

## Comparison between Plasma gel (Filler) and Polydioxone (PDO) Threads in Treating Fine and Medium Sized Infra-Orbital Wrinkles Using 3D Antera Camera

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### ABSTRACT

**Background:** Plasma gel is a new procedure in the aesthetic field. It has been used for various dermatological conditions including wound healing, anti-inflammatory, and cosmetic uses. Infra-orbital dark circles possess no medical harm but signifies cosmetic and psychological burden.

**Objective:** Evaluation the efficacy and safety of plasma gel (Filler) injection and comparing its result with polydioxone (PDO) mono threads in peri-orbital rejuvenation by subjective measure using a 3D computerized camera which gives a report with very fine details.

**Patients and methods:** 40 patients with infra-orbital fine wrinkles were included and by the Antera 3D camera, these fine wrinkles were divided to small sized and medium sized wrinkles and evaluated for the changes in the size and depth, indentation index and texture roughness of the wrinkles. Patients underwent plasma gel injections into the infra-orbital area of the left eye and PDO mono threads insertion in the right side. All patients were evaluated using the Antera camera at day (0m), after one month (1m) and after 6 months (6m) of the therapy.

**Results:** Antera reports of the side injected with the plasma gel showed very good response. Also PDO mono threads insertion revealed marked cosmetic results, yet the efficacy of the plasma filler was superior as regards wrinkle's size, indentation index and texture roughness. .

**Keywords:** Infra-orbital fine wrinkles, 3D Antera camera, Plasma gel, PDO thread.

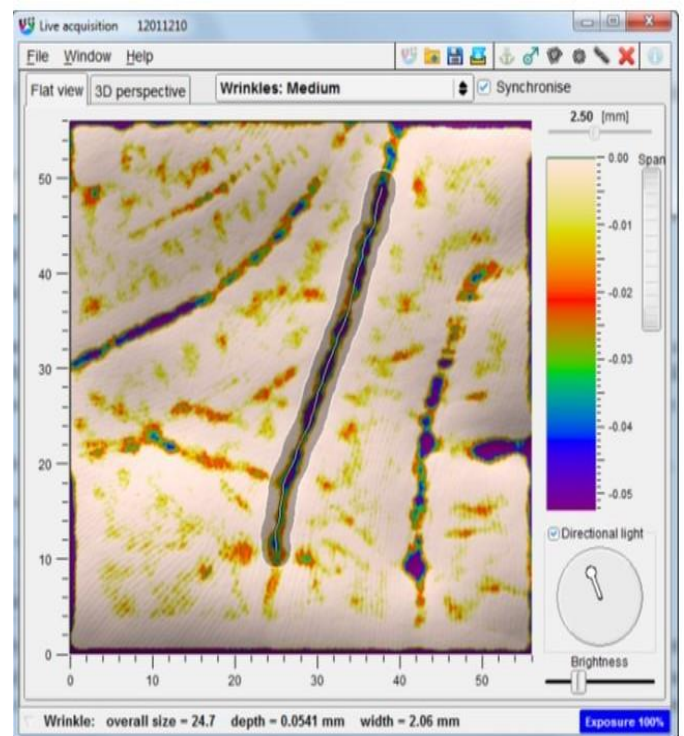
### INTRODUCTION

**A- Antera 3D camera:** Antera 3D allows you to analyse a number of parameters related to the skin. Thanks to sophisticated algorithms, the software allows users to analyse and measure topographic features of the skin (such as texture, wrinkles, fine lines, etc.) <sup>(1)</sup>.

**B- Wrinkles:** This mode allows you to measure a set of parameters relating to fine lines, wrinkles and folds.

The first thing you need to do when measuring a wrinkle is to select the appropriate filter. You can choose between four options: Small (1mm filter): suitable for the analysis of fine lines. Medium (2mm filter): this is the default selection suitable for most wrinkles, e.g. crow's feet, forehead wrinkles, marionette lines. Large (3mm filter): suitable for large deep wrinkles, furrows and folds, and custom: this option allows you to define your own filter and it spans from 0.5mm to 40mm <sup>(1-2)</sup>.

In our study, we chose the small and medium sized wrinkles. The color image will change to a false color map, where the violet indicates the deepest features and the white corresponds to the top of the surface. You can now select the particular wrinkle then the software will display the following parameters in the Data Display bar (Figure 1).

