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Evaluation of Injectable Platelet-rich Fibrin (i-PRF) as an Autologous Tissue Regenerator in Facial Aesthetics

Fernanda Pirossi Brodt [a*], Roberto Puertas Garcia [b*], Michelle Fechine Costa [c], Carolyne Martins De Marchi [d], Paulo Roxo Barja [e], Anelise Cristina Osorio Cesar Doria [a], Gisele Rosada Donola Furtado [f], Kledson Lopes Barbosa [f] and Josne Carla Paterno [a]

[a] University of Paraiba Valley, Sao Paulo, Brazil.
[b] Research Support Foundation – FAPES, São Paulo, Brazil.
[c] University of Manchester, England.
[d] University of Sao Paulo, Bauru Campus, Brazil.
[e] University of São Paulo, Brazil.
[f] International Association of Orofacial Harmonisation – ASSIHOF, Sao Paulo, Brazil.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Cutaneous ageing, an inherent process with advancing time, often detrimentally impacts self-esteem due to manifestations like wrinkles, blemishes, dehydration, sagging, and reduced tissue vitality. A contemporary trend seeks natural approaches to facial rejuvenation.

**Corresponding author: E-mail: fernandabrodt@yahoo.com.br;*

Injectable Platelet-Rich Fibrin (i-PRF) emerges as a noteworthy solution owing to its biological origin and autologous nature.

Materials and Methods: Evaluating i-PRF's efficacy in counteracting ageing signs, we employed a 16 MHz high-frequency ultrasound device and meticulous photographic documentation. 26 females, aged 35-55, underwent three i-PRF sessions. Statistical scrutiny utilised a paired t-test ($\alpha = 0.05$) to assess dermal modifications. Self-Perception Index scores underwent Wilcoxon testing ($\alpha = 0.05$) for significant enhancements. Comparisons of newly captured frontal and profile photographs (D and E) with initial images aided visible change assessment.

Results and Discussion: Compelling data analysis evidenced a notable dermal thickness increase post-intradermal i-PRF application. P-values for examined regions were: glabella ($P < .00269$), frontal D ($P < .00018$), frontal E ($P < .00014$), cheek D ($P < .00709$), and cheek E ($P < .0008$). These results underscore substantial dermal thickness alterations. Statistical examination of the Self-Perception Index yielded a P-value < .0001, signifying significant self-perception change post-treatment. Conclusion: Intradermal i-PRF application markedly increased dermal thickness, endorsing its potential for dermal restructuring. Furthermore, this approach presents an accessible, cost-effective, and unbiased alternative for facial rejuvenation.

Keywords: Platelet-rich Fibrin; tissue regeneration; autologous tissue; ageing; rejuvenation; facial aesthetics; ultrasound.

1. INTRODUCTION

The skin, comprising 16% of body weight, is essential for protection, nourishment, pigmentation, insulation, and sensory functions [1]. Collagen, an insoluble fibrous protein in the connective tissue, imparts strength and resilience [2]. Constituting 25-30% of body proteins, collagen maintains skin elasticity [3]. Collagen production declines with age, leading to cutaneous ageing [4].

Cutaneous ageing results from intrinsic and extrinsic factors [5]. Intrinsic factors involve cellular wear and tear, while extrinsic factors encompass UV exposure, pollution, smoking, alcohol, and lifestyle choices [5]. This process leads to morphological, physiological, and molecular changes at cellular, histological, and anatomical levels [6].

Excessive sun exposure degrades collagen, causing wrinkles [7]. The Telomere hypothesis links cellular ageing to fibroblast telomere loss [8,9].

Aesthetic practices often fall short [10]. Platelet concentrates with abundant growth factors aids tissue repair and rejuvenation. Platelet-derived growth factors trigger fibroblast activities [11].

Platelet-Rich Plasma (PRP) aids regeneration [6,12,13]. PRP is obtained through double centrifugation, but limited leukocytes impede healing [14]. Platelet-Rich Fibrin (PRF) enhances PRP, devoid of chemicals [15].

