have a single syringe containing the two diluted products (HA + CaHA). The injection was performed using a 100-unit BD insulin syringe with a 30-gauge needle, employing a micro-aliquot technique. Three injection points were designated within the interdental papillary region: the first at 3 mm from the papillary tip, the second at the distal line angle of the adjacent tooth, and the third at the mesial line angle. A total volume of 0.1 mL was distributed per the whole site. Post-injection, gentle massage with a cotton-tipped applicator was applied to ensure uniform distribution. (**Figure 1**)

Postoperative care and follow up

Patients were advised to avoid excessive manipulation of the treated area for the first 48 hours and to maintain proper oral hygiene using non-abrasive toothpaste. Follow-up assessments were scheduled at 2 weeks, 1 month, 3 months, and 6 months to monitor treatment efficacy and longevity.

Outcome Measures

(A) Objective Measures:

- **Interdental Papillary Height:** The height of the interdental papilla was assessed using a calibrated periodontal probe (e.g., UNC-15, Hu-Friedy, USA), measuring from the gingival margin to the most apical point of the contact area

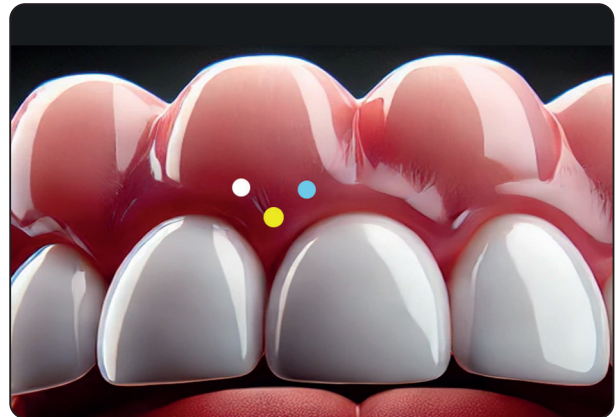


Fig (1) Original drawing using software showing the injection technique for papillary regeneration using hyperdiluted Radiesse. The diagram illustrates the three key injection points within the interdental papilla. The first injection site is marked by the yellow dot, located 3 mm from the base of the papilla. The second injection site is represented by the white dot corresponding to the mesial line angle of adjacent teeth, positioned slightly above the first site. The third injection site, marked by the blue dot, corresponding to the distal line angle of the adjacent teeth.

between adjacent teeth. To ensure measurement consistency, standardized anatomical reference points were used, and all assessments were conducted at baseline and subsequent follow-up visits by a single calibrated examiner.

- **Papillary Fill Index (PFI):** Evaluated using a standardized scoring system to determine the degree of papillary fill within the interdental space¹².

(B) Subjective Measures:

- **Patient Satisfaction Score:** A Likert scale questionnaire was used to evaluate patient perception of improvement¹¹.
- **Visual Analog Scale (VAS) for Aesthetics:** Patients rated their satisfaction with papillary enhancement on a scale from 0 to 10. Patients were asked to evaluate their level of satisfaction with papillary enhancement using a continuous scale ranging from 0 to 10. A score of 0 indicated complete dissatisfaction or no

improvement, while a score of 10 represented maximum satisfaction or the ideal result. This scale provides a simple yet effective means of quantifying patient-reported outcomes, facilitating a comprehensive understanding of the aesthetic results achieved following treatment. The VAS is widely used in aesthetic procedures due to its ease of application and the reliable data it yields in reflecting the patient's personal perception of the treatment effect¹³.

Statistical analysis

Statistical analysis was performed using SPSS software. A repeated measures ANOVA was applied to compare results at different time points. A significance level of $p < 0.05$ was considered statistically significant.

RESULTS

A total of 20 Egyptian female patients, aged between 35 and 45 years, were included in this study. All participants received treatment with the combined injectable (hyperdiluted calcium hydroxylapatite + diluted hyaluronic acid) for interdental papilla regeneration.

Patients treated with the combined injectable demonstrated noticeable improvements in interdental papilla regeneration. Over the follow-up period, objective assessments revealed a significant

increase in papillary height and a more complete interdental fill, as evidenced by higher scores on the Papillary Fill Index (PFI). The mean PFI score increased significantly compared to baseline values, with the most substantial gains observed at the two-week mark. These improvements were maintained, though a slight regression was noted at the six-month follow-up, still remaining significantly higher than pre-treatment levels.

Subjective evaluations aligned with these objective findings, as patients reported a marked enhancement in aesthetics and overall satisfaction. Participants consistently rated their smile appearance as significantly improved, with higher scores on the Visual Analog Scale (VAS) for aesthetics. The VAS scores ranged from 1 to 10, with the majority of patients rating their satisfaction between 7 and 9, reflecting a high level of satisfaction. Notably, satisfaction levels remained stable across all follow-up intervals, reinforcing the durability of the treatment outcomes.