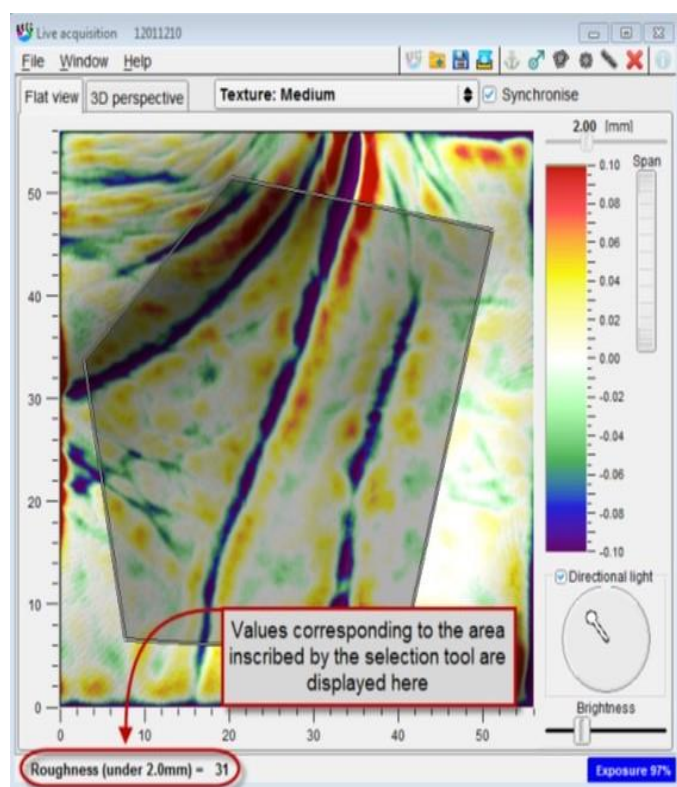


**Figure (1):** Measuring a wrinkle's depth, width and overall size.

- Overall size. This value corresponds to the average cross section of the wrinkle selected and has the dimensions of an area.
- Depth. It is the average depth of the wrinkle selected and is measured in millimeters.
- Width. It is the average width of the wrinkle selected and is measured in millimeters.
- Indentation index. This parameter is similar to the roughness definition, used to determine the texture of the skin. The difference lies in the fact that only the negative vertical deviations of the surface from its ideal form are considered, leading to a value of roughness that is solely dependent on indentations in the skin and not on protrusions.

When selecting certain wrinkle by the Antera 3D to determine the values of depth and width, the other wrinkles features will be discarded by the software and will not be used to compute the values of depth and width.

**C- Texture:** The precise analysis of the topography of the epidermis is an indispensable tool for assessing the progress achieved through cosmetic treatment. The texture of the skin is determined by the Antera software by measuring the average roughness (Ra), using a roughness plane correction option. Roughness is quantified by the vertical deviations of a real surface from its ideal form. If these deviations are large, the surface is rough; if they are small the surface is smooth (**Figure 2**).



**Figure (2):** The Texture of the skin is determined by measuring the average roughness (Ra).

Plasma Rich Platelets (PRP) is obtained from autologous blood that contains different growth factors that may act on tissues involved in the wound healing and regeneration<sup>(3)</sup>.

Activation of platelet poor plasma (PPP) by thermal measures and /or, adding an activator gives rise to a gelatinous material formation, which is known as plasma filler. The plasma gel is the bio skeleton of filler, which provides a dense environment for a 3 dimensional configuration of dermal fibroblasts<sup>(4)</sup>. It contains fibrin that provides the formula with greater consistency and resistance than ordinary P.R.P. or P.P.P., and gelled proteins that provide constant stability and volume<sup>(5)</sup>.

In other words plasma gel is simply a gelatinous form of PRP containing all the growth factors of ordinary PRP and PPP but with a longer duration inside the tissues<sup>(3)</sup>. The gel formula serves to stop the diffusion of both activated platelets and their pre synthesized growth factors in the treatment area and sustain their therapeutic effects for several months after the last treatment injection<sup>(6)</sup>.

PRP gel has numerous applications, particularly in the cardiac and neurosurgical areas. Also, it can be used in skin rejuvenation and acts as soft tissue natural filler in addition to oral and maxillofacial surgery bone grafting procedures<sup>(7)</sup>.

Wrinkles are visible creases or folds in the skin. Wrinkles less than 1 mm in width and depth are defined as fine wrinkles and those greater than 1 mm as coarse wrinkles. Wrinkles may be caused by intrinsic factors and by extrinsic factors<sup>(8)</sup>. The presence of wrinkles is a sign that the skin's recovery ability has declined progressively with age and is linked to undesirable cosmetic effects of aging<sup>(9)</sup>.

Complication of filler injection in the lower eyelid; irregularities of the skin, hematoma formation, Tyndall effect, inflammatory reactions, infection, and ischaemic complications<sup>(10)</sup>.

Studies evaluating the effects of platelet rich plasma in infraorbital circles revealed improvement in colour homogeneity of the region, but larger studies are required for external validity of the results<sup>(11)</sup>. In fact, plasma gel has proved to reverse the solar photoaging process, by inducing dermal fibroblast proliferation, which stops cellular apoptosis, which is translated into a thickening in the skin and the new formation of collagen and elastin<sup>(12)</sup>. These changes in collagen persisted for up to 12 months<sup>(13)</sup>.

Polydioxanone threads differ from the other bio-stimulators because they gradually induce a minimal foreign body reaction. This granulation tissue forms a scaffold which supports the sagging tissue and tightens the skin. It also improves skin vitality and elasticity<sup>(14)</sup>.

In this study, we evaluated the efficacy and safety of autologous plasma gel in the rejuvenation of infra-orbital fine wrinkles and texture and compare these results with PDO threads.

## PATIENTS AND METHODS

### A Study population:

**Inclusion criteria:** The current study included 40 adult male and female patients with infra-orbital fine wrinkles recruited from dermatology outpatients' clinics.

