Original Research Article

Evaluation of Injectable Platelet-Rich Fibrin (i-PRF) As an Endogenous and Autologous Tissue Regenerator

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. Injectable Platelet-Rich Fibrin (i-PRF) emerges as a noteworthy solution owing to its biological origin and autologous nature. **Materials andMethods:** Evaluating i-PRF's efficacy in counteracting ageing signs, we employed a 16 MHz high-frequency ultrasound device and meticulous photographic documentation. ~~26~~ Twenty-sixfemales~~,~~ aged 35-55 years~~,~~ underwent three i-PRF sessions. Statistical scrutiny utilised a paired t-test (α = 0.05) to assess dermal modifications. Self-Perception Index scores underwent Wilcoxon testing (α = 0.05) for significant enhancements. Comparisons of newly captured frontal and profile photographs (right~~D~~ and left~~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. The p-~~P~~-values for examined regions were: glabella (~~P~~*p*<.00269), frontal right~~D~~ (*p*~~P~~<.00018), frontal left~~E~~ (~~P~~*p*<.00014), cheek right~~D~~ (*p*~~P~~<.00709), and cheek left~~E~~ (*p*~~P~~<.0008). These results underscore substantial dermal thickness alterations. Statistical examination of the Self-Perception Index yielded a ~~P~~*p*-value < .0001, ~~signifying~~ meaningsignificant 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, ageing, rejuvenation, 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 aging [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 [13]. Platelet concentrates with abundant growth factors aid~~s~~ tissue repair and rejuvenation. Platelet-derived growth factors trigger fibroblast activities [14].

Platelet-Rich Plasma (PRP) aids regeneration [6,16,17]. PRP is obtained through double centrifugation, but ~~limited~~ the presence ofleukocytes impedesthe healing [15]. Platelet-RichFibrin (PRF)~~, enhances PRP, devoid of chemicals [22].~~

~~PRF,~~ a second-~~-~~generationof platelet concentrates, supports tissue engineeringwhile providing cells, growth factors, and a scaffold[22]. ~~Known as L-PRF, it provides cells, growth factors, and a scaffold~~

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~~[22].~~ High-force centrifugation (2700 rpm, 12 minutes) yields a dense fibrin matrix producing the standard platelet-rich fibrin (S-PRF)[25,26]. Advanced ~~-~~PRF(A-PRF)made with low-force centrifugation (1500 rpm, 14 minutes) ~~utilises low force,~~ results in ~~producing~~ a more porous matrix, more appropriate forwound healing and tissue regeneration[28,29].

The injectable PRF (i-PRF) was introduced by Mourão et al. (2015) [30];~~,~~ and comprehensively explained by Miron et al. (2017) [25, 26]; and Wang et al. (2018) [31, 32]. Plastic tubes~~,~~ and centrifugation modifications slow coagulation [25,31]. The i-PRF~~,~~is suitable for facial rejuvenation~~,~~ allowing~~s~~ extended working time [32,33].

The ~~F~~fibrin matrix captures and releases growth factors for tissue healing [14,25,34]. Fibrin's sustained action leads to increased growth factor concentrations [35]. Using ani-PRF from autologous blood enhances safety [25].

Blood centrifugation activates platelets, releasing growth factors for cell migration and proliferation [36]. Transforming growth factor-beta 1 (TGF-1), platelet-derived growth factor (PDGF), and others contribute to regeneration [22,37].

The use of i-PRF is reported in various healthcare fields [13,38,39]. However, there is ~~L~~limited data ~~exist~~ on using i-PRF in facial rejuvenation [13,40]. This study ~~assessesi-PRF's impact on facial rejuvenation using objective analysis, self-perception, and photos~~uses objective analysis, self-perception, and photos to assess the impact of intradermal application of i-PRF on facial rejuvenation, dermal restructuring, and aesthetic enhancement across the face.

~~Facial aesthetics benefit from platelet concentrate growth factors, promoting skin rejuvenation [40]. This study evaluates i-PRF's intradermal application for dermal restructuring and aesthetic enhancement across the face.~~

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2. MATERIAL AND METHODS

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.

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.

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.

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.

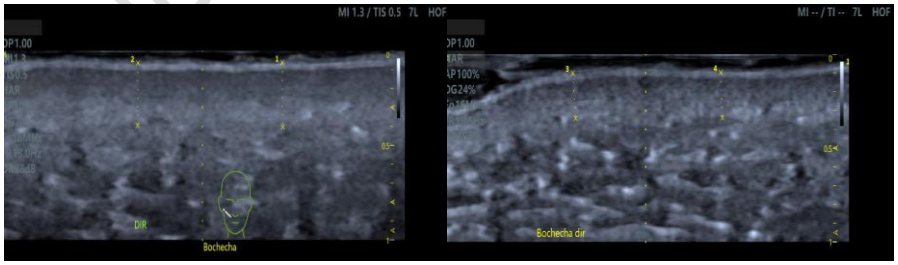
3. RESULTS AND DISCUSSION

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. Figures 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 assumesd a normal distribution of values and employsed a two-tailed model with a significance level set at *P p-value*<.05. The test results (*pP*-values) for the glabella region (*pP*<.00269), right frontal area (*Pp*<.00018), left frontal region (*pP*<.00014), tragus to the corner of the mouth (cheek) on the right side (*Pp*<.00709) and left side (*Pp*<.0008) indicate highly significant alterations in dermal thickness in these regions.