PRF, a second-gen platelet concentrate, supports tissue engineering [15]. Known as L-PRF, it provides cells, growth factors, and a scaffold [15]. High-force centrifugation yields a dense fibrin matrix [16,17]. A-*PRF utilises low force, producing a porous matrix [18,19].*

iPRF was introduced by Mourão et al. (2015) and comprehensively explained by Miron et al. (2017) and Wang et al. (2018). Plastic tubes and centrifugation modifications slow coagulation [16,20]. i-PRF, suitable for facial rejuvenation, allows extended working time [21,22].

Fibrin matrix captures and releases growth factors for tissue healing [11,16,23]. Fibrin's sustained action leads to increased growth factor concentrations [24]. i-PRF from autologous blood enhances safety [16].

Blood centrifugation activates platelets, releasing growth factors for cell migration and proliferation [25]. Transforming growth factor-beta 1 (TGF-1), platelet-derived growth factor (PDGF), and others contribute to regeneration [15,26].

i-PRF reported in various healthcare fields [10,27,28]. Limited data exist on i-PRF in facial rejuvenation [10,29]. This study assesses i-PRF's impact on facial rejuvenation using objective analysis, self-perception, and photos.

Facial aesthetics benefit from platelet concentrate growth factors, promoting skin rejuvenation [29]. This study evaluates i-PRF's intradermal application for dermal restructuring and aesthetic enhancement across the face.

2. MATERIALS AND METHODS

The study involved 26 participants at the University of Vale do Paraiba and Ciclo Oral Odontologia Ltda clinic from November 2021 to August 2022. The study adhered to WHO's COVID-19 protocols, ensuring safety measures like mask usage, hand hygiene, disinfecting with 70% alcohol, and temperature screening.

Inclusion criteria focused on females aged 35 to 55 exhibiting signs of facial ageing such as wrinkles, sagging, radiance loss, and dermal thinning. Exclusion criteria comprised conditions like pregnancy, allergies to pre-procedure ointment (dermomax), lactation, neoplasms, anaemia, diabetes, deep venous thrombosis, autoimmune diseases, infections, recent botulinum toxin or filler use, dermatological conditions at the treatment site, tanned skin, recent surgeries (within 30 days), and use of NSAIDs, antibiotics, or anticoagulants.

Participants received three intradermal i-PRF sessions spaced 21 days apart. Standardised photographs captured frontal and profile views. A self-perception questionnaire gauged skin quality and improvement perception. A Self-Perception Index assigned values (0 or 1) to responses, with a score range of zero to four, evaluating improvements.

Ultrasound examined facial areas using a 16 MHz linear transducer to measure dermal thickness. Initial and final measurements were analysed.

Participants applied Dermomax anaesthetic cream before venous puncture. Six tubes of whole blood were collected and processed by centrifugation (2700 rpm/700g RCF, 3 min). The "buffy coat" area (1.5 ml/tube) was collected, yielding 9 ml. Infiltrate (i-PRF) was isolated, transferred, and face-treated using intradermal injections (1 ml/region).

Post-procedure instructions included area manipulation avoidance for 12 hours, sun/temperature exposure for seven days, and no anti-inflammatory drugs for seven days. SPF 30 sunscreen use for 30 days, makeup abstention for 24 hours, and other recommendations were advised.

After the final session, ultrasound measured dermal thickness after 21 days. Paired t-tests analysed measurements; the Wilcoxon test evaluated Self-Perception Index scores. New photographs were compared with the initial ones, assessing outcomes through visual and graphical analysis.

3. RESULTS AND DISCUSSION

The participants underwent the described procedures without experiencing any complications during the treatment.

