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Contents

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LARGE INCREASES IN AMERICANS' CONSUMPTION OF sugar-sweetened beverages (SSB) have been a topic of concern. Between 1977 and 2002, the intake of "caloric" beverages doubled in the United States, with most recent data showing that children and adults in the United States consume about 172 and 175 kcal daily, respectively, from SSB,[1] it is estimated that SSB account for about 10% of total energy intake in adults[2,3]. High intake of SSB has....

References Section Example

References

1. Duffey KJ. Popkin BM. Shifts in patterns and consumptions of beverages between 1965 and 2002. *Obesity.* 2007:15(11):2739-2747.
2. Nielsen SJ. Popkin BM. Changes in beverage intake between 1977 and 2001. *Am J Prev Med.* 2004;27(3):205-210.
3. Drewnowski A. Bellisle F. Liquid calories, sugar, and body weight. *Am J Clin Nutr.* 2007;85(3):651-661.

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Original Article

The "Dorsal Reshaping Pencil Technique"- An Innovative Method for Nasal Sculpturing, 4-years' Experience of a Single Surgeon

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Short running head: Dorsal Nasal Reshaping Pencil Technique

Abstract
Background: the nose is the most prominent and centrally located part of the face and contributes greatly to facial aesthetics. Dermal fillers have gained popularity as an acceptable technique to correct and reshape the nose. This study presents the senior author's (AL) novel technique for nose reshaping in a case series of 167 consecutive patients.
Methods: this single surgeon, nonrandomized, retrospective study was conducted from December 2016 to April 2020. A total of 167 consecutive cases were eligible for non-surgical nose reshaping. Patients were divided into 4 groups based on their facial profile and nose defect. All patients were injected using the "dorsal reshaping pencil technique."
Results: a total of 48 (27.3%) men and 119 (72.7%) women, with a mean age of 36.2 years (range 16 to 78 years) were included. 138 (82.6%) members of the study group had never undergone any previous surgical nose procedures and 29 (17.4%) were post-rhinoplasty. Five cases experienced minor complications and no vascular accidents were recorded. Most patients 162 (97%) were satisfied or very satisfied with the procedure.
Conclusions: the dorsal pencil technique is simple, safe and reproducible, with a high satisfaction rate. Using the presented guidelines and specific patient selection methods can further improve patients' and physicians' satisfaction.

Keywords
Non-surgical rhinoplasty, dermal fillers, nose reshaping

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Introduction

The nose is the most prominent and centrally located part of the face. In addition to its important functions, it contributes greatly to the perception of facial aesthetics. In the past, surgery was the only way to modify the shape of the nose, with the drawbacks of prolonged recovery time, morbidity, reoperations and high costs.
Dermal fillers have gained popularity over the last two decades due to their versatility, safety, and immediate results, with minimal lifestyle disruptions and relatively acceptable pricing[1,2]. Although the longevity of hyaluronic acid filler material remains effective for about 8 months and around 4 years with polycaprolactone (Ellansé®, Sinclair Pharmaceuticals, London, UK)[3,4], it is gaining acceptance among plastic surgeons for nose correction and reshaping[2,5,6-8].
This study presents the senior author's (AL) novel technique for nose reshaping in a case series of 167 consecutive patients.

Material and methods

Ethics approval

All patients provided written informed consent. Patients provided authorization for use of images. The study was approved by the Meir Medical Centre Institutional Review Board and complied with the Helsinki guidelines.

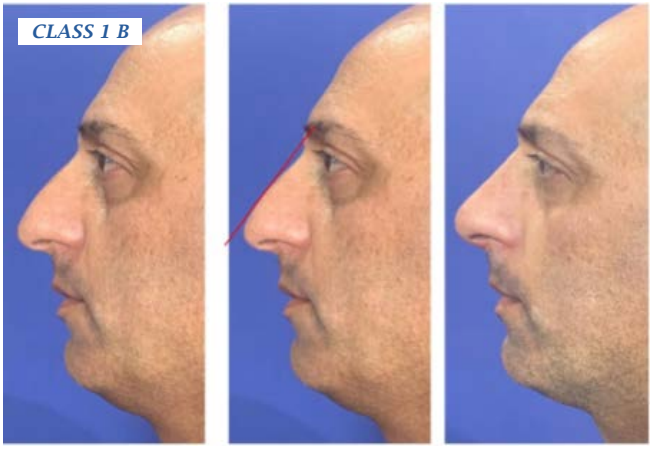
Study design

This single surgeon, nonrandomized, retrospective study was conducted from December 2016 to April 2020. A total of 167 consecutive patients were eligible for non-surgical nose reshaping. Data regarding age, gender, previous nose surgery (rhinoplasty or tumour removal) and previous nose injection were recorded.
Exclusion criteria were sensitivity to lidocaine, hyaluronic acid or polycaprolactone, connective tissue disease, antithrombotic therapy, pregnancy, bleeding disorder, or a diagnosis of dysmorphic syndrome.
All patient pictures were taken in a standard manner using a Canon EOS 65 camera (Canon Inc., Huntington, NY). The result was assessed by the patients using a simple 3-grade scale (not satisfied, satisfied or very satisfied) and by the physician using a scale ranging from 1- very poor result to 10- excellent results.
Patients were divided into 4 groups by the surgeon, based on their facial profile and additional nose defect (*Figure 1*):
Class I - Patients with concave nose profile and
a) prominent cephalic dorsal hump
b) middle dorsal hump
c) caudal dorsal hump.
Class II- Straight dorsum
Class III- Convex dorsum
Class IV- Other nasal deformities.
After analyzing the nose and obtaining informed consent, topical anaesthetic cream (EMLA®, AstraZeneca, Wilmington, DE) was applied for approximately 30 minutes. The nose was reshaped based on the "dorsal reshaping pencil technique". The type and amount of material and the anatomic location of the injection were recorded. Patients were photographed immediately after the procedure, 2 weeks later (during the fine-tuning second injection) and at 3 months. All complications were recorded. Data were gathered on Excel digital spread sheet (Microsoft, Redmond, WA) and were analyzed for descriptive statistics.

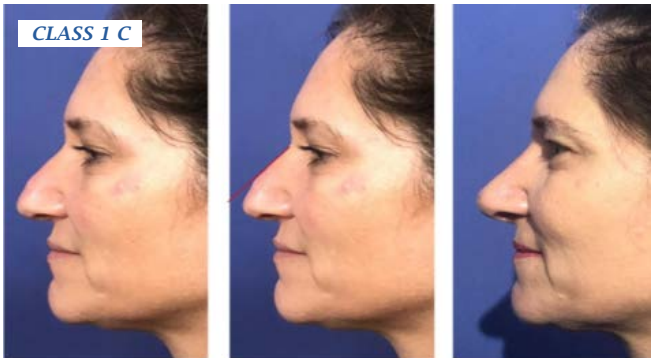
Injectable materials

Two main injectables were used. Patients who were anxious about the final result received hyaluronic acid with high G prime density, and for self-assured patients, Ellansé® was used.

Figure 1 *- Classification of Patients Based on Facial Profile and Nasal Defects.*
Class 1
Patients with concave nose profile and
a. Prominent cephalic dorsal hump. Most filler was injected into the radix.



b. Middle dorsal hump. The filler was injected into the radix and nasal dome.



c. Caudal dorsal hump. Most filler was injected into the dome and tip.

Class 2
Patients with straight dorsum. The filler was injected into the tip.

Class 3
Patients with convex dorsum. The filler was injected into the entire dorsum.