**Exclusion criteria** included pregnancy and lactation, acute skin infection, history of keloid formation, extreme age, use of isotretinoin, autoimmune diseases and previous treatments for the infra-orbital region in the last 1 year.

A full history taking, occupation of medical importance as outdoors for long duration and special habits of medical importance, such as smoking, alcohol or substance abuse, onset and duration of wrinkles, previous treatment of wrinkles, history of autoimmune diseases, drug history, history of autoimmune diseases such as hypo or hyperthyroidism, pernicious anemia and Addison disease.

### Treatment plan:

#### Plasma gel filler preparation:

**Gupta** prepared the plasma gel in his study by centrifuging the plasma serum, then adding 0.01 ml calcium gluconate to every 1 ml of P.P.P., then incubation in hot water at 100° C for 5min, after that he putted the tube in cold water bath in a metal container with initial temperature 7° C for 5 min<sup>(15)</sup>.

In our study, we modified the technique by using 10 ml of the patient's blood, then it was mixed with 1 ml acid citrate dextrose (as an anticoagulant) and centrifuged at 3000 rotations per minute (RPM) for 10 minutes. The platelet-poor plasma (P.P.P.) in the upper part (rich in fibrinogen needed in the viscous filler preparation) and the platelet-rich plasma (P.R.P.) in the lower precipitate were withdrawn to 5 syringes 1 ml each. 0.01 ml of Ca-gluconate was then added to each 1 ml syringe. The prepared formula was then placed into a plasma filler machine where it was heated 5 min. to 90° C then another 5 min. 70° C and finally 5 min. to 40° C. A viscous gel is formed and is ready for the injection.

The infra-orbital region anatomy extends superiorly; from the lower upper eyelid, inferiorly; the inferior orbital rim, medially; the medial canthus angle and laterally to the lateral canthus angle.

In the present study, we injected the infra-orbital area of the left eye by (1 ml, 4 mm, 30 G) needle, every month (for three consecutive months) in the deep dermis as multiple injections; 0.1 ml in each point and 5 mm apart.

PDO mono threads (Venus, korean) (30 G, 25 mm, Thread 30 mm) were inserted in one session, the numbers of threads were about 3 -5 threads inserted in the deep dermis (Figure 3).



**Figure (3):** Insertion of PDO threads in right eye of the patient.

Sunscreen cream was applied after each session, to be used daily before sun exposure and to be re-applied every 2 hours.

**Results evaluation** is done by photographic documentation by the Antera 3D camera, (Miravex, Ireland) which is a multi-LED handheld camera with accompanying software that has area matching functions to ensure a direct comparison of the same area. Taking baseline facial photographs of the right eye and the left eye, for each patient (when they first presented, before each session, as well as one month after the last session, and six months after). Photos were standardized as to area, distance, illumination, angle of exposure and background so that there were no major differences between any of the series of photographs. By the **Antera 3D camera**, a computerized report recording the fine wrinkles' indentation index, overall size, depth and width of the small (0.1-1 mm) and medium sized (1-2mm) wrinkles, the texture (roughness) score.

### Ethical approval:

**After taking the approval of the research ethics committee (FMASU M S 28212019-15/9/2019), a written consent was obtained from each patient. The Declaration of Helsinki for human beings, which is the international medical association's code of ethics, was followed during the conduct of this study.**

### Statistical analysis

Statistical Package for Social Sciences (SPSS) version 22 for Windows was used to code, process, and analyze the obtained data (IBM SPSS Inc, Chicago, IL, USA). Using the Shapiro Walk test, the distribution of the data was examined for normality.

Frequencies and relative percentages were used to depict qualitative data. To determine differences between two or more sets of qualitative variables, use the chi square test ( $X^2$ ). Quantitative information was presented as mean $\pm$ SD (Standard deviation). Two independent groups of normally distributed variables were compared using the independent samples t-test



(parametric data). P value less than 0.05 was regarded as significant.

**RESULTS**

Mean age of included cases was 42 (± 9) years, 17 (42.5%) of them were males and 23 (57.5%) were females, 25 cases were skin photo-type 3 (62.5%) and 15 had skin photo-type 4 (37.5%). 13 were nonsmokers (32.5%), 16 (40%) were smokers less than 10 and 11 (27.5%) were smokers of more than 10 cigarettes daily. 29 (72.5 %) of included cases do not use sunblock or cosmetics, 10 patients (25%) reported use of sunblock or cosmetics sometimes and only 1 patient always used sunblock and cosmetics (2.5%).

The 3D Antera Camera assessment of treatment response with both treatments revealed that both PDO thread insertion and plasma gel injection exerts beneficial effects in improving peri-orbital wrinkles. However, plasma gel revealed more potent effects compared to PDO threads. PDO threads treatment response in small-sized and medium sized wrinkles revealed significant improvement of wrinkle size after 1 & 6 months, wrinkle depth after 1 month, wrinkle width after 6 months, indentation index after 1 & 6 months and texture roughness after 1 & 6 months. Assessment of plasma gel treatment response in small-sized wrinkles revealed significant improvement of wrinkle size after 1 & 6 months, wrinkle depth after 1 month & 6 months, wrinkle width after 1& 6 months, indentation index after 1 & 6 months, texture roughness after 1 & 6 months. While, medium-sized wrinkles response revealed significant improvement of wrinkle size after 1 & 6 months, wrinkle depth after 1 month & 6.

