Facial Plastic Surgery & Aesthetic Medicine
Volume 00, Number 00, 2025

DOI: 10.1089/fpsam.2024.0253

Facial Plastic Surgery & Aesthetic Medicine

Open camera or QR reader and scan code to access this article and other resources online.

ORIGINAL INVESTIGATION Aesthetic

Effectiveness of an Autologous Filler in Patients with Moderate-to-Severe Nasolabial Folds: A Pilot Study

Angela Cong, BS,[1,*] LaRyel Waldon, BS,[1] Aurelio Aquila, BS,[1] Sharon Stewart, PA-C,[1] Amit Kochhar, MD,[1,2] and Kian Karimi, MD, FACS[1,*]

Abstract

Background: Nasolabial folds, commonly known as smile lines, are a cosmetic concern for individuals.

Objective: To measure the change in facial volume at the nasolabial folds among adults injected with an autologous blood filler, as measured by three-dimensional (3D) photography and aesthetic surveys.

Methods: Fifteen participants above the age of 22 received up to three autologous filler injections, to bilateral nasolabial folds, over a 24-week treatment period. Based on investigator's discretion, injections ranged from 0.6 to 3.0 cc at the initial visit, week 4, and week 16. Follow-ups were conducted at weeks 2, 6, 8, 20, and 24 with measurements completed at the beginning of each treatment and follow-up visit. Standardized 3D photography with Vectra® and QuantifiCare® cameras measured volume for before and after comparison. Patients and investigator completed the Wrinkle Severity Rating Scale and Global Aesthetic Improvement Scale.

Results: Fifteen patients, 1 male and 14 female, age 32–63, were followed-up for 24 weeks. The treatment improved nasolabial fold appearances and patient satisfaction. The 3D imaging revealed increased volume in the treated areas.

Conclusion: The autologous filler effectively fills moderate-to-severe nasolabial folds in this pilot study and future studies are needed to evaluate safety.

Introduction

Autologous treatments, using one's own cells or tissues, were initially introduced as a method for treatment in severe burn victims. They have been the cornerstone of dermatological and reconstructive therapy for subcutaneous and superficial injury for almost 30 years.[1] This approach has paved the way for innovative therapies, including skin substitutes, serum therapy, immunotherapy, fat transplantation, and platelet-rich plasma (PRP) treatments. The primary advantage of using autologous treatment is the significant reduction in adverse events (AEs) such as allergic reactions, abscesses, and granuloma formation to foreign materials.[1]

Recently, notable advancements have been made in the use of platelet-rich fibrin (PRF) over PRP. PRF was initially utilized in maxillofacial procedures, enhancing bone regeneration and soft tissue healing. This success is attributed to its application in aesthetic and regenerative treatments, including facial rejuvenation.[2,3] Injectable PRF contains essential growth factors such as platelet-derived growth factor (PDGF), transforming growth factor beta (TGF-β), vascular endothelial growth factor (VEGF),

[1]*Rejuva Medical Aesthetics, Los Angeles, California, USA.*
[2]*Pacific Neuroscience Institute, Santa Monica, California, USA.*

*Address correspondence to: *Kian Karimi, MD, Rejuva Medical Aesthetics, 11645 Wilshire Blvd. Suite 605, Los Angeles, CA 90025, USA,* Email: Kiankarimi@gmail.com

KEY POINTS

Question: Does an autologous filler, improve the appearance of smile lines with no serious adverse events?

Findings: The filler, made from the body's own blood components, restored volume to smile lines through aesthetic surverys and 3D photography.