Class 4
Other nasal areas deformities. The filler was injected according to the deformity.

Injection guidelines

Several precautions were taken to avoid vascular complications:

1) Injections were administered at a slow rate.
2) A very small amount of material was injected in each location; never more than 0.6 ml in a single session.
3) All patients were invited for touch-up treatments two weeks later.
4) A 27-gauge, 13 mm long needle was used.
5) Retrograde injection was recommended.
6) If any colour change was noticed during or immediately after the injection, the injection was stopped immediately and the patients were instructed to wait an hour in the waiting room. If the area did not recover, hyaluronidase was injected.
7) Most injections were in the midline, which is a safe zone. Smaller boluses were injected in paramedian areas.
8) At the alar base, the "beauty triangle", either very deep or very superficial injections were performed, due to the location of the angular artery, which lies at a medium depth in this region.
9) Only superficial injections were performed at the glabella, as the supratrochlear artery emerges in this area and becomes superficial as it extends to the forehead.
10) During midline injection, we pinched the area strongly to avoid displacement of injectable material and to compress neighbouring vessels.
11) Aspiration was used before each injection.
12) Hyaluronidase was always immediately accessible.

The "dorsal pencil technique" for nasal sculpturing

The first step of cosmetic nasal sculpturing consists of elevating the nasal tip and domes to their normal or even over-corrected location. This decreases the distance from tip to radix and decreases the amount of material injected into the nasal dorsum. This is achieved by injecting the filler into the base of columella (about 0.1-0.2 cc). The second step is completed using the "dorsal reshaping pencil technique", in which a ruler or a pencil is used as a straight scale to determine the location of the filler injected to correct the specific deformity.

The pencil is laid upon the most prominent point of the dorsum, which serves as a pivot point to determine the perfect nose profile; thereby creating a normal naso-frontal angle (135-145 degrees)[7].

Any gaps appearing under the device demonstrate the volume of the deficit to be corrected (*Figure 2*).

The pencil can be gently rotated vertically to observe at which angle the least amount of substance should be injected, to obtain the ideal result. The manoeuvre is repeated between each injection, until the desired result is achieved.

Treatments of specific areas or specific deformities

Radix

In cases of a deep radix due to saddle nose, frontal bossing and prominent dorsal humps, a small bolus should be injected to the radix at the midline supra-periosteal level, while pinching the lateral sidewalls to prevent lateral displacement and vascular accidents. We recommend that a maximum of 0.15 ml is injected at each session. Further injections should be performed at

Figure 2 *- A 32-year-old male with a type Ia nose, treated with 0.6 cc hyaluronic acid, injected into nasal tip and columella using the dorsal pencil reshaping technique.*

2-week intervals to build the radix projection in layers, thus preventing lateral displacement and broadening of the radix.
In the event of a projected radix, seen mainly due to iatrogenic over injection to this area to camouflage a high, prominent dorsal hump, a small amount of material can be injected superficially to the glabellar area, to balance radix projection .

Crooked nose

Crooked noses are usually the result of old fractures, septal deviations, congenital deviations and post-rhinoplasty or other surgeries such as Mohs. Fillers are used to camouflage the defect. The effect achieved is similar to that of surgeries using spreader grafts, diced on lay graft and others. Firstly, we address the cause of the deviated nose bony/septal/lateral collapse, etc. Then the injection is aimed at the areas that will camouflage it, similar to "dorsal reshaping pencil technique", but on the lateral walls of the nose.
Lateral wall injection should be performed with the utmost caution with small slow boluses followed by a layering technique over several successive visits. To avoid the lateral nasal artery, the injection should start from the midline at a deep supraperiostal/perichondral level and slide laterally.

Droopy nose

To elevate the nasal dome and tip, we advocate injection into the columellar base. This is done by direct bolus injection at the nasolabial angle of the columella. The needle is pointed to the midline at 45 degrees to the lip; 0.1-0.3 ml is injected at the subdermal level. Over-injecting can lead to a hanging columella, which can be treated by injecting the alar bases or by massage. For final beautification and to create a small superior tip break, a small amount of filler material is injected into the tip.

Saddle nose

This deformity is typical of patients of ethnic Asian or African descent, trauma and post-rhinoplasty patients with over-resected dorsum or septal collapse. Due to the large amount needed to correct this deformity, multiple sessions of injections are recommended (not more than 0.5 ml per session) to avoid complications; mainly skin necrosis, material displacement and blindness.

Pollybeak deformity

These patients are usually post-rhinoplasty. All post-rhinoplasty patients should be considered vascularly compromised, so extra caution should be taken. This deformity is addressed using the "pencil technique", usually leading to injection to the columella to elevate the droopy nose, and above the supra-tip up to the radix. We recommend such patients should not be treated sooner than 6 months after surgery, giving the nose enough time to settle into its final shape.

Inverted v-deformity

These patients are characterized by collapsed upper lateral cartilage from the nasal bone, and narrow nose at the middle third. Such cases should be addressed by filling the gap between the two structures and

smoothing the lateral side walls. The needle is inserted in the midline into the soft tissue, filling the gap and the depression in retrograde slow injection and with small boluses.

Alar collapse and notched ala

Alar collapse and notched ala usually occur secondary to rhinoplasty, mainly due to over-resectioning of alar cartilage. These deformities can be treated with extremely small subdermal bolus injection of fillers. The notched ala is treated by directly filling the notch or by liner injection, simulating alar rim graft. For collapsed ala, augmentation and reinforcing the alar base can be helpful.

Pinched nose deformity

Aggressive cephalic trimming of lower lateral cartilage during rhinoplasty and over-tight inter-cartilaginous suturing can lead to pinched nose deformity, sometimes with visible cartilage bulging over the dome. This deformity can be treated with direct injections to the pinched area in small boluses. Extra caution should be exercised in this area due to the possibility of vascular compromise.

Results

During the study period, 167 consecutive patients underwent dorsal reshaping with dermal fillers using the pencil technique. 48 (27.3%) were men (average age 36.3 years) and 119 (72.7%) were women, (average age 35.7 years). The average age of patients was 36.2 years, (ranging from 16 to 78 years). 138 members of the study group (82.6%) had never undergone any previous surgical nose procedures and 29 (17.4%) were post-rhinoplasty.

According to the surgeon's physical examination, 89 patients (53.2%) were classified as having a high dorsal hump, Class 1a; 14 (8.4%) medium dorsal hump, Class 1b; 22 (13.2%) low dorsal hump, Class 1c; 14 (4.7%) normal dorsum, Class 2; 19 patients (11.2%) convex dorsum, Class 3, and 1.2% had a combination of high and low humps (Classes 1a and 1c; Figures 1,2).

The 29 post-rhinoplasty patients had at least one of the following complications: asymmetry in 13 (45%), over-resected dorsum in 12 (41%), graft deformation in 1, pollybeak deformity in 4 (14%), alar deformity in 6 (21%) and inverted v-deformity in 5 (17%).

The most common dermal filler was Ellanse-E®, used in 112 subjects (67%), followed by hyaluronic acid in 55 subjects (32.3%). One patient was injected with Radiesse® (Merz, Frankfurt/Main, Germany) due to their personal request. The total mean volume injected was 0.7 ml (0.2ml – 1.6 ml), 0.77 ml for men and 0.6 for women (P=NS). One hundred and forty-seven patients (86.9%) were injected over 2 sessions; in the first session, a maximum of 0.6 ml was injected, and the fine-tuning second injection was administered 2 weeks later. Three patients who received Ellansé-E® underwent a third touch-up session.