Dermal thickness measurements were conducted using a 16 MHz ultrasound in the glabella, right (R) and left (L) frontal regions, and from the tragus to the corner of the mouth (cheek) on the right (R) and left (L) sides. These measurements were taken before initiating the treatment and 21 days after the third session. Figs. 1A and 1B visually display the increase in superficial dermal thickness, appearing as hypoechoic (grey), and deep dermal thickness, appearing as hyperechoic (white). All the areas measured and analysed are presented in Tables 1 and 2. A paired t-test was applied for statistical analysis using the initial value (dermal thickness before the treatment) and the final value (dermal thickness 21 days after the third session). The null hypothesis (H0) assumed no difference in dermal thickness before and after the application, while the alternative hypothesis (H1) indicated a significant change in dermal thickness 21 days after the third session. The paired t-test assumes a normal distribution of values and employs a two-tailed model with a significance level set at $P < .05$. The test results (P-values) for the glabella region ($P < .00269$), right frontal area ($P < .00018$), left frontal region ($P < .00014$), tragus to the corner of the mouth (cheek) on the right side ($P < .00709$) and left side ($P < .0008$) indicate highly significant alterations in dermal thickness in these regions.

Furthermore, the statistical analysis conducted on the Self-Perception Index yielded a P-value of less than .0001, indicating a highly significant change in participants' self-perception after the treatment.

Figs. 1A and 1B present the results of the ultrasonography measurements. In Fig. 1A, the dermal thickness measured before the start of the treatment was 2.41 mm, while in Fig. 1B, the dermal thickness measured 21 days after the third treatment session increased to 3.35 mm. The observed increase in dermal thickness indicates a positive response to the treatment, as visually depicted in the images.

Table 1. Glabella measurements, right frontal(D) and left (E)

	Pre-application mm	Post-application mm	Variation	%	Pre-application mm	Post-application mm	Variation	%	Pre-application mm	Post-application mm	Variation	%
1	2,13	3,84	1,71	0.8	1,93	2,43	0,50	0.26	1,69	2,22	0,53	0.31
2	2,24	2,39	0,15	0.07	1,94	2,08	0,14	0.07	1,77	2,05	0,29	0.16
3	1,92	2,56	0,64	0.33	1,79	2,45	0,66	0.37	1,66	2,22	0,56	0.34
4	1,60	3,02	1,42	0.89	1,74	2,45	0,71	0.41	1,64	2,05	0,42	0.25
5	1,89	3,02	1,13	0.6	1,85	2,24	0,39	0.21	1,18	1,76	0,58	0.49
6	2,29	3,45	1,16	0.51	2,26	2,54	0,28	0.12	2,52	2,40	-0,12	-0.05
7	2,08	2,23	0,15	0.07	2,12	1,86	-0,26	-0.12	1,92	2,19	0,27	0.14
8	1,87	2,57	0,7	0.37	1,75	1,69	-0,06	-0.04	1,38	1,70	0,32	0.23
9	1,52	2,95	1,43	0.94	1,26	2,28	1,02	0.81	1,25	2,62	1,37	1.1
10	1,68	2,51	0,83	0.49	1,67	1,90	0,23	0.13	1,97	2,42	0,45	0.23
11	1,85	2,97	1,12	0.61	1,49	2,01	0,52	0.35	1,69	1,93	0,24	0.14
12	1,76	2,33	0,57	0.32	1,80	2,27	0,47	0.26	1,67	2,06	0,39	0.23
13	2,13	2,26	0,13	0.06	1,47	1,91	0,44	0.3	1,83	2,23	0,40	0.22
14	2,05	1,98	-0,07	-0.03	1,77	2,04	0,27	0.15	1,79	1,92	0,13	0.07
15	2,05	2,13	0,08	0.04	1,48	1,78	0,30	0.2	1,83	1,66	-0,17	-0.09
16	2,44	2,61	0,17	0.07	1,92	1,98	0,06	0.03	1,76	1,88	0,12	0.07
17	2,48	2,24	-0,24	-0.1	1,72	2,37	0,65	0.38	1,75	1,76	0,01	0.01
18	2,29	2,21	-0,08	-0.03	1,78	1,74	-0,04	-0.02	1,51	1,67	0,16	0.11
19	1,98	1,83	-0,15	-0.08	1,54	1,82	0,29	0.19	1,60	1,74	0,14	0.09
20	2,53	2,18	-0,35	-0.14	1,65	1,98	0,33	0.2	1,49	1,96	0,47	0.32
21	2,33	1,98	-0,35	-0.15	1,84	1,85	0,01	0.01	1,69	1,69	0,00	0
22	2,1	2,51	0,41	0.2	1,97	2,16	0,20	0.1	1,98	2,22	0,24	0.12
23	2,26	1,9	-0,36	-0.16	2,08	1,89	-0,19	-0.09	2,05	1,85	-0,20	-0.1
24	2,01	2,28	0,27	0.13	2,15	2,08	-0,07	-0.03	1,92	2,02	0,10	0.05
25	1,7	1,72	0,02	0.01	1,74	1,99	0,26	0.15	1,46	1,68	0,22	0.15
26	2,38	2,31	-0,07	-0.03	2,36	2,21	-0,16	-0.07	1,90	2,12	0,22	0.12
	Average		**0,40**	**22%**	**Average**		**0,27**	**17%**	**Average**		**0,27**	**18%**
	Variance		**0,38**	**11%**	**Variance**		**0,10**	**4%**	**Variance**		**0,10**	**5%**
	DP		**0,61**	**33%**	**DP**		**0,31**	**20%**	**DP**		**0,31**	**23%**