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

Figures 1A and 1B present the results of the ultrasonography measurements. In Figure 1A, the dermal thickness measured before the start of the treatment was 2.41 mm, while in Figure 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.



Source: The author (2022)

Table 1: Glabella measurements, right frontal(RD) and left (LE)

	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)

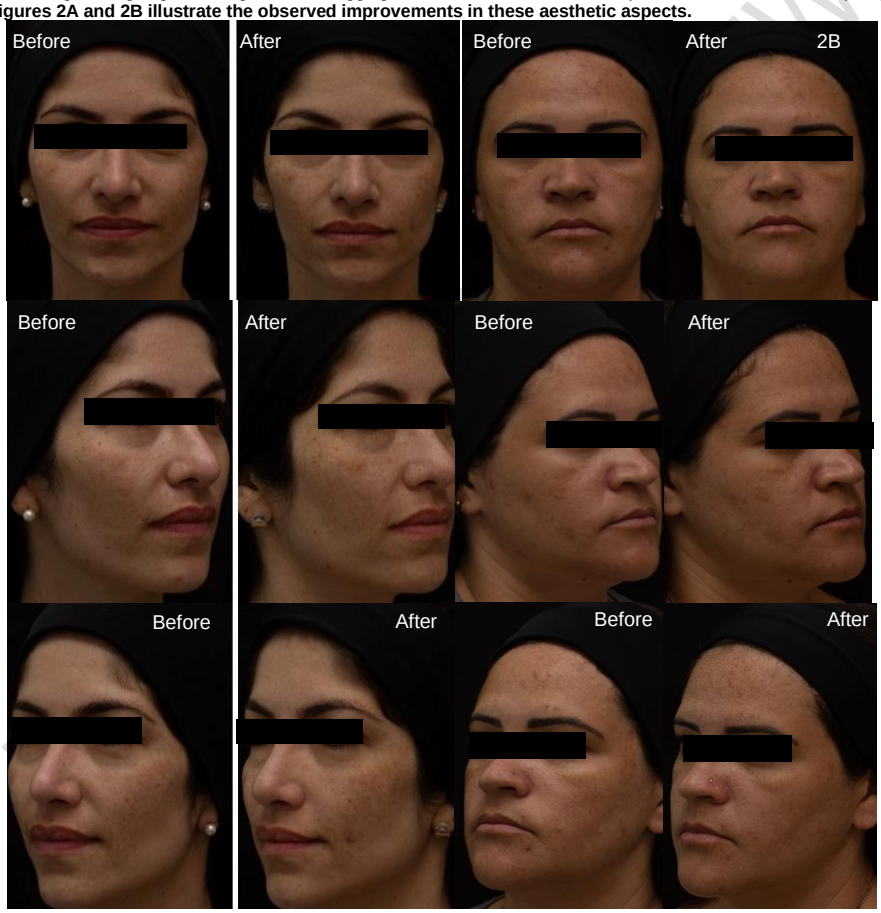
Table 2: Tragus mouth corner (cheek), right (RD) and left (LE)

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)~~

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. **Figures 2A and 2B illustrate the observed improvements in these aesthetic aspects.**

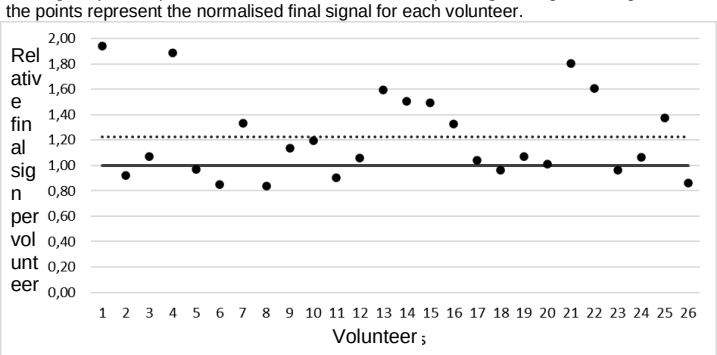


~~Source: The author (2022)~~

The graphical representations of the relative final signals in the analysed areas (Figures 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

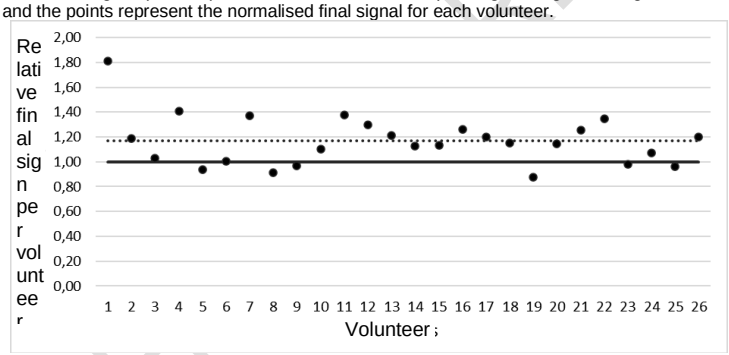
on the comprehensive analysis, it was observed that the administration of three sessions of intradermal i-PRF resulted in a significant increase in dermal thickness and an overall improvement in skin condition.