Five patients experienced minor complications: 1 early hematoma and 4 had delayed redness at the injection site, primarily due to visible telangiectasis which disappeared in all patients without intervention, after 3-4 months.

Most patients 162 (97%) were satisfied or very satisfied with the procedure and only 5 (3%) were dissatisfied. One was a young female, post-rhinoplasty patient who was not satisfied with the result; 3 were dissatisfied due to the short longevity of results and were satisfied after additional injections;1 patient was dissatisfied with the new look of her nose. The surgeon's overall satisfaction rate was 8.6 (on a scale of 1- very poor result to 10-excellent results). No vascular accidents occurred.

Discussion

In this retrospective study, we found that the dorsal pencil technique was safe and effective in 167 consecutive patients, with excellent clinical results and very high patient and surgeon satisfaction rates.

The pencil technique is a powerful and easy tool to master. Once the entire nose is examined and the most prominent point of the dorsum is identified, rotating the pencil over this pivot point helps the surgeon to better visualize areas requiring filling. Repeating this technique during the procedure further increases the accuracy of the result.

Recommended use of this technique, by starting from the columella and only then reshaping the dorsum, reduces the amount of the injected substance required, which in turn decreases expenses, substance tissue burden and therefore, the complication rate. While performing dorsal pencil reshaping, visualization of the deformity is obvious, which is important for surgeons inexperienced in nasal aesthetic treatments. Visualization can be done on a photograph or on the patient's nose.

As opposed to rhinoplasty, the advantages of using injectables for nose reshaping are that it is inexpensive, easily available, a simple office procedure, with a short recovery time (one can return to work the same day)[1,6,7], does not require anaesthesia, and has fewer potential complications[5,6]. The procedure has a shorter learning curve compared to rhinoplasty, with more precise and predictable results. This treatment is a good solution for patients who are anxious about having surgery and those who are concerned about a permanent change to their face[6].

The main disadvantages of this procedure are the relatively short-term results (1-4 years), the inability to reduce the overall size of the nose, and possible complications[2,6].

Conclusion

The dorsal pencil technique has proven to be simple, safe, short and reproducible, with a high satisfaction rate. The ability to effectively visualize a patient's problem using our classification system and "pencil technique" enables the physician to quickly understand the problem and effectively provide an efficient result.

Adherence to guidelines involving the slow injection of small amounts to respect nasal vascular anatomy, coupled with specific patient selection methods, can further improve patients' and physicians' satisfaction.

Authors' contributions

Study conception and design: AL and AS. Data analysis was performed by AL, AB and OSA. The first draft of the manuscript was written by AL, AB and OSA. All authors commented on subsequent versions and contributed substantially to its revision. All authors read and approved the final manuscript.

Conflict of interest

None to declare.

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REFERENCES

1. Palomar-Gallego MA, Gómez-Esquer F, Gómez-Sánchez SM, Díaz-Gil G, Linares García-Valdecasas R. Influence of the topographic vascular distribution of the face on dermal filler accidents. *Dermatology*. 2019; 235(2):156-163.

2. Singh P, Vijayan R, Nikkhah D. Filler rhinoplasty: Evidence, outcomes, and complications. *Aesthet Surg J.* 2018;38(11):NP165-NP167.

3. Master M. Hyaluronic acid filler longevity and localization - MRI evidence. *Plast Reconstr Surg.* 2021; 147:50e-53e.

4. Christen M, Vercesi F. Polycaprolactone: how a well-known and futuristic polymer has become an innovative collagen-stimulator in esthetics. *Clinical, Cosmetic and Investigational Dermatology*. 2020; 13:31-48.

5. Mehta U, Fridirici Z. Advanced techniques in nonsurgical rhinoplasty. *Facial Plast Surg Clin North Am.* 2019; 27(3):355-365.

6. Bertossi D, Lanaro L, Dorelan S, Johanssen K, Nocini P. Nonsurgical Rhinoplasty: Nasal Grid Analysis and Nasal Injecting Protocol. *Plast Reconstr Surg.* 2019; 143(2):428-439.

7. Jung GS. Clinical aesthetics of the nose for filler injection. *Facial Plast Surg.* 2019; 35(5):561-562.

8. Moon HJ. Injection rhinoplasty using filler. *Facial Plast Surg Clin North Am.* 2018; 26(3):323-330.

aesthetic medicine

Original Article

Hyper electromagnetic field technology: a novel therapeutic option to reduce abdominal fat

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Running title: **HyperEM technology to reduce abdominal fat**

Abstract

Background: abdominal fat is a health related issue to this day, physical activity is considered the best method to reduce it. However daily exercise can be a struggle for many as it is quite time consuming, which has therefore caused for people to ask about other ways to reduce belly fat.
Objective: to evaluate the effectiveness of an approach based on Electro-Magnetic Field focused on Hyper-Maximum Intensity (HyperEM) technology in abdominal modelling.
Methods: the study was carried out in 32 female patients (37.3 ± 9.4 years) under informed consent. Before and after treatment, anthropometric parameters (weight, height, BMI, skinfolds), subcutaneous abdominal fat thickness (echo-sonogram), and tone muscle (digital photography) were all measured. All patients underwent 6 sessions of treatment for over two weeks (3 times per week). Each session lasted 30 minutes.
Results: a significant decrease ($p<0.0001$) in the values corresponding to the supra-ilium and abdominal skinfolds was observed. In agreement with the skinfold values, significant differences were observed ($p<0.0001$) regardless of the location (supraumbilical, infraumbilical or lateral) in the subcutaneous abdominal fat thickness measured by using ultrasound. The component that highly contributed to these differences was the variation in the subcutaneous superficial fat thickness ($p<0.0001$). However, the muscles' tone was positively increased post treatment.
There were no clinical symptoms in any of the participants indicating the presence of major physiological abnormalities related to muscle damage for up to two months after application.
Conclusions: the Electro-Magnetic Field focused on Hyper-Maximum Intensity is a safe and effective technological approach for non-invasive body shaping, increasing muscle tone, strengthening the abdominal muscles and reducing abdominal fat.

Keywords
HyperEM, abdominal fat reduction, abdominal muscles strengthening

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Introduction

The accumulation of abdominal fat is one of the most frequent disorders in overweight, obese, or even anthropometrically normal people[1,2]. Subcutaneous fat is an important factor affecting the patient's body contours as it embraces approximately 25% of the human body's composition. However, muscle tissue comprises even a larger portion of the human body (around 42% in males and 36% in females) which may vary according to individual characteristics. The condition of the patient's muscle plays indeed an important role in defining the overall aesthetic appearance[3]. Abdominoplasty and liposuction offer a permanent solution to fat reduction. However, the removal of excess fat does not solve the problem of muscle flaccidity developed through increased intra-abdominal pressure and reduced muscular tension[4]. Nonetheless, physical workout is currently the most available method for natural muscle strengthening. Unfortunately, finding the time to do so seems to be an issue for most people, which causes for there to be a constant demand for more practical and non-invasive methods to reduce belly fat, while strengthening abdominal muscles. This situation has driven the market to the development of new body shaping procedures. In this regard, Hyper Electromagnetic Field technology appears as a new non-invasive approach. It is applied through high-intensity focused electromagnetic fields. This procedure consists of approximately 23,000 muscle contractions. The electromagnetic pulses are delivered at a high frequency rate that prevents muscle relaxation, resulting in supramaximal contractions, which are not reproducible by voluntary muscle contraction. Previous studies have shown that the application of the high-intensity focused electromagnetic field based on focused magnetic stimulation works by strengthening the internal muscles of the abdomen and reducing fat deposition[4,5]. Another study showed that this approach used in a therapy scheme composed of four sessions lasting 30 min lead to an increase (16%) in abdominal muscle thickness and a reduction of 19% in the abdominal fat layer[6], however the mechanisms by which its application causes a reduction in abdominal fat are still not very clear. The use of a high-intensity electromagnetic field in a porcine model resulted in adipocyte apoptosis[7]. Supramaximal contractions may lead to an increased metabolic activity of adipocytes in the region of stimulation and subsequent breakdown of lipids into free fatty acids (FFA) and glycerol[8]. It has been proposed that in the case of supramaximal contractions, the lipid breakdown could lead to an overflow of FFA in the intracellular space. When the amount of FFAs exceeds a certain level in the intracellular space, this may lead to an adipocyte dysfunction. An increased intracellular concentration of FFA may also lead to the natural death of affected cells by a mechanism of the endoplasmic reticulum (ER) stress-induced apoptosis[7].
The objective of this study was to evaluate the short-term effects of the use of Electro-Magnetic Field Focused on Hyper-Maximum Intensity (HyperEM) technology on the reduction of the subcutaneous abdominal fat thickness and the strength of abdominal muscle tone in a group of adult female Venezuelan volunteers.