Statistical analysis demonstrated a significant improvement across all measured parameters when compared to baseline values, with a p -value of < 0.05 . The most substantial improvements were observed at the two-week mark, and while a slight regression was noted at the six-month interval, the improvements remained significantly higher than pre-treatment levels.

TABLE (1) Changes in interdental papillary height and papillary fill index over different time intervals following hyperdiluted calcium hydroxylapatite injection. Values are presented as mean $\pm$ standard deviation (SD). A p -value of < 0.05 indicates statistical significance.

Time Interval	Interdental Papillary Height (Mean $\pm$ SD)	Papillary Fill Index (Mean $\pm$ SD)	p-value	Significance
Baseline	1.20 $\pm$ 0.17	1.50 $\pm$ 0.17	-	-
2 Weeks	1.80 $\pm$ 0.29	2.50 $\pm$ 0.29	< 0.05	Significant
1 Month	2.00 $\pm$ 0.25	3.00 $\pm$ 0.25	< 0.05	Significant
3 Months	2.10 $\pm$ 0.22	3.20 $\pm$ 0.22	< 0.05	Significant
6 Months	2.00 $\pm$ 0.13	3.00 $\pm$ 0.13	< 0.05	Significant

The treatment was well tolerated by all participants, with no major complications reported. Mild discomfort was observed in a few cases but resolved within a few days without the need for

intervention. These findings support the feasibility of hyperdiluted calcium hydroxylapatite as a minimally invasive and effective option for interdental papillary regeneration.

TABLE (2) Patient-reported satisfaction scores and Visual Analog Scale (VAS) ratings for aesthetics over different follow-up intervals after treatment. Values are presented as mean $\pm$ standard deviation (SD). A p-value of <0.05 indicates statistical significance.

Time Interval	Patient Satisfaction Score (Mean $\pm$ SD)	VAS for Aesthetics (Mean $\pm$ SD)	p-value	Significance
Baseline	3.00 $\pm$ 0.25	4.00 $\pm$ 0.25	-	-
2 Weeks	6.50 $\pm$ 0.22	7.00 $\pm$ 0.22	<0.05	Significant
1 Month	7.80 $\pm$ 0.46	8.50 $\pm$ 0.46	<0.05	Significant
3 Months	8.20 $\pm$ 0.38	9.00 $\pm$ 0.38	<0.05	Significant
6 Months	7.90 $\pm$ 0.41	8.70 $\pm$ 0.41	<0.05	Significant

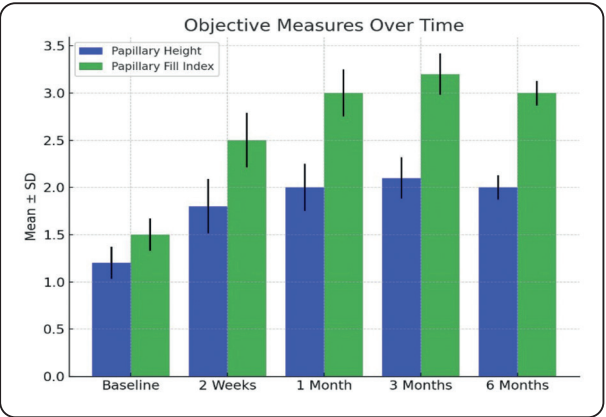


Fig. (2) Changes in interdental papillary height and Papillary Fill Index (PFI) over different follow-up intervals. Error bars represent standard deviation. Significant improvement was observed compared to baseline values ($p < 0.05$).

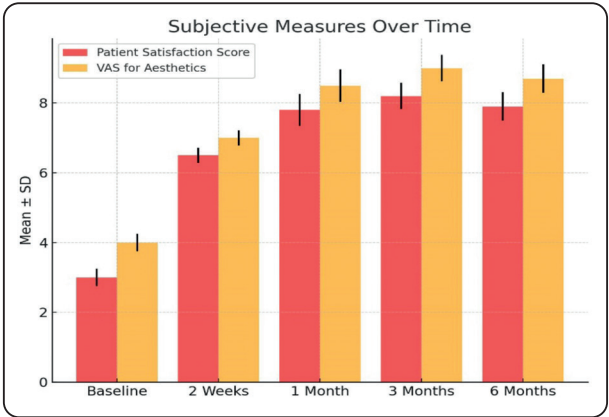


Fig. (3) Subjective assessment of patient satisfaction and Visual Analog Scale (VAS) for aesthetics across follow-up intervals. Error bars represent standard deviation. Patient-reported outcomes showed significant improvement over time ($p < 0.05$).