Meaning: The findings of the study suggest effective and compounding results of the autologous filler.

epidermal growth factor (EGF), and insulin-like growth factor 1 (IGF-1).[3] With no additives and a reduced cost, PRF offers the potential for longer-lasting results, thanks to its prolonged growth factor release. PRF also forms a fibrin matrix and contains multipotent stem cell markers, enhancing its rejuvenating properties.[4] When injected into the periorbital region, it has been shown to reduce rhytids, hyperpigmentation, and improve skin texture.[5]

In 2023, 83% of plastic and reconstructive surgery treatments performed were minimally invasive, while only 17% were surgical.[6] With a growing demand for maintenance of aging and preventative treatment, there are opportunities to improve the delivery of aesthetic facial care with more cost-effective and longer-lasting technology. Autologous filler emerges as a promising solution. ezGEL (CosmoFrance, Miami, USA) is a biostimulating serum that combines PRF and heated albumin to create a 100% autologous filler for patients.[7] It offers natural rejuvenating properties through the subject's own blood and has been used to restore volume loss to the under-eye area and other hollows. With the increased market potential of autologous treatments, it is crucial to understand the encompassing side effects. In this study, we sought to measure the change in nasolabial fold volume among patients before undergoing injection of an autologous filler compared with after the injection, as measured by three-dimensional (3D) photography and standard aesthetic rating systems.

Materials and Methods

Consent and compensation

This study (protocol #CLN-PRF-NLF) was approved and reviewed by the Allendale IRB to ensure compiance with applicable regulations, common ethical standards, and adequate research participant protection. Subjects signed study consent and photo release forms prior to study-related activities. In study compensation, subjects received $60 for in-person visits and $100 for treatments.

Inclusion and exclusion criteria synopsis

Inclusion criteria required subjects to be previously healthy, English speaking, age >22 years old, and have grade 3 (moderate) to 4 (severe) nasolabial fold depth based on the Wrinkle Severity Rating Scale (WSRS) that was performed by the principal investigator (PI) at the first visit. Additionally, subjects were asked to maintain their body weight within 10% of baseline during the study to prevent confounding of 3D analysis. Exclusion screenings for significant medical conditions or diseases that would put subjects at undue risk or compromise study integrity were done based on the PI's judgment. Exclusion criteria included a history or presence of a skin condition/disease in the treatment area, such as connective tissue diseases, atopic dermatitis, psoriasis, and open wounds. Tendency to form keloids, hypertrophic scars, or pigmentation disorders were excluded. Prior history of facial plastic surgery, tissue augmentations with absorbable substances, bleeding disorders, or current uses of anticoagulant/thrombolytic medications within 10 days preinjection and 3 days postinjection were excluded. Subjects also were not allowed to have facial dermal filler, microneedling, botulinum toxin, dermabrasion, or mesotherapy in the treatment area within the last 12 months.

Study protocol

The autologous filler was injected into the patient's nasolabial folds. Subjects refrained from aesthetic and surgical treatments to this area for the duration of the study and used routine skin care and makeup products. All subjects were offered the same product and treatment regimens.

This was a 24 week, single-institution, open-label study. Fifteen subjects met the criteria and were enrolled. The study consisted of nine in-person visits and three phone call assessments. During the screening (visit 1-day 0), the PI assessed the nasolabial folds using the WSRS scale to determine eligibility. Visits 1 and 2 both occurred on day 0. In-person assessments included urine pregnancy tests, digital photographs, vital signs, and subject evaluations with questionnaires. 3D imaging and assessments were given at the beginning of each visit, prior to treatment and touch ups. Treatment occurred on day 0 with an optional touch-up treatment at weeks 4 and 16 as deemed necessary by the investigator and subject agreement. A safety phone call assessment was conducted 3 days after each treatment and touch-up visit to screen for AEs and changes in medication. All other in-person visits at weeks 2, 6, 8, 20, and 24 were conducted for progress and satisfaction assessments.

Preparation of autologous filler

A 23 gauge butterfly needle was used to draw blood into two separate 13 mL CosmoFrance ezPRF tubes for an average collection of 26 mL. The PRF and albumin collected varied based on patient anatomy and hydration levels. Tube 1 was spun via the EZminispin centrifuge device with a counterweight at 2600 RPM for 7 min to collect serum proteins. Tube 2 was placed in the EZ cool

bath to prevent coagulation. Albumin from tube 1 was then collected into a 5 mL heat-proof syringe and heated within the EZHEAT heat block at 75°C for 10–14 min. Tube 2 was spun in the centrifuge with a counterweight at 1100 RPM for 5 min. PRF was drawn up into a syringe and placed in the cool bath. A 3.5 cc heated albumin to 0.5 cc PRF ratio was mixed via a luer-to-luer connector and transferred into 1 mL syringes. The remaining PRF and hematocrit contents stored in the cool bath were discarded in appropriate sharps containers.