Methods

Population

32 female patients who attended the UNIMEL clinic, Caracas, Venezuela, were evaluated for non-invasive body modelling from August 2019 to November 2019. Prior to treatment, according to the declaration of Helsinki[9,10], informed consent of each patient was obtained as well their compliance in the use of the data including photographs for scientific and educational purposes. The project was approved by the Ethics Committee for the UNIMEL Center, constituted independently by professors of the Faculty of Medicine and the School of Law of the Central University of Venezuela as well as of members of the Community in accordance with the applicable laws of the Bolivarian Republic of Venezuela, following the guidelines established by the WHO[11].

Clinical evaluation

Patients were examined clinically with an emphasis on cardiovascular, renal, chronic diseases that compromise the respiratory and gastrointestinal systems. Patients undergoing cardiovascular disorders, pregnancy, recent deliveries, recent surgeries, anticoagulant therapy, pacemakers, electronic implants, drug pumps, defibrillator, implanted neurostimulator and metal implants or underwent cosmetic or surgical body treatments 6 months before were excluded from this study. A medical history was assessed including records of personal diseases and habits (smokers, exercise practice, type of nutrition). Weight was determined by an OMRON BF511 Bioelectrical Impedance Monitor (OMRON Healthcare UK Ltd). Standing height was measured by a Harpender Portable Stadiometer (Holtain Ltd., UK) to the nearest 0.1 cm. Height information was stored for each patient in in the OMROM BF511 device. The Body Mass Index (BMI) was calculated for each patient as weight (kg) divided by the squared height (meters)[12,13] using the OMROM BF511 software[14].
Suprailium and abdominal skinfolds measurements were performed by the same anthropometrist before and after treatment using a Lange caliper (Cambridge Scientific Industries Inc., Cambridge, Maryland, USA) on the right side of the body with the subject standing in a relaxed condition as previously reported[15,16]. Suprailium skinfolds were taken directly above the most lateral side of the iliac tubercle in the ilio-axillary line. Abdominal vertical folds were taken 5 cm at the right of the umbilicus. Measurements were performed in quadruplicate and the average value was reported.
Abdominal fat thickness was also measured before and during treatment by ultrasound (Phillips HD7XE Ultrasound system, Philips Medical Systems. The Netherlands) following the protocol reported by Katz and his coworkers[4]. Changes in muscle tone were evaluated through 3D digital photography studies.

Patient's treatment using HyperEM technology

All participants underwent abdomen modelling using a HyperEM based device (Hypersculpt, VioSculpt™, San José, California USA). The complete procedure consisted of 6 sessions spread over two weeks (3 times per day, repeated 3 times per week). Each session lasted 30 minutes under the supervision of specialized

personnel. The treatment was carried out applying the device onto the abdominal area, acting on the rectus abdominis muscle and the external and internal oblique muscles. The position of the applicator was adjusted at the beginning of the treatment. The initial intensity was established according to the patient's tolerance threshold starting from 10%, increasing approximately every 15 seconds until reaching a maximum of 100%. All patients reached 100% intensity.

Statistical analysis

Data analysis was performed using the Graph Pad Prism version 5.00 for Windows (Graph Pad Software, San Diego California USA). The averages of the values for the different parameters obtained before and after treatment were compared by two-tailed paired t-test with a 95% confidence interval. Percentages were compared using the Fisher's exact test.

Results

Characteristics of the group

Thirty two (32) females with an average age of 37.3 ± 9.4 years participated as volunteers in this project. According to the WHO classification[17,18], 54.1% of the participants who were overweight (BMI: 25-29) (37.5%), and obese (BMI ≥ 30) (9.4%), exhibited a normal BMI (18-24.9). It was also found that 11.1% of the participants were smokers, 33% of them reported alcohol intake at least once a week, 48% include fats and sugars regularly in their daily diet and 80% include fruits and vegetables at least twice a week in their diet. In addition, 16.5% of the participants reported that they practiced some type of physical exercise at least twice a week.

Effect of HyperEM treatment on anthropometric measures

Table 1 shows that BMI values in the overall group did not vary significantly after treatment with HyperEM. However, an extremely significant decrease of the values corresponding to middle abdominal circumference as well as of the supra-ilium and abdominal skinfolds was observed after six treatment sessions (*Table 1*) indicating a significant decrease in abdominal fat. Moreover, 66.7% as well as 70% of the overall group showed a decrease > 2mm in the values of the abdominal and supra-ilium skinfolds respectively (*Figure 1*) which was more noticeable in overweight and obese patients (*Figure 2*).

	Normal			Overweight			Obese		
	Before	After		Before	After		Before	After	
	Mean (95% CI)	Mean (95% CI)	p	Mean (95% CI)	Mean (95% CI)	p	Mean (95% CI)	Mean (95% CI)	p
BMI (kg/m2)	**22.2** (21.3-23.1)	**21.9** (21.2-22.8)	0.08	**27.0** (25.9-28.1)	**26.8** (24.8-28.8)	0.62	**34.4** (29.3-39.6)	**33.7** (29.0-38.5)	0.06
Middle abdominal circumference (cm)	**74.7** (73.6-75.9)	**71.5** (69.4-73.7)	<0.0001	**88.3** (86.3-90.2)	**87.8** (84.7-90.8)	0.0002	**101.0** (93.9-108.0)	**93.0** (78.0-108.0)	0.04
Abdominal skin fold	**23.6** (20.2-26.9)	**20.4** (18.2-22.6)	0.002	**32.3** (26.4-38.2)	**24.5** (18.7-30.4)	0.007	**38.5** (27.1-49.9)	**31.2** (27.2-35.2)	0.04
Suprailium skin fold	**27.4** (23.1-31.7)	**22.5** (19.1-25.9)	0.0003	**35.9** (29.9-41.9)	**28.1** (22.9-33.4)	0.01	**39.8** (25.0-54.6)	**34.3** (20.7-47.9)	0.003

Table 1 *- Variations in anthropometric measures after six sessions of treatment using HyperEM.*