Source: The author (2022)

Table 2. Tragus mouth corner (cheek), right (D) and left (E)

P	Right Mouth Tragus				Left Mouth Tragus			
	Pre-application mm	**Post-application mm**	**c**	**%**	**Pre-application mm**	**Post-application mm**	**Post-application mm**	**%**
1	2,46	3,09	0,64	26%	2,63	3,24	0,62	23%
2	1,74	1,65	-0,09	-5%	1,95	1,99	0,03	2%
3	1,94	2,27	0,33	17%	1,79	2,30	0,51	28%
4	2,41	3,35	0,94	39%	2,00	3,18	1,18	59%
5	1,40	1,70	0,30	21%	1,55	1,92	0,37	24%
6	2,72	2,91	0,19	7%	2,35	3,20	0,85	36%
7	2,07	2,23	0,16	8%	1,84	2,17	0,33	18%
8	1,54	1,81	0,28	18%	1,62	1,99	0,37	23%
9	1,61	2,21	0,61	38%	1,64	2,43	0,79	48%
10	1,79	1,96	0,17	9%	1,84	2,02	0,18	10%
11	1,58	2,04	0,47	30%	1,69	2,28	0,60	35%
12	1,76	2,05	0,29	16%	1,40	2,15	0,75	54%
13	2,08	2,45	0,37	18%	1,84	1,86	0,02	1%
14	2,47	2,52	0,05	2%	2,36	2,10	-0,27	-11%
15	2,00	2,17	0,17	8%	1,74	1,99	0,26	15%
16	2,34	1,86	-0,48	-20%	1,86	1,99	0,14	7%
17	2,13	2,62	0,49	23%	2,35	2,19	-0,16	-7%
18	2,22	2,07	-0,15	-7%	2,12	1,93	-0,20	-9%
19	1,88	1,96	0,08	4%	2,03	1,96	-0,07	-3%
20	2,23	2,07	-0,16	-7%	2,03	2,17	0,14	7%
21	2,22	2,02	-0,20	-9%	2,12	2,24	0,12	6%
22	2,60	2,35	-0,25	-10%	2,18	2,34	0,16	7%
23	1,93	1,96	0,03	2%	2,24	2,04	-0,20	-9%
24	2,03	1,97	-0,07	-3%	2,30	2,50	0,20	8%
25	1,75	1,94	0,19	11%	1,50	1,63	0,13	8%
26	1,84	2,14	0,30	16%	1,82	1,99	0,18	10%
	Average		**0,18**	**10%**	**Average**		**0,27**	**15%**
	Variance		**0,10**	**2%**	**Variance**		**0,13**	**4%**
	DP		**0,31**	**15%**	**DP**		**0,36**	**19%**