Injection of autologous filler

The treating investigator (S.S., Natalia Guzman, and K.K.) made a port with a 23G DermaSculpt (Cosmo-France, Miami, FL) hypodermic needle on each lateral cheek in the perioral region. The autologous filler was injected with the paired 25G DermaSculpt cannula on a 1 mL syringe. Injection amounts ranged from 1 to 2 cc, depending on the subjects' needs and the investigator's assessment. Average baseline injection was 1.93 cc per nasolabial fold. Fourteen subjects received touch up injections at week 4 with an average of 1.76 cc per nasolabial fold, and at week 16 with an average of 1.66 cc per nasolabial fold. Autologous filler was also injected with a McKesson (McKesson, Irving, TX) 27G hypodermic needle on a 1 mL syringe based on the investigator's assessment of the nasolabial folds. Autologous filler was injected into the subcutaneous, subdermal, and periosteal planes of the nasolabial folds depending on investigator's injection technique and subjects' anatomy.

Wrinkle Severity Score and Global Aesthetic Improvement Scale

The average Wrinkle Severity Score (WSRS) was compiled from both the left and right side assessments of patients' faces. This scale objectively measures depth and severity of wrinkles ranging from 1 (least severe) to 5 (most severe). The Global Aesthetic Improvement Scale (GAIS) was also compiled from both the left and right side assessments of the patients' face. This is rated on a 5 point scale: 0 = much worse; 1 = worse; 2 = no change; 3 = improved; 4 = much improved. Treating investigator and patients indicated their responses on both scales. Baseline WSRS measurements were taken before treatment began and GAIS was used starting at the first follow-up assessment.

3D imaging

Vectra® 3D Analysis Module (VAM) (Canfield Scientific, Parsippany, NJ) was utilized for photographic documentation and midfacial volume instrumental evaluations. The system facilitated the capture of 3D images, enabling comprehensive analysis of facial features and volume changes over time. To compare images captured at different time points, the VAM was employed, ensuring accurate and reliable data interpretation.

QuantifiCare LifeViz® Infinity 3D (QuantifiCare Inc, Suwanee, GA) imaging system was utilized to assess the 3D morphology and surface characteristics of the skin. This advanced imaging device provided a reliable and precise method for capturing and analyzing the 3D structure of the skin, enabling a comprehensive assessment of the treatment effects.

Standardized methods of uniform subject distance and illumination intensity were implemented to maintain consistency and comparability across images. Subjects also cleansed their skin prior to imaging to remove any makeup, oils, or debris that might interfere with the imaging process.

Results

Patient satisfaction

Patient satisfaction was assessed using the GAIS during in-person evaluations (Table 1). At the primary study endpoint, which occurred at the last study visit, the GAIS results showed:

- 46% of patients reported "Very Much Improved"
- 30.8% of patients reported "Much Improved"
- 15.4% of patients reported "Improved"
- 7.7% of patients reported "No change"

The data showed a progressive decrease in the WSRS with each treatment. Pretreatment bilateral nasolabial fold was moderate (mathematical average of 2.2). At the primary study endpoint, the average WSRS was mild (mathematical average of 0.75) (Fig. 1).

Volume enhancement

Advanced diagnostic tools from VAM and QuantifiCare LifeViz Infinity 3D viewer + revealed a notable increase in volume in the treated areas, contributing to the overall reduction in the appearance of nasolabial folds as demonstrated in Figure 2, Figure 3.