**Comparison of wrinkles indentation index with different demographic data before start of treatment:** Comparison of indentation index with small and medium sized wrinkles on both right and left sides in relation to patients' gender before treatment revealed

that female patients had a higher indentation index compared to males without any statistically significant difference. (**Table 1**).

**Table (1):** Comparison of indentation index relation to patients' gender.

Indentation index	Gender (Number of patients)	Mean ± SD	Test value	P value
Small wrinkles (Rt)	Male (17)	17.5±5.1	0.660	0.513
	Female (23)	18.8±7.1		
Small wrinkles (Lt)	Male (17)	17.1±4.7	1.485	0.146
	Female (23)	20.6±8.9		
Medium wrinkles (Rt)	Male (17)	37.6±12.4	0.460	0.648
	Female (23)	39.6±14.4		
Medium wrinkles (Lt)	Male (17)	36.8±9.9	1.586	0.121
	Female (23)	46.6±23.9		

Smoking status before treatment revealed that non-smokers had the lowest indentation index compared to smokers but without any statistically significant difference. Moreover, increased cigarette consumption was associated with a higher indentation index.

**Comparison of treatment response in small-sized wrinkles with both PDO threads and plasma gel:** revealed significantly better response with plasma gel compared to PDO threads regarding wrinkles' size, depth, width, indentation index, texture. (**Table 2**).

**Table (2):** Assessment of treatment response in **small-sized wrinkles** with both PDO threads and plasma gel.

	PDO threads response		Plasma gel response		P value (after 1 month of both treatments)	P value (after 6 months of both treatments)
	After 1 month	After 6 months	After 1 month	After 6 months		
Wrinkle size	-5.99±1.6	-6.61 ± 2.2	-8.83±3.9	-7.9±2.8	<b>0.001</b>	<b>0.001</b>
Wrinkle depth	-0.017±0.001	0.023±0.01	-0.032±0.01	-0.02±0.006	<b>0.021</b>	<b>0.001</b>
Wrinkle width	-0.004±0.001	-0.061±0.02	-0.084±0.02	-0.089±0.03	<b>0.001</b>	<b>0.042</b>
Indentation Index	-3.75±1.2	-3.91±1.8	-5.077±2.2	-4.49±1.3	<b>0.009</b>	<b>0.035</b>
Texture Roughness	-4.7±2.1	-4.67±1.9	-6.11±2.1	-5.76±2.2	<b>0.005</b>	<b>0.025</b>

**Comparison of treatment response in medium-sized wrinkles with both PDO threads and plasma gel:** revealed significantly better response with plasma gel compared to PDO threads regarding wrinkles' size, depth, width, indentation index and texture roughness (Table 3).

**Table (3):** Assessment of treatment response in **medium-sized wrinkles** with both PDO threads and plasma gel.

	PDO threads response		Plasma gel response		P value (after 1 month of both treatments)	P value (after 6 months of both treatments)
	After 1 month	After 6 months	After 1 month	After 6 months		
<b>Wrinkle size</b>	-13.26 ± 5.9	-15.94 ± 7.3	-21.74 ± 9.2	-17.19 ± 5.9	<b>0.001</b>	<b>0.021</b>
<b>Wrinkle depth</b>	-0.04 ± 0.012	-0.006 ± 0.002	-0.06 ± 0.02	-0.04 ± 0.015	<b>0.046</b>	<b>0.001</b>
<b>Wrinkle width</b>	-0.025 ± 0.01	-0.122 ± 0.02	-0.037 ± 0.01	-0.4 ± 0.11	<b>0.042</b>	<b>0.001</b>
<b>Indentation Index</b>	-8.31 ± 2.5	-10.93 ± 3.9	-12.2 ± 3.5	-12.03 ± 4.4	<b>0.001</b>	<b>0.022</b>
<b>Texture Roughness</b>	-9.29 ± 2.8	-7.49 ± 5.1	-11.28 ± 4.8	-12.2 ± 2.9	<b>0.035</b>	<b>0.01</b>

**PDO threads** treatment response in small-sized and medium sized wrinkles revealed significant improvement of wrinkle size after 1 & 6 months, wrinkle depth after 1 month, wrinkle width after 6 months, indentation index after 1 & 6 months, texture roughness after 1 & 6 months.

Assessment of **plasma gel** treatment response in small-sized wrinkles revealed significant improvement of wrinkle size after 1 & 6 months, wrinkle depth after 1 month & 6 months, wrinkle width after 1& 6 months, indentation index after 1 & 6 months and texture roughness after 1 & 6 months.

While, medium-sized wrinkles response revealed significant improvement of wrinkle size after 1 & 6 months, wrinkle depth after 1 month & 6 months, indentation index after 1 month and texture roughness after 1 & 6 months.

The following figures show the Antera scoring record showing pictures and graphs for the wrinkle overall size, depth, width, indentation index and roughness for each type of wrinkles in before, a month and after 6 months for each treated eye (Figures 4, 5, 6, 7, 8).