Source: The author (2022)

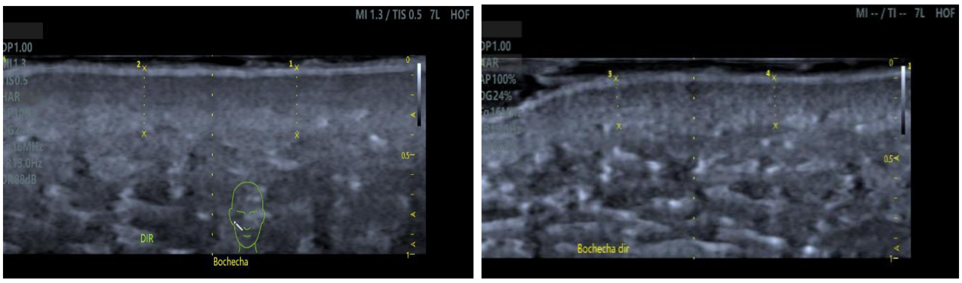

Fig. 1A and 1B: Results of the ultrasonography measurements
Source: The author (2022)

Figs. 2A and 2B illustrate the observed improvements in these aesthetic aspects
Source: The author (2022)

The photographic documentation provided a subjective visual assessment of the treatment's efficacy in addressing various signs of ageing, including wrinkles, sagging, loss of radiance, reduction in pore size, and overall skin quality.

The graphical representations of the relative final signals in the analysed areas (Figs. 3 to 7) precisely visualise the treatment's effectiveness by quantifying the increase in dermal thickness. These graphs display the relative final signal for each participant, obtained by dividing the last signal by the initial signal, along with a visual guideline at a value of 1 and a dashed line representing the final normalised average value for the entire participant group. Based on the comprehensive analysis, it was observed that the administration of three sessions of intradermal i-PRF resulted in a significant increase in dermal thickness and an overall improvement in skin condition.

Fig. 3. Relative final signs of the Glabella region before and after the procedure. The straight line represents the normalised initial signal (value 1), and the dotted line is the corresponding average final signal for each volunteer (value 1.22); the points represent the normalised final signal for each volunteer.

Fig. 4. Relative final signs of the R frontal region before and after the procedure. The straight line represents the initial normalised signal (value 1), the dotted line represents the corresponding average final signal for each volunteer (value 17), and the points represent the normalised final signal for each volunteer.

Fig 5. Relative final signs of frontal region E before and after the procedure. The straight line represents the initial normalised signal (value 1), and the dotted line is the corresponding average final signal for each volunteer (value 1.18); the points represent the normalised final signal for each volunteer.