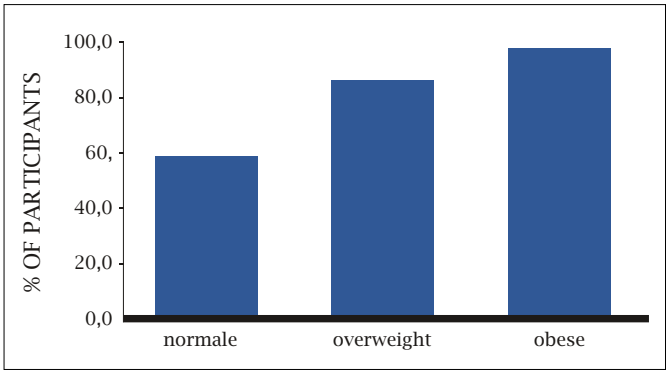

Figure 1 *- Proportion of participants with a decrease > 2mm in the abdominal skinfold.*

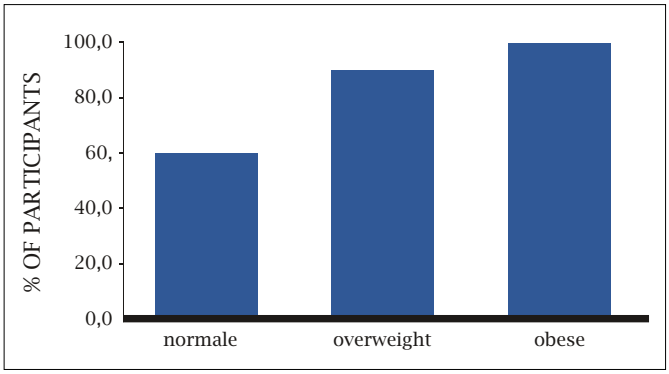

Figure 2 *- Proportion of participants with a decrease > 2mm in the supra-ilium skinfold.*

	before (mean ± Sd)	after (mean ± Sd)	P*
Supraumbilical			
Superficial	1.07 ± 0.56	0.90 ± 0.51	0.038
Deep	1.48 ± 0.81	1.31 ± 0.86	0.037
Total	2.55 ± 1.25	2.22 ± 1.27	0.002
Infraumbilical			
Superficial	1.14 ± 0.54	0.93 ± 0.50	0.009
Deep	1.22 ± 0.55	1.01 ± 0.56	0.014
Total	2.27 ± 1.07	1.94 ± 1.02	0.0006
Right lateral			
Superficial	1.23 ± 0.64	0.96 ± 0.59	0.001
Deep	1.31 ± 0.60	1.17 ± 0.64	0.028
Total	2.54 ± 1.12	2.13 ± 1.13	< 0.0001
Left lateral			
Superficial	1.17 ± 0.57	0.99 ± 0.47	0.0007
Deep	1.29 ± 0.63	1.09 ± 0.60	0.006
Total	2.47 ± 1.11	2.09 ± 0.98	< 0.0001

Table 1 *- Variations in anthropometric measures after six sessions of treatment using HyperEM.*

Effect of HyperEM on abdominal fat thickness measured by ultrasound

Consistent with both abdominal and suprailium skinfold values, there was a significant decrease in the abdominal fat thickness measured by ultrasound in the group overall (*Table 2*). These differences were statistically significant regardless of the abdominal location (supraumbilical, infraumbilical, or lateral). A greater decrease was observed for the superficial subcutaneous fat thickness compared to that observed for deep or total subcutaneous fat thickness.

Effect of HyperEM on abdominal muscle strengthening

The evaluation of digital photographs showed a reduction in the overall abdominal volume and an improvement in muscle tone that correlated with variations in ultrasound studies (*Figure 4*). After 6 sessions, no patient presented side effects such as bruising, petechiae, muscle pain or redness after each session. Only 15% of the patients manifested feeling pain, and out of these only 1% felt severe pain.

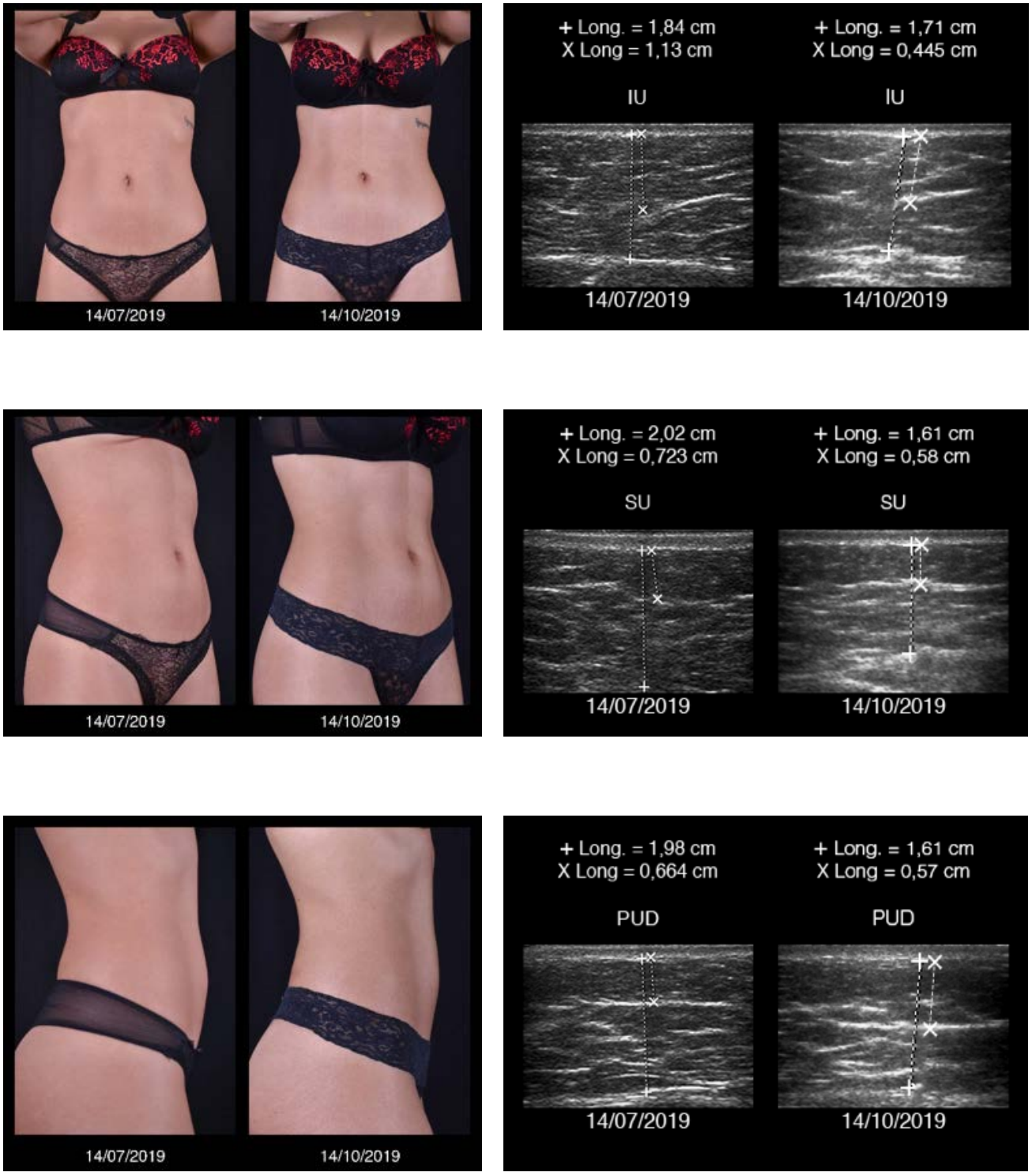

Figure 4a *- Reduction in the overall abdominal volume and an improvement in muscle tone correlating with variations in ultrasound studies in an anthropometrically normal patient.*