**Figure (4):** Photos with 8 mega pixels digital camera; before beginning of the sessions (left), 1 month after (center) and 6 months (right) of the treated eye with the PDO threads (top) and Plasma gel (bottom):

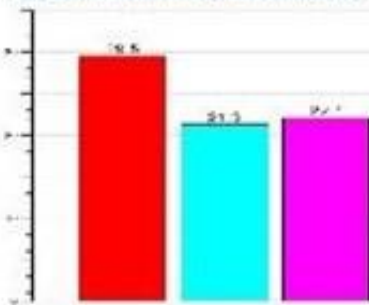
Wrinkles: Small (0.1 - 1 mm)



● a7md a7md rghit before

- Overall size = 29.5  
 - Depth = 0.0824 mm  
 - Width = 2.41 mm

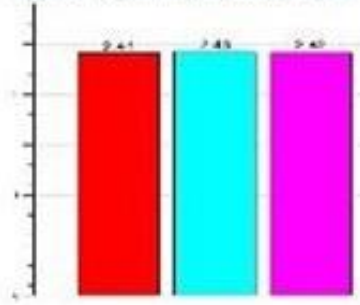
Wrinkle overall size under 1.0 mm of lateral size



● a7md a7md right after 1 m

- Overall size = 22.1  
 - Depth = 0.064 mm  
 - Width = 2.42 mm

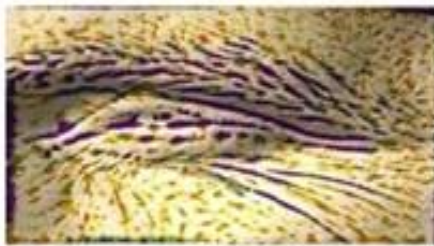
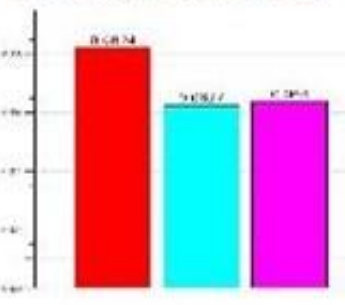
Wrinkle average width [mm] under 1.0 mm of lateral size



● a7md a7md right after 6 m

- Overall size = 21.3  
 - Depth = 0.0627 mm  
 - Width = 2.43 mm

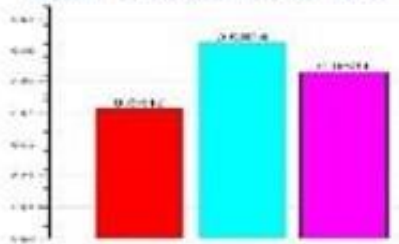
Wrinkle average depth [mm] under 1.0 mm of lateral size



● a7md a7md left before

- Overall size = 14.4  
 - Depth = 0.0624 mm  
 - Width = 1.02 mm

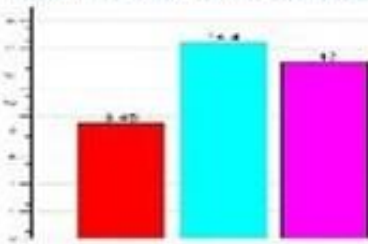
Wrinkle average depth [mm] under 1.0 mm of lateral size