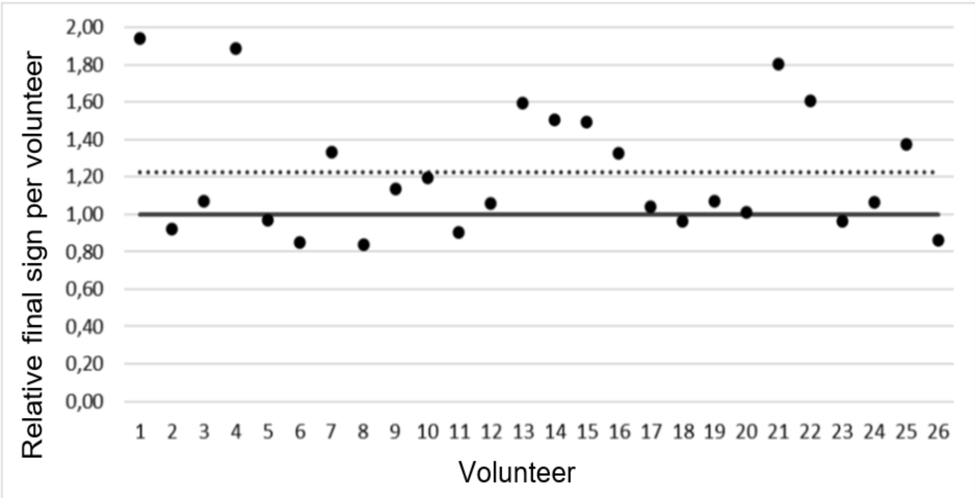

Fig. 3. Relative final signs of the Glabella region before and after the procedure
Source: The authors (2022)

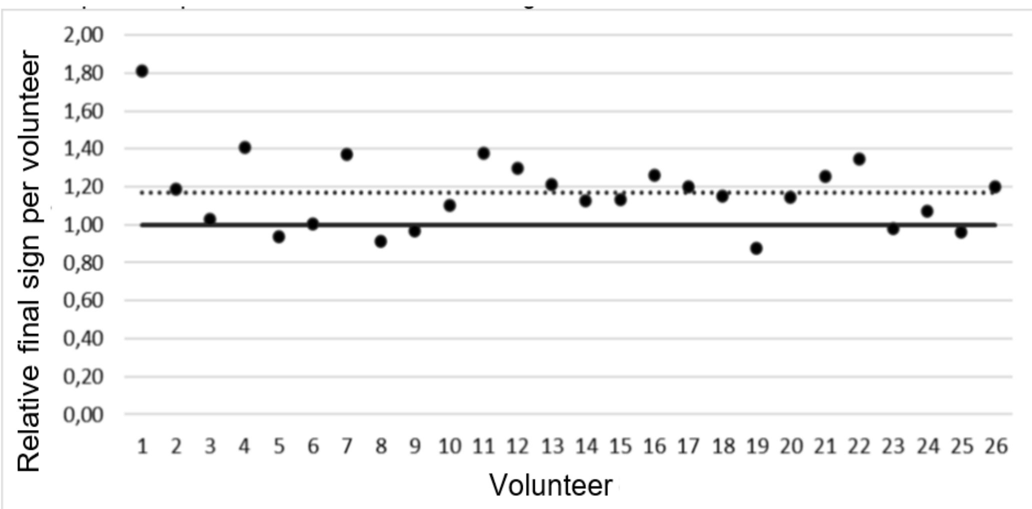

Fig. 4. Relative final signs of the R frontal region before and after the procedure
Source: The authors (2022)

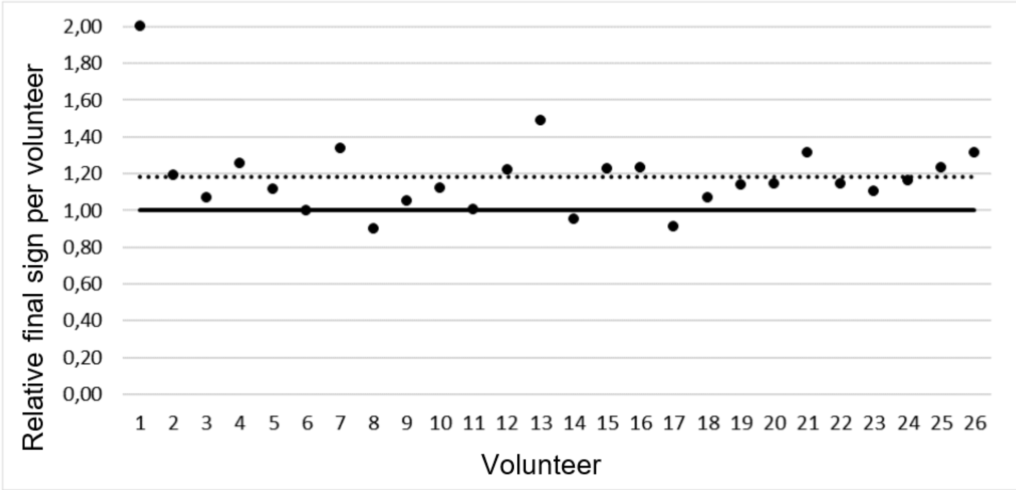

Fig. 5. Relative final signs of frontal region E before and after the procedure
Source: The authors (2022)