Statistical analysis

The analysis of variance (ANOVA) test yielded an F-statistic of 2.863 and a statistically significant p-value of 0.032 (Table 2). The changes in volume from baseline across the different weeks are not uniform. The average volume increase is highest from baseline to week 16 at 1.312 cc, and the lowest average volume increase is from baseline to week 20 at 0.638 cc (Figure 4).

AEs and protocol deviations

The study had one reported AE. The subject contracted COVID-19 during the study timeline and experienced prolonged swelling up to 2 weeks after injection. Treatment for swelling was provided at no cost.

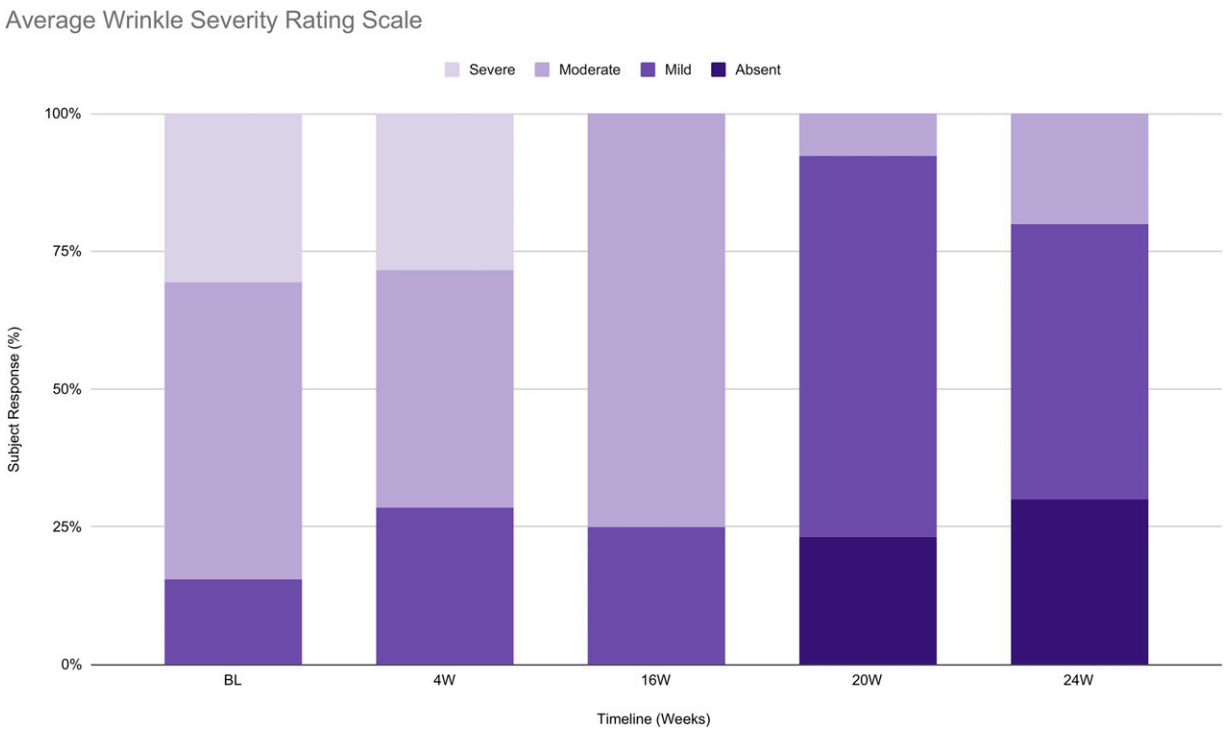

Fig. 1. Average Wrinkle Severity Rating Scale (WSRS) scores were obtained from investigator assessments of both the left and right nasolabial folds over the course of the study. The WSRS scores were calculated by averaging the severity of wrinkles observed on each side of the face at baseline (BL) and at follow-up appointments: 4 weeks (4W), 16 weeks (16W), 20 weeks (20W), and 24 weeks (24W) post initial treatment.

Protocol deviations included excessive missed visits from three subjects. Subjects with insufficient data (i.e., missed visits) were excluded from statistical analysis. All subjects received safety follow-up phone calls regardless of the number of protocol deviations to document any AEs or changes to medication.