Figure 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.



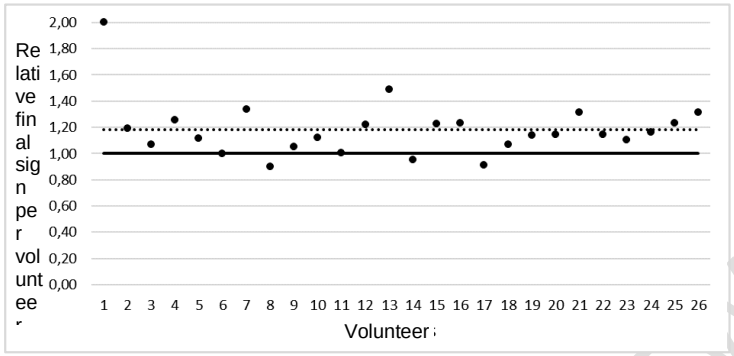
~~Source: The authors (2022)~~

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



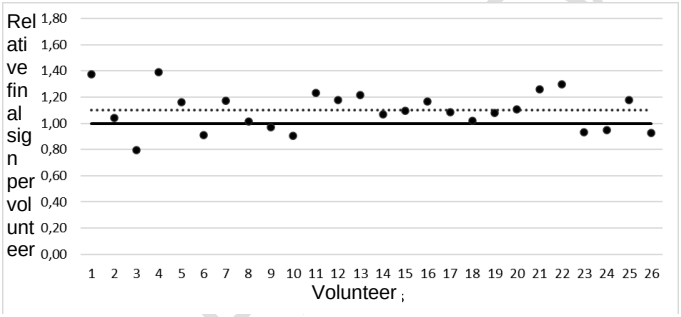
~~Source: The authors (2022)~~

Figure 5: Relative final signs of the left 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.



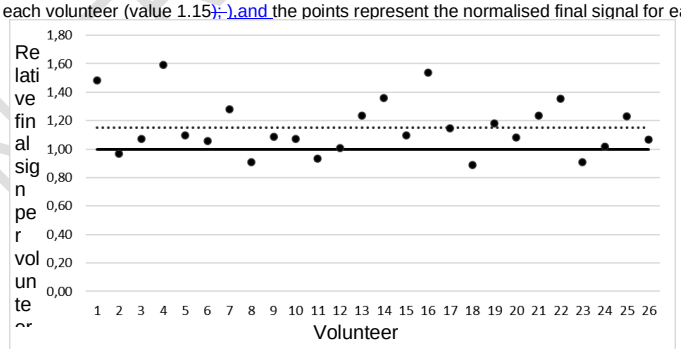
~~Source: The authors (2022)~~

Figure 6: Relative final signs from the tragus region to the corner of the mouth rightD 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.



Source: The authors (2022)

Figure 7: Relative final signs from the tragus region to the left 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~~);),~~ and the points represent the normalised final signal for each volunteer.



~~Source: The authors (2022)~~

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 large component sizes may compromise post-micro-needling platelet concentrate application [42].

Results affirm suggest thei-PRF's potential in forattracting fibroblasts for dermal restructuring, supported by growth factor presence. Vascular endothelial growth factor (VEGF) fosters restructuring through angiogenesis [22,36,37,43]. Applying i-PRF-driven rejuvenation yielded volume effects, angiogenesis, collagen, and fibronectin production [44]. Fibroblast division, migration, adhesion, gene expression, and growth factor activation were evidenced.

Tables 1 and 2 data reveal some negative adverse 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 [25,28,29,31,32,45]. 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, which is crucial for clinical efficacy evaluation.

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

4. CONCLUSION

The application ofApplying 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 ratherprogressive. 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.

CONSENT ~~(WHEREEVER APPLICABLE)~~

All authors declare that ~~'~~written informed consent was obtained from the patient (or other approved parties) ~~for publication of~~to publish this case report and accompanying images. A copy of the written consent is available for review by the~~ Editorial office/Chief Editor/Editorial Board members of this journal~~is journal's Editorial office/Chief Editor/Editorial Board members.

ETHICAL APPROVAL ~~(WHEREEVER APPLICABLE)~~

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have, therefore ~~been performed in accordance with~~, been performed according to the ethical standards laid down in the 1964 Declaration of Helsinki.

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