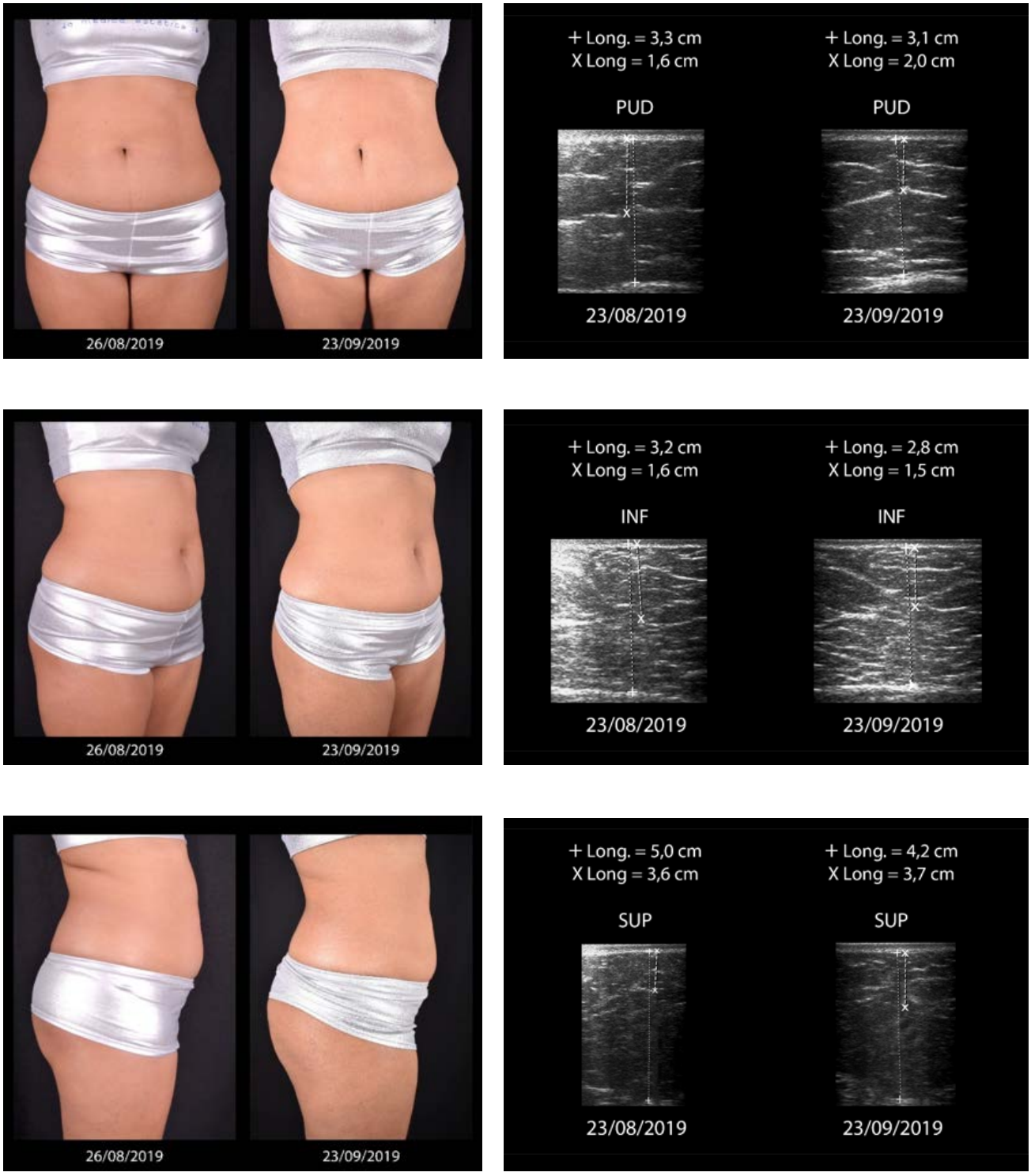

Figure 4b *- Reduction in the overall abdominal volume and an improvement in muscle tone correlating with variations in ultrasound studies in an overweight patient.*

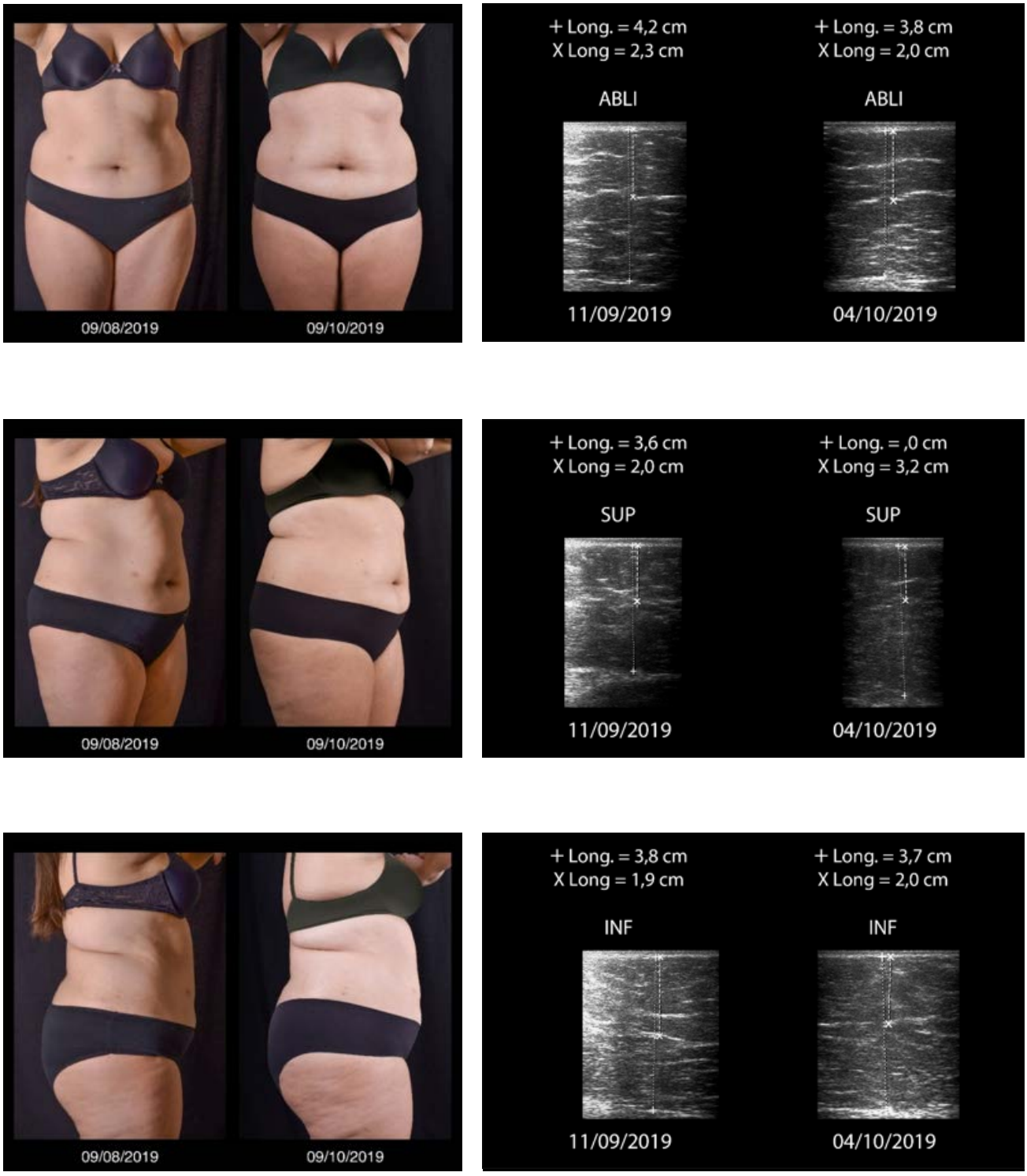

Figure 4c *- Reduction in the overall abdominal volume and an improvement in muscle tone correlating with variations in ultrasound studies in an obese patient.*