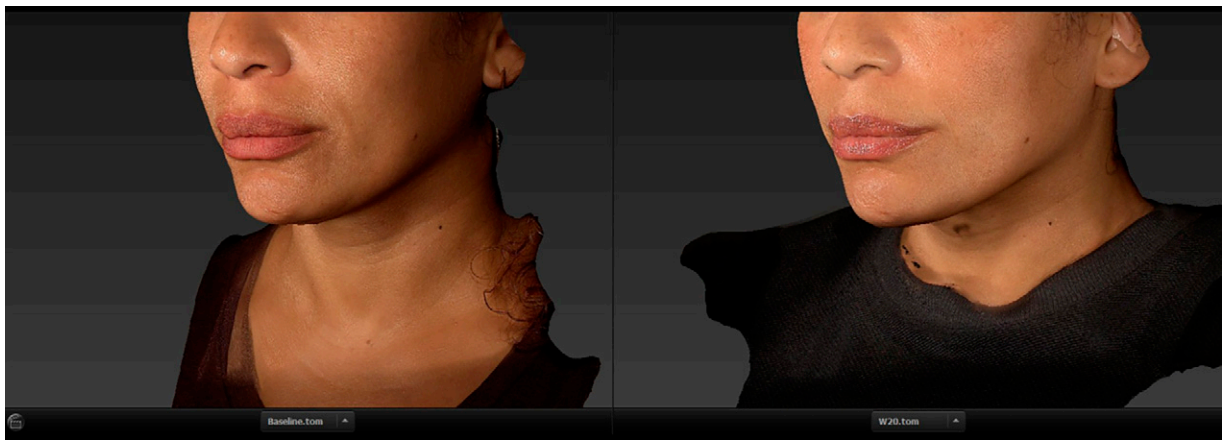

Fig. 2. Visual comparison of the nasolabial folds 20 weeks from baseline using the Vectra® 3D Analysis Module (VAM). The baseline image (left) is compared with the image taken 20 weeks postinitial treatment (right). The subject received one initial autologous filler treatment and two touch-up treatments according to the study protocol, showing a visible decrease in the nasolabial folds.