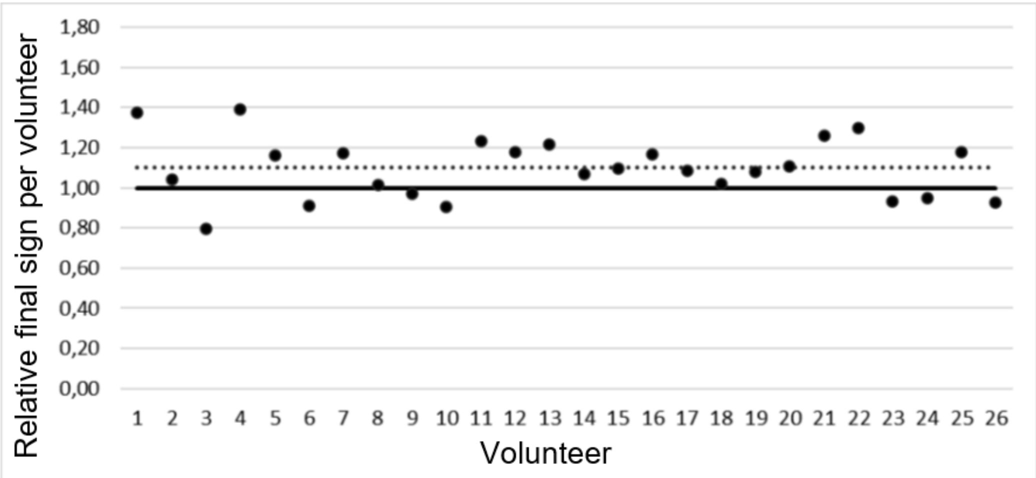

Fig. 6. Relative final signs from the tragus region to the corner of the mouth D before and after the procedure
Source: The authors (2022)

Fig. 6 Relative final signs from the tragus region to the corner of the mouth D before and after the procedure. The straight line represents the initial normalised signal (value 1), and the dotted line is the corresponding average final signal for each volunteer (value 1.10); the points represent the normalised final signal for each volunteer.

Fig. 7. Relative final signs from the tragus region to the corner of the mouth E before and after the procedure. The straight line represents the normalised initial signal (value 1), and the dotted line is the corresponding average final signal for each volunteer (value 1.15); the points represent the normalised final signal for each volunteer.

The data reveals that dermal thickness increased across studied regions, with variable response magnitudes, suggesting potential lifestyle influence on i-PRF efficacy. Monitoring inflammatory markers and modulating variables could optimise therapy outcomes. Limited studies on intradermotherapy via i-PRF exist; however, this study's promising outcomes underscore its proper dermal depth functionality. Dhurat's findings suggest that the large size of the components may compromise their passage through the skin via transdermal delivery, making it clear that platelet concentrates should be applied via intradermotherapy [30].