Discussion

This study investigated the potential use of HyperEM technology for non-invasive body modeling in a group of 32 Venezuelan volunteer women. The approach proved to be effective by toning abdominal muscles and reducing subcutaneous abdominal fat in all the patients who participated in the study. As explained in the introduction, HyperEM technology induces almost 20,000 pulses in a 30-minute session. Such a frequency of nerve stimuli leads to supramaximal muscle contractions that are not voluntarily achievable. Muscle tissue is forced to adapt to this stress, resulting in hyperplasia and muscle hypertrophy, significantly improving muscle tone. These results confirm previous findings reported in other studies[3,5,19,20] using Hyper Electromagnetic Field technology for muscle toning. Because the application of this approach does not affect nociceptors, it is not painful[21] causing minimal discomfort in the women participating in the program.
The data presented in this study showed a substantial reduction in abdominal subcutaneous fat measured either with anthropometrics or ultrasound. These results confirm previous findings of another recent study where a similar approach was used to reduce abdominal fat[4]. In that study, ultrasound analyses report that 1 month after 4 sessions, patients showed a significant reduction of the fat layer (average 19.0%), and this reduction was sustained for up to 3 months after treatment (average 23.3%). Similarly, Kinney et al found a reduction average of 18.6% in abdominal fat, evaluated with an MRI 2 months after four sessions using Hyper Electromagnetic Field technology[6]. In the current study the reduction in abdominal fat was significant in all patients regardless their anthropometric status including overweight and obese women. The accumulation of abdominal fat particularly in overweight individuals is related to other clinical conditions such as cardiovascular diseases[22] and the development of non-alcoholic fatty liver diseases[23]. This entails that the use of HyperEM technology to decrease abdominal fat would benefit particularly overweight patients who usually do not practice any type of exercise by preventing other important clinical conditions.
The results observed in terms of adipose tissue reduction using this approach are comparable to those obtained with thermal technologies, which routinely report reductions ranging from 20% to 29%[24,25]. However, unlike thermal devices that externally affect the adipocyte cell membrane, HyperEM works on the muscle, causing supramaximal contractions. As explained above, these contractions may cause metabolic disturbances that can lead to the release of locally saturated free fatty acids[7] that may cause the apoptosis of adipocytes[26]. Findings from experimental models support these results[7,27,28]. In contrast, a recent clinical study designed to investigate adipose tissue responses to electromagnetic muscle stimulation (EMMS) in comparison to cryolipolysis, indicates that EMMS does not induce any injury in the adipocytes. Histological analysis harvested from the superficial and deep subcutaneous fat layers of the patients that underwent EMMS did not evidenced any postinflammatory response that would normally follow the adipocytes' injury[29] while cryolipolysis treated tissues exhibits an inflammatory response in the fat layer evidenced by loss of perilipin, which is a characteristic of an irreversible adipocyte injury[29]. Nevertheless, more studies in larger populations would be required to confirm these results. On the other hand, the possibility that supramaximal contractions would induce metabolic changes leading to abdominal fat reduction should also be investigated. Hence, HyperEM appeared as an outstanding new approach among a variety of non-invasive body contouring procedures, such as cryolipolysis, radiofrequency heating, 1060 nm laser heating, high-intensity focused ultrasound, and non-thermal focused ultrasound[29]. The choice of one of these the procedures to reduce abdominal fat will depend on the particular characteristics of the patient and the availability of the respective devices. The results of this work confirm that HyperEM is an effective, safe and successful approach for non-invasive abdomen shaping, increasing muscle tone and reducing abdominal fat. All study participants were satisfied with the results and pleased with the new appearance of their abdomen. However the mechanisms by which reduction of abdominal fat occurs needs further elucidation.

Acknowledgements

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Declaration of Interest

The authors declare that they have no competing interests.