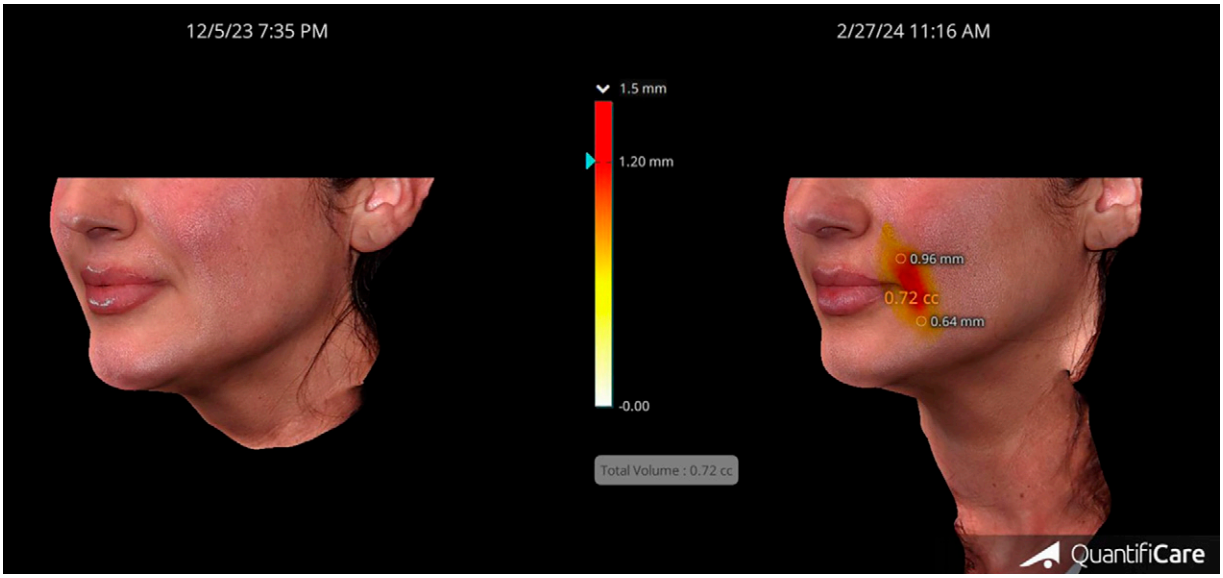

Fig. 3. Comparison of volumetric measurements taken 12 weeks from baseline using the QuantifiCare LifeViz® Infinity 3D viewer. At 12 weeks, the subject received one initial autologous filler treatment and one touch-up treatment according to the study protocol. The baseline image (left) is compared with the image taken 12 weeks postinitial treatment (right), with volume assessments displaying a 0.72 cubic centimeters (cc) change.

Discussion

The primary focus of this study was to evaluate the effectiveness of autologous filler as a biostimulant filler for the reduction of moderate-to-severe nasolabial folds. The findings affirm the autologous filler is an effective treatment option, with no significant AEs directly attributable to the treatment itself. Notably, one reported AE was likely related to an external factor (COVID-19) and

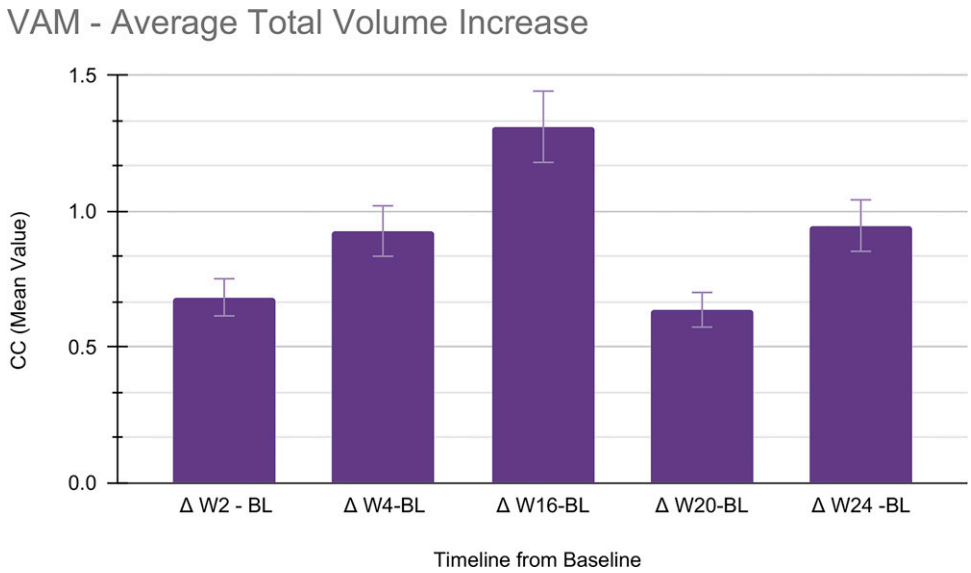

Fig. 4. Instrumental evaluation of nasolabial fold volume by Vectra® 3D Analysis Module (VAM) facial volume imaging analysis. The figure shows the average increase in total volume (cc) from baseline to time points at 2, 4, 16, 20, and 24 weeks.

Table 1. The baseline characteristics and demographic data of 15 subjects enrolled in the study, including follow-up duration and wrinkle severity scores

Characteristic	*Left side*	*Right side*	p-*Value*
Total patients	15	15	
Gender (n = %)			1
Male	1 (6.7%)	1 (6.7%)	
Female	14 (93.3%)	14 (93.3%)	
Age (years)			1
Mean	47.67	47.67	
Median	46	46	
Range	32–63	32–63	
Follow-up (weeks)			N/A
Mean	14	14	
Median	12	12	
Range	4–24	4–24	
Wrinkle severity at baseline (n = %)			
Absent (1)	0	0	
Mild (2)	1 (6.7%)	2 (13.3%)	
Moderate (3)	8 (53.3%)	8 (53.3%)	
Severe (4)	6 (40%)	5 (33.3%)	
Extreme (5)	0	0	
Mean severity score	3.33	3.2	0.78