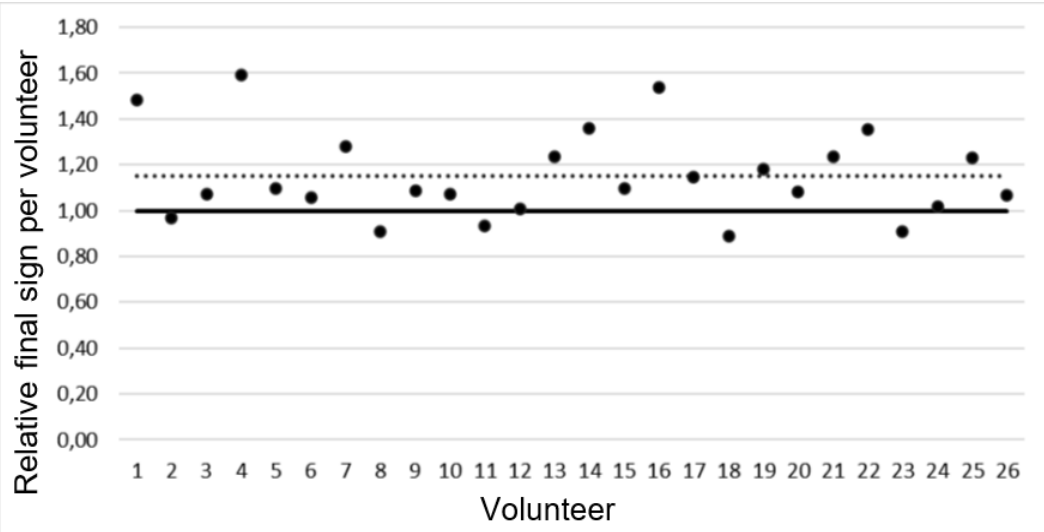

Fig. 7. Relative final signs from the tragus region to the corner of the mouth E before and after the procedure

Source: The authors (2022)

Results affirm i-PRF's potential in attracting fibroblasts for dermal restructuring, supported by growth factor presence. Vascular endothelial growth factor (VEGF) fosters restructuring through angiogenesis [15,25,26,31]. i-PRF-driven rejuvenation yielded volume effects, angiogenesis, collagen and fibronectin production [32-36]. Fibroblast division, migration, adhesion, gene expression, and growth factor activation were evidenced [37-39].

Tables 1 and 2 data reveal some negative outcomes, possibly linked to pre-existing subclinical inflammation, subsequently reduced by i-PRF, or ultrasound measurement variability due to evaluator pressure or gel thickness. Evaluators received training to mitigate bias. Visual outcomes in photos (e.g., Figure 2B, patient 22) require multifactorial analysis, considering subcutaneous layers, inflammation, and skin type.

Although i-PRF intradermotherapy seems promising, standardised protocols and comparative effectiveness studies are lacking. The debate on high vs. low-force PRF protocols persists [16,18,19,20,21,40]. Our high-force i-PRF protocol yielded favourable results, warranting further comparative investigations.

This research employed varied assessment techniques: ultrasonography, photography, and self-perception questionnaires. Ultrasonography demonstrated increased dermal thickness post-treatment, correlating with improved texture, wrinkles, and radiance. Analysis of ultrasonographic data 21 days after treatment revealed enhanced dermal thickness. Participant responses underscored treatment satisfaction, crucial for clinical efficacy evaluation.

Treatment displayed minimal complications—transient oedema and occasional hematomas, resolving within a week. Pain during application was manageable [41-45]. Future investigations could enhance comprehension by incorporating biochemical, haematological, and lifestyle analyses.

4. CONCLUSION

The application of three sessions of high-force centrifugation i-PRF via intradermotherapy significantly increased dermal thickness, proving to be an effective dermal restructurer and a cost-effective alternative accessible to all. The results of i-PRF bio-stimulation are short-term but rather progressive. The positive evaluation from the self-perception questionnaire demonstrated the significant importance of clinical analysis and should be associated with the positive outcomes of increased dermal thickness. Further standardisation of the technique for different clinical scenarios is still necessary.

ETHICAL APPROVAL AND CONSENT

The study protocol received approval from the Research Ethics Committee of the University of

Vale do Paraíba [Opinion 4,930,500/CAAE 48019521.5.0000.5503], aligning with the guidelines set forth by the National Health Council through resolution 466/2012. Informed consent was obtained from all participants after providing comprehensive information about the procedures.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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