● a7md a7md left after 1 month

- Overall size = 8.5  
 - Depth = 0.0415 mm  
 - Width = 0.785 mm

Wrinkle overall size under 1.0 mm of lateral size



● a7md a7md left after 6 m

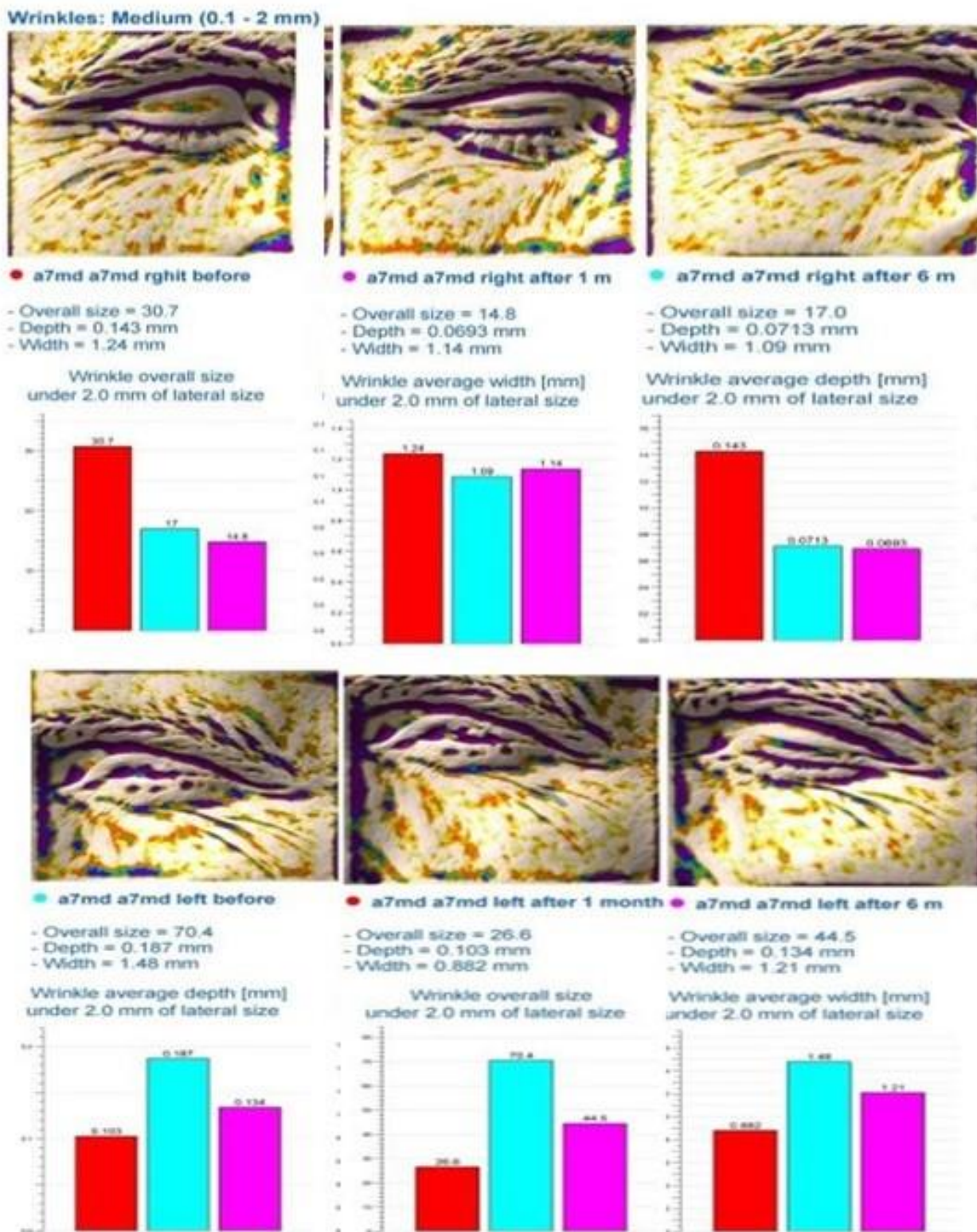
- Overall size = 13.0  
 - Depth = 0.0531 mm  
 - Width = 0.99 mm

Wrinkle average width [mm] under 1.0 mm of lateral size



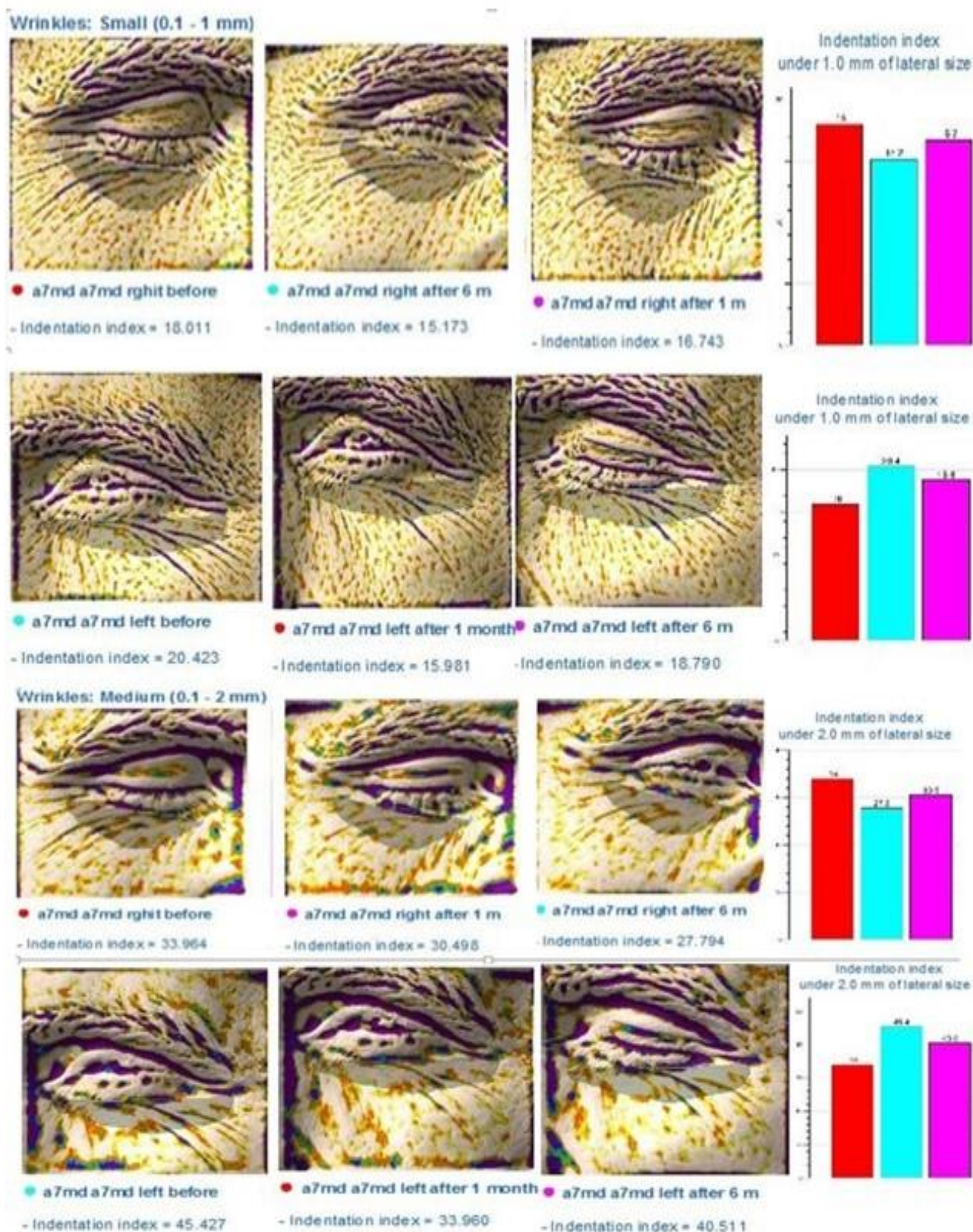
**Figure (5):** Showing antera report of the overall size, depth and width of *small sized wrinkles* (0.1-1mm); of **upper PDO threads side** and **bottom plasma gel treated side**; at months 0m (left), 1m (center) and 6m (right) of the beginning of treatment.