Gender distribution was compared using the chi-square test for independence. A permutation test was performed for wrinkle severity score comparisons between the left and right sides. p-Values are included to assess statistical significance between the left and right nasolabial fold areas at baseline.

overactive immune response rather than the treatment procedure or the composition of autologous filler. The AE resolved without sequelae. This indicates a potential safety profile for autologous filler, particularly in the context of autologous treatments where compatibility with the patient's body is significant. Further studies are needed to validate the safety profile.

These findings are consistent with prior reports referenced in the introduction section. The sustained release of growth factors and the 3D fibrin network of injectable PRF supports tissue regeneration as confirmed with literature. As demonstrated in this pilot study, incorporating PRF with heated albumin in autologous filler has a potential role in correcting moderate-to-severe nasolabial folds.

Results effectively demonstrated significant improvements in nasolabial fold appearance at the 6-week posttreatment mark. This short-term effectiveness is vital in showcasing the immediate benefits of autologous filler in reducing wrinkle severity and restoring volume. The data supports the cumulative and progressive effects, while indicating a level of variability in compounding effects. Patients experienced continuous improvement and satisfaction exhibited by GAIS and WSRS measurements. Substantial proportions of patients and treating investigator reported "Much Improved" and "Improved" on the GAIS with nearly all (92.3%) of the participants experiencing improvement by 20 weeks. This demonstrates the majority of patients observed noticeable enhancement in their appearance.

To continue, volumizing effects are more pronounced around week 16, and less at week 20. The significant ANOVA result suggests the autologous filler has a differential effect on volume increase from baseline to various time points, not due to random chance. Interestingly, patients and investigator reported the highest levels of satisfaction (i.e., WSRS and GAIS results) at the 20- and 24-week time points despite not experiencing the most significant average volume increase at these time points. This finding suggests volume increase alone may not be the sole determinant of aesthetic improvements and PRF growth factors contribute a key component. PRF stimulates tissue regeneration and collagen production in injected areas over time. Improved Wrinkle Severity Scores and overall GAIS ratings are likely due to biostimulating effects of PRF in autologous filler. Thus, visible effects of tissue regenerative and collagen production appear at 20 and 24 weeks postinjection.

Additionally, despite only injecting the autologous filler to the NLF and not the midface, some patients experienced an overall lifting effect in the midface. This lifting effect likely further corrects nasolabial folds, enhances facial contour and structure, leading to higher satisfaction rates. This highlights the importance of targeted placement and suggests clinicians should focus on volume and strategic enhancement of facial features to achieve optimal results. However, the lifting aspect of the treatment's impact was not systematically measured. Future studies should collect and analyze data on the lifting effects in the midface to better clarify their contribution to patient satisfaction and overall aesthetic outcomes. Understanding nasolabial fold improvement over time and the need for additional maintenance treatments would also provide valuable information to clinicians.

While the study provided valuable insights into the short-term effects of this autologous filler, the data must be interpreted in the context of the study design. This single center pilot study had a total of 15 participants within a 24-week timeline. An increase in the study population would further solidify the statistical significance of the present results. Diversifying the patient population to include more males also allows for broader applications.

Table 2. The results of the ANOVA test, which assesses the significance of differences in mean volume increase between various timeframes

ANOVA

Source of variation	*SS*	*df*	*MS*	*F*	p-*Value*	*F crit*
Between groups	3.46	4	0.86	2.863	0.032	2.54
Within groups	16.60	55	0.30			
Total	20.06	59				

The groups are the timeframes: BL-W2, BL-W4, BL-W16, BL-W20, BL-W24.

ANOVA, analysis of variance.