DISCUSSION

Interdental papilla loss is a significant aesthetic and functional issue, often arising due to periodontal disease, aging, or dental interventions. Over time, this condition can lead to a compromised smile and affect oral hygiene, resulting in a substantial decline in both aesthetic and functional quality of life. Historically, interventions for interdental papillary

loss have ranged from surgical techniques to the use of non-surgical, minimally invasive options¹⁴. Among these, injectable fillers have gained prominence as effective alternatives, offering both safety and convenience for patients. Specifically, hyaluronic acid (HA) fillers have been widely utilized for papillary volumization. However, while HA fillers provide immediate results, they offer

only temporary improvements and lack the ability to stimulate tissue regeneration over time. On the other hand, calcium hydroxylapatite (CaHA) fillers stand out for their dual benefit of immediate volumization and long-term biostimulation, providing a more durable and regenerative solution for tissue augmentation^{15,16}.

The results of this study demonstrate that the combined use of hyperdiluted CaHA and diluted HA injections significantly improved interdental papillary height and the Papillary Fill Index (PFI) over the course of the follow-up period. Notably, the increase in papillary height was evident as early as two weeks post-injection, with continued improvements observed at one and three months. Remarkably, the improvements remained stable at six months, with only minimal regression from peak values. These findings suggest that the regenerative effects of CaHA are not only immediate but also sustained, a feature that differentiates it from other fillers such as HA. The enhancement in papillary volume was coupled with subjective improvements, with patients reporting higher satisfaction and more favorable aesthetic outcomes. This corroborates the notion that injectable fillers can effectively address aesthetic concerns, with the added advantage of being minimally invasive.

The mechanism underlying the observed improvements likely involves both immediate volumization and long-term tissue remodeling. CaHA microspheres serve as a scaffold that stimulates fibroblast activity, enhancing collagen and extracellular matrix deposition. This biostimulatory effect contributes to sustained tissue augmentation and structural support, explaining the prolonged improvements seen in this study^{14,16,17}.

Our results are consistent with previous studies on HA and CaHA for soft tissue regeneration, which also highlight the potential of these materials in oral and peri-oral regions. Research on HA fillers has indicated temporary improvements in papillary volume, with effects often diminishing after three

to six months due to the natural degradation of the product. For instance, some studies found that HA fillers showed a transient increase in papillary volume, but significant reabsorption occurred within six months, necessitating repeat injections for sustained results^{18,19}.

In contrast, CaHA's biostimulatory properties provide a distinct advantage, promoting long-term collagen synthesis and soft tissue regeneration. A study supporting this finding demonstrated that CaHA injections could increase tissue volume and stimulate collagen deposition for up to 12 months in peri-oral applications. Although their research did not focus specifically on the interdental papilla, it is reasonable to assume that similar regenerative mechanisms could be occurring in the papillary region²⁰.

Furthermore, our findings are in line with those of other studies on CaHA in soft tissue augmentation. For example, research demonstrated that CaHA injections in the facial region resulted in sustained volumization and enhanced tissue elasticity. These results were attributed to the dual action of the CaHA microspheres, which not only provide immediate volume but also stimulate fibroblast activity and collagen formation. This regenerative effect likely accounts for the continued improvement in papillary height observed in our study, as CaHA provides a scaffold for tissue remodeling and supports long-term augmentation²¹.

While the present study contributes valuable data on the efficacy of hyperdiluted CaHA in papillary regeneration, it is important to consider the limitations and areas for further research. Future studies should investigate different dilution protocols and injection techniques to refine the approach and optimize clinical outcomes. Additionally, comparative studies between CaHA and other biomaterials, including emerging bioactive fillers, would provide a broader understanding of the relative effectiveness and longevity of these treatments. The integration of radiographic data and

software analysis could also enhance our ability to precisely monitor and evaluate changes in papillary volume and height. Expanding the study to include a more diverse patient population with varying periodontal conditions would further enhance the generalizability of the results. This would provide a more comprehensive perspective on the potential of hyperdiluted CaHA to address interdental papillary loss in different clinical settings.

CONCLUSION

This study highlights that the combined injection of hyperdiluted Radiesse and diluted Belotero Balance is a safe and effective minimally invasive method for promoting interdental papillary regeneration. Notable improvements in papillary height and the Papillary Fill Index, coupled with high patient satisfaction, support its volumizing and biostimulatory properties. The technique successfully preserved bone integrity while enhancing soft tissue volume, providing a promising alternative to conventional treatments. Future research with larger sample sizes and extended follow-up periods is necessary to assess long-term stability.

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