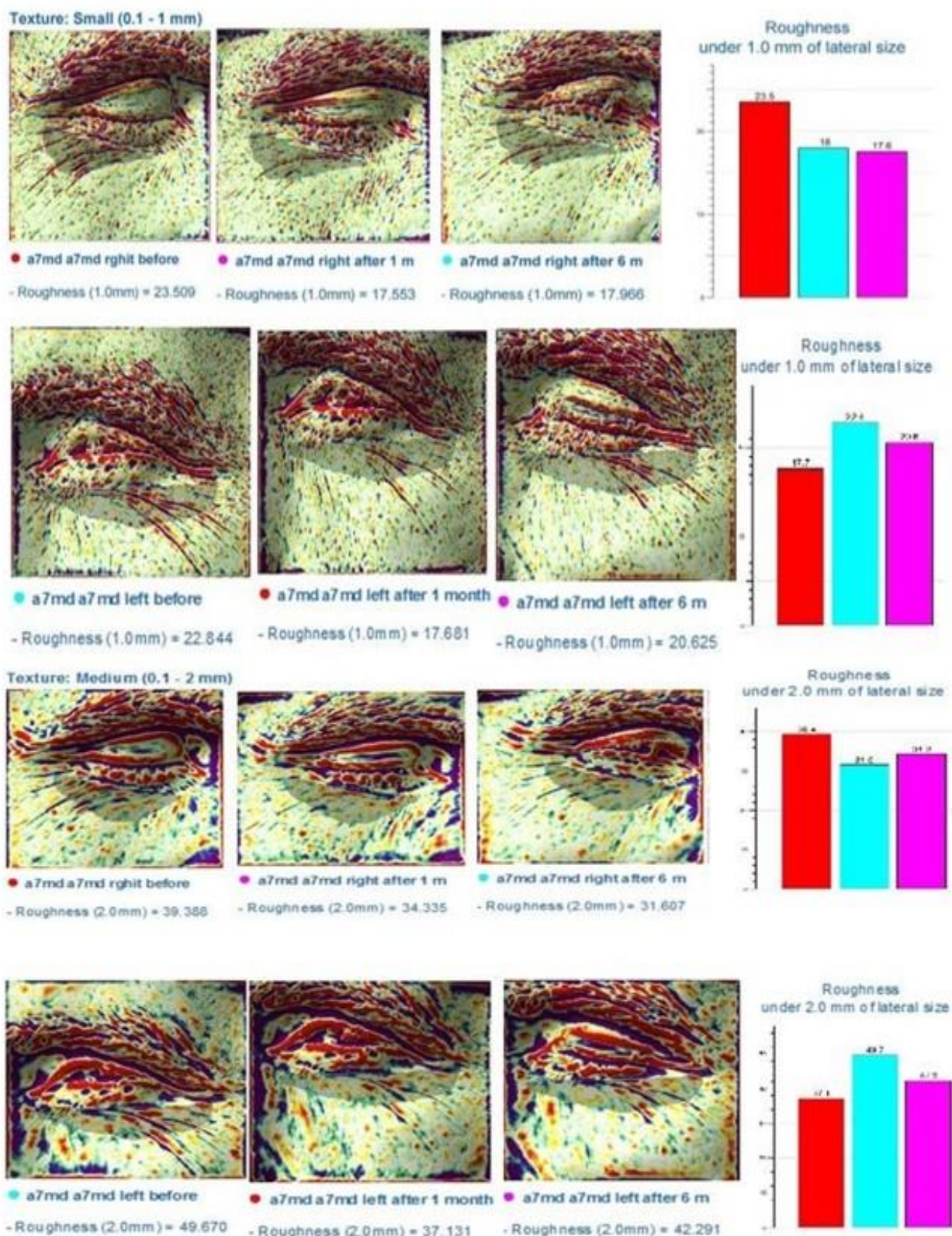
**Figure (6):** Showing antera report of the overall size, depth and width of the *medium sized wrinkles* (1-2mm); of the **upper PDO threads** side and **bottom plasma gel** treated side; at months 0m (left), 1m (center) and 6m (right) of the beginning of treatment.