Lastly, longitudinal studies with extended follow-up periods could shed light on the longevity of the autologous filler's effects and continued safety. This study sets the stage for broader applications of this treatment in aesthetic medicine. Traditional hyaluronic acid filler has numerous usages, including facial balancing in patients with facial paralysis.[8] It's also worth exploring autologous filler in these facets, broadening options for patients with varying needs.

In conclusion, autologous filler shows improvement in restoring volume as a treatment for moderate-to-severe nasolabial folds, without significant AEs. High patient satisfaction indicated by GAIS scores and significant aesthetic improvements were noted particularly at the 20-week mark. The average Wrinkle Severity Score (WSRS), which progressively decreased with treatment sessions, underscores the cumulative effect of the autologous filler injections in reducing wrinkle depth and severity over time. Furthermore, the statistical analysis supports these findings, confirming the effectiveness of the autologous filler. Investigating other factors such as the frequency dosage and patient characteristics might help explain the observed variations in volume increases. Autologous treatments also vary in the amount of growth factors per patient. Future directions may include quantifying PRF levels in the autologous filler samples and standardizing the texture of the gel. This may be explored using QC tests with a viscometer to compare the viscosity of autologous filler to other injectable autologous treatments.

Authors' Contributions

A.C.: Writing—original draft, writing—review and editing. L.W.: Data curation, formal analysis, investigation, methodology, project administration, resources, supervision, validation, visualization, writing—original draft, writing—review and editing. A.A.: Writing—review and editing. A.K.: Investigation, supervision, writing—review and editing. S.S.: Data curation, investigation, supervision, writing—review and editing. K.K.: Conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, supervision, validation, visualization, writing—original draft, writing—review and editing. All co-authors have reviewed and approved the article prior to submission.

Author Disclosure Statement

K.K. is the medical director of CosmoFrance, which manufactures and distributes PRF centrifuges and blood collection tubes. A.C., L.W., A.A., S.S., and A.K. have no financial conflicts of interest or disclosures relating to this study.

Funding Information

This study was supported, in part, by CosmoFrance.

References

1. Kumar S, Mahajan BB, Kaur S, et al. Autologous therapies in dermatology. *J Clin Aesthet Dermatol.* 2014;7(12):38–45.
2. Choi YJ, Kim HS, Nam JH, et al. A clinical study of the usefulness of autologous plasma filler in the treatment of NLF wrinkles. *J Cosmet Laser Ther.* 2017;19(3):174–180; doi: 10.1080/14764172.2016.1248443
3. Shashank B, Bhushan M. Injectable PRF: The newest biomaterial and its use in various dermatological conditions in our practice: A Case series. *J Cosmet Dermatol.* 2021;20(5):1421–1426; doi: 10.1111/jocd.13742
4. Pourang A, Rockwell H, Karimi K. New frontiers in skin rejuvenation, including Stem Cells and autologous therapies. *Facial Plast Surg Clin North Am.* 2020;28(1):101–117; doi: 10.1016/j.fsc.2019.09.009
5. Ahmadi Mahmoodabadi R, Golafshan HA, Pezeshkian F, et al. Evaluation of the effect of platelet rich fibrin matrix in the correction of periorbital wrinkles: An experimental clinical trial. *Dermatol Pract Concept.* 2023; 13(1):e2023050; doi: 10.5826/dpc.1301a50
6. *American Academy of Facial Plastic and Reconstructive Surgery, inc.* American Academy of Facial Plastic and Reconstructive Surgery. February 1, 2024. Available from: https://www.aafprs.org/Media/Press_Releases/2024_02_01_PressRelease.aspx?WebsiteKey=5d3e122f-6cba-47ca-a903-c75cb1c94f61
7. *The autologous bio-stimulatinggel.* ezGEL · Autologous Biostimulating Serum. n.d. Available from: https://ezgel.net/
8. Liu RH, Yau J, Derakhshan A, et al. Facial filler in facial paralysis: A prospective case study and Multidimensional assessment. *Facial Plast Surg Aesthet Med.* 2024;26(4):426–430; doi: 10.1089/fpsam.2023.0048