**Figure (7):** Showing antera report of the **Indentation index** of *upper small sized wrinkles and bottom medium sized wrinkles*; of the **PDO threads side (row 1 and 3)** and the **plasma gel (row 2 and 4)** treated sides; at months 0m (left), 1m (center) and 6m (right) of the beginning of treatment.





**Figure (8):** Showing antera report of the **Texture** of upper *small sized wrinkles* and *bottom medium sized wrinkles*; of the **PDO threads** side (row 1 and 3) and the **plasma gel** (row 2 and 4) treated sides; at months 0m (left), 1m (center) and 6m (right) of the beginning of treatment.

## DISCUSSION

Plasma gel is an autologous growth factor rich formula that has been used extensively in dermatology and cosmetic procedures<sup>(2)</sup>.

Eye dark circles is a complex in its pathogenesis that negatively affects the quality of life of the patients and is considered a challenge for dermatologist to treat. It worsens with aging as sagging of the skin and subcutaneous fat loss occurs<sup>(16)</sup>.

In this study, we compared the efficacy and safety of autologous plasma gel injections and the PDO threads in the treatment of infra-orbital fine wrinkles and texture rejuvenation. We included 40 adult male and female subjects with infra-orbital dark circle, wrinkle or eye bags.

Blinded doctor assessment after 1 month and after 6 months with PDO threads, revealed better response after 6 months compared to after 1 month but without statistical significance. Plasma gel on the other hand revealed significantly better response after 6 months compared to over a month.

Assessment of patients' indentation index as regards demographic data before the start of treatment revealed that female gender, skin photo-type 3, smoking and sun exposure had a higher indentation index but without any statistically significance.

**Assessment of PDO threads** treatment response in **small-sized and medium sized wrinkles** revealed significant improvement of wrinkle size after 1 & 6 months, wrinkle depth after 1 month, wrinkle width after 6 months, indentation index after 1 & 6 months, texture roughness after 1 & 6 months.

PDO thread insertion possessed marked significant improvement in wrinkle's size followed by indentation index then texture roughness. Insertion of PDO threads causes mechanical damage resulting in inflammatory response and platelets, neutrophils aggregation. This inflammatory response activates fibroblasts triggering new collagen synthesis that reduces wrinkles' size, depth, width, indentation index and texture roughness.

Newly formed fibrous tissue and many WBCs, including eosinophils, are gathered forming a fibrous granulomas surrounding the inserted thread. In this fibrous band, newly made collagenous connective having fibroblasts and myofibroblasts inside it<sup>(9)</sup>. Myofibroblasts are related to the wound contracture in the healing process, and serves as a key role in causing elasticity in the procedure area and help to tighten the dermis after the thread is inserted<sup>(13)</sup>. Also, the eosinophil cells induce fibrosis process in the wound healing<sup>(17)</sup>. In addition, there is fat cell denaturation by the granulomas only in the inserted thread area, while the other areas showed no changes<sup>(18)</sup>.

**Assessment of plasma gel treatment** response in **small-sized and medium-sized wrinkles** revealed significant improvement of wrinkle (size, depth, width,

indentation index, texture and roughness) after 1 & 6 months. Plasma gel injection possessed marked significant improvement to wrinkle's depth followed by wrinkle's size then indentation index and finally texture roughness.

Plasma gel exerts this beneficial role as it contains several growth factors as (PDGF, TGF and VEGF) that participate in angiogenesis, fibrous tissue turnover and re-epithelialization. Also, plasma gel contains fibrin, fibronectin, and vitronectin, which are important adhesive molecules that exerts a beneficial role in cell migration and regeneration. That is why plasma gel markedly reduces wrinkles' size, depth, width, indentation index and texture roughness.

**Comparison of treatment response** with both treatment modalities revealed significantly better response with plasma gel compared to PDO threads regarding wrinkles' size, depth, width, indentation index and texture roughness. The plasma gel contains a higher concentration of growth factor compared to PRP, thereby sustains growth factors and other critical cells enabling prolonged secretion<sup>(19)</sup>. A study done by Di-Liddo detected multi-potent stem cell markers within the gel. Thus, plasma gel establishes a local environment that enhances MSC migration and serve as a stem cell source<sup>(20)</sup>.

Another similar study by Lee and colleagues evaluated the outcomes of facial rejuvenation using PDO threads in 35 Asian patients. They evaluated the results using digital photography and patient satisfaction. 33 patients (94.3 %) were satisfied with the results. While the objective photography showed: good improvement (68.6%), moderate improvement (25.7%), and mild improved (5.7%)<sup>(21)</sup>.

The PDO monothreads and plasma filler were safe, cheap and easy office procedures, we encourage using them in the office procedures, with no series side effects, only; minimum erythema and bruising which lasts only for several hours to a maximum two days.

We recommend further studies on a large number of patients are needed with long term follow up to detect the delayed and prolonged effect of PDO threads and plasma gel.

## CONCLUSION

PDO threads insertion and Plasma gel injection in the periorbital area improved wrinkles' size, depth, width, indentation index and texture roughness. However, plasma gel revealed more potent effects compared to PDO threads.

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**Competing interests:** Nil.

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