REFERENCES

1. Popa IR, Sotolongo OCG, Gámez ÁA. El índice cintura-talla como variable de acumulación de grasa para valorar riesgo cardiovascular. *Rev Cuba Med Mil.* 2013; 42(4).
2. Scarsella C, Després J-P. Tratamiento de la obesidad: necesidad de centrar la atención en los pacientes de alto riesgo caracterizados por la obesidad abdominal. *Cad Saude Publica.* 2003; 19(suppl 1):S7-S19.
3. Jacob C, Kinney B, Busso M, et al. High intensity focused electromagnetic technology (HIFEM) for non-invasive buttock lifting and toning of gluteal muscles: A multi-center efficacy and safety study. *J Drugs Dermatology.* 2018; 17(11):1229-1232.
4. Katz B, Bard R, Goldfarb R, Shiloh A, Kenolova D. Ultrasound Assessment of Subcutaneous Abdominal Fat Thickness After Treatments With a High-Intensity Focused Electromagnetic Field Device. *Dermatologic Surg.* 2019; 45(12):1542-1548.
5. Kinney BM, Lozanova P. High intensity focused electromagnetic therapy evaluated by magnetic resonance imaging: Safety and efficacy study of a dual tissue effect based non-invasive abdominal body shaping. *Lasers Surg Med.* 2019; 51(1):40-46.
6. Kinney BM, Kent DE. MRI and CT Assessment of Abdominal Tissue Composition in Patients After High-Intensity Focused Electromagnetic Therapy Treatments: One-Year Follow-Up. *Aesthetic Surg J.* 2020; 40(12):NP686-NP693.
7. Weiss RA, Bernardy J. Induction of fat apoptosis by a non-thermal device: Mechanism of action of non-invasive high-intensity electromagnetic technology in a porcine model. *Lasers Surg Med.* 2019; 51(1):47-53.
8. Gorski J. Muscle triglyceride metabolism during exercise. *Can J Physiol Pharmacol.* 1992; 70(1):123-131.
9. Manzini JL. DECLARACIÓN DE HELSINKI: PRINCIPIOS ÉTICOS PARA LA INVESTIGACIÓN MÉDICA SOBRE SUJETOS HUMANOS. *Acta Bioeth.* 2000; 6(2):321-334.
10. GANDEVIA B, TOVELL A. DECLARATION OF HELSINKI. *Med J Aust.* 1964; 2:320-321.
11. Organization WH. Operational Guidelines for Ethics Committees That Review Biomedical Research. Published online 2012. LINK PDF.
12. Heart N, Lung U, Institute B. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. WMJ. 1998; 97(9).
13. Executive summary of the clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. *Arch Intern Med.* 1998; 158(17):1855-1867.
14. OMRON BF511 Bioelectrical Impedance Monitor Instruction Manual. LINK PDF.
15. Durnin JVGA, Womersley J. Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 Years. *Br J Nutr.* 1974; 32(1):77-97.
16. NORTON K, OLDS T. Antropométrica: Um Livro Sobre Medidas Corporais Para o Esporte e Cursos Da Área as Saúde.; 2005. Accessed September 19, 2021. LINK PDF.
17. Materko W, Benchimol-Barbosa PR, Carvalho ARS, Nadal J, Santos EL. Accuracy of the WHO's body mass index cut-off points to measure gender- and age-specific obesity in middle-aged adults living in the city of Rio de Janeiro, Brazil. *J Public health Res.* 2017; 6(2):904.
18. Hunma S, Ramuth H, Miles-Chan JL, et al. Body composition-derived BMI cut-offs for overweight and obesity in Indians and Creoles of Mauritius: Comparison with Caucasians. *Int J Obes (Lond).* 2016; 40(12):1906-1914.
19. Abulhasan JF, Rumble YLD, Morgan ER, Slatter WH, Grey MJ. Peripheral electrical and magnetic stimulation to augment resistance training. *J Funct Morphol Kinesiol.* 2016; 1(3):328-342.
20. Jacob CI, Paskova K. Safety and efficacy of a novel high-intensity focused electromagnetic technology device for noninvasive abdominal body shaping. *J Cosmet Dermatol.* 2018; 17(5):783-787.
21. Tyler DJ. Peripheral nerve stimulation. In: Neuroprosthetics: *Theory and Practice: Second Edition.* World Scientific Publishing Co. Pte. Ltd.; 2017:300-347.
22. Lee JJ, Pedley A, Hoffmann U, Massaro JM, Fox CS. Association of Changes in Abdominal Fat Quantity and Quality With Incident Cardiovascular Disease Risk Factors. *J Am Coll Cardiol.* 2016; 68(14):1509-1521.
23. Kim D, Chung GE, Kwak MS, et al. Body Fat Distribution and Risk of Incident and Regressed Nonalcoholic Fatty Liver Disease. *Clin Gastroenterol Hepatol.* 2016; 14(1):132-138.
24. Ingargiola MJ, Motakef S, Chung MT, Vasconez HC, Sasaki GH. Cryolipolysis for fat reduction and body contouring: safety and efficacy of current treatment paradigms. *Plast Reconstr Surg.* 2015; 135(6):1581-1590.
25. Kennedy J, Verne S, Griffith R, Falto-Aizpurua L, Nouri K. Non-invasive subcutaneous fat reduction: a review. *J Eur Acad Dermatology Venereol.* 2015; 29(9):1679-1688.
26. Hardy S, El-Assaad W, Przybytkowski E, Joly E, Prentki M, Langelier Y. Saturated fatty acid-induced apoptosis in MDA-MB-231 breast cancer cells. A role for cardiolipin. *J Biol Chem.*
27. Duncan D, Dinev I. Noninvasive Induction of Muscle Fiber Hypertrophy and Hyperplasia: Effects of High-Intensity Focused Electromagnetic Field Evaluated in an In-Vivo Porcine Model: A Pilot Study. *Aesthetic Surg J.* 2020; 40(5):568-574.
28. Halaas Y, Bernardy J. Mechanism of nonthermal induction of apoptosis by high-intensity focused electromagnetic procedure: Biochemical investigation in a porcine model. *J Cosmet Dermatol.* 2020; 19(3):605-611.
29. Zachary CB, Burns AJ, Pham LD, Lozano JNJ. Clinical Study Demonstrates that Electromagnetic Muscle Stimulation Does Not Cause Injury to Fat Cells. *Lasers Surg Med.* 2021; 53(1):70-78.

aesthetic medicine

Case Report

Management of post-radiotherapy edema in patients with previous labial silicone implants

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Abstract
A 58 years-old patient, who underwent lips silicone implants in 1994, was diagnosed with Hodgkin Lymphoma of the hypopharynx, and was treated with radiotherapy. She developed an oedema, inflammation and felt pain 10 days after the last session. Corticosteroids and antibiotics were started. After an initial improvement, the patient relapsed due to the discontinuation of therapy. Steroids were initiated once again, in association with 300 mg of oral fermented Maltodextrin. The intake of steroids was interrupted after 20 days while Maltodextrin was continued for 3 months resulting in a complete recovery.
Oedema and inflammation are common complications of radiotherapy, especially in patients with silicone implants. Pathogenic mechanisms rely on innate immunity activation, pro-inflammatory cytokine secretion, bacteremic seeding and silicone exposure. Conservative methods, corticosteroids and antibiotics are commonly used as treatment. However, prolonged exposure to these medications could lead to steroid-related side effects and antibiotic resistance. Maltodextrin is a starch derived polysaccharide with anti-inflammatory properties. It inhibits the secretion of IL-6 and gamma interferon and has the capacity to disrupt bacterial biofilm in vitro.
In our patient, this treatment associated with corticosteroids and antibiotics relieved symptoms and reduced exposure to steroids and antibiotics.
Short periods of treatment with Maltodextrin, in association with other treatments could be an option to relieve symptoms and reduce exposure to steroids and antibiotics as it provides a good safety profile. To the best of our knowledge this is the first report describing the use of Maltodextrin in post radiation inflammation in a patient with silicone implants.

Keywords
Silicone implants, radiotherapy, inflammation, oral maltodextrin

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Introduction

The outbreak of the Coronavirus disease in 2019 (COVID-19) has drastically changed life and the approach to Medicine. Since March 2020 most governments across the globe have imposed the closure of all non-essential services in order to prevent the spreading of the virus and an overload in the healthcare system. This has temporarily reduced the access to dermatological and aesthetic treatments. However, ever since the situation improved and things started reverting to normality, an increasing number of patients asking for aesthetic treatments have been registered. As revealed by Bourleigh et al.[1], this was mostly related to the need to "feel better", to "gain confidence" or "as a gift for myself" after a period of anxiety, depression and social isolation.
Along with an increased number of performed treatments, a rising number of complications related to such procedures have also been registered. Therefore, it is of great importance to quickly recognize, prevent and manage those complications in order to ensure the best aesthetical result and preserve the patient's safety. Here below we describe a case of lips oedema which appeared after radiotherapy in a patient with lip silicone implants.

Case description

A 58 years-old female, who underwent lips silicone implants in 1994, was diagnosed with Hodgkin Lymphoma of the hypopharynx and treated with radiotherapy in May 2020. She developed lips oedema, local inflammation and pain 10 days after the last session (*Figure 1*). The patient's past medical history and clinical examinations were unremarkable except for recent radiotherapy exposure and signs of limited phlogosis. Ultrasound was performed in order to evaluate the morphological conditions of the labial tissue and the characteristics of the silicone implants, and did not reveal any abnormality. After a discussion with the oncologist, a treatment of oral prednisone was selected, with the dose of 0,3 mg/kg once daily (25 mg) in the morning after meals. Even in the absence of any signs of infection, oral antibiotics (clarithromycin 500 mg twice daily) were prescribed in association with prednisone in order to help the healing process. Symptoms rapidly improved and antibiotics could have been stopped 7 days after the appearance of symptoms while steroids could have been quickly tapered until discontinuation within 10 days. However, symptoms relapsed once cortisone was stopped. Oral corticosteroids in the dose of 0,3 mg mg/kg once daily (Prednisone 25 mg per day) in the morning after meals, were re-initiated. Antibiotics were not prescribed in order to avoid the development of resistant bacteria and because the relapsed clearly occurred after the discontinuation of cortisone.
The patient then began taking Fermented Maltodextrin (Serrados® Anatek Health, capsules) in the dose of 300 mg twice daily, taken away from meals. Symptoms alleviated within one week after the beginning of treatment. Corticosteroids could have been tapered within 10 days leading to a complete discontinuation on day 20 after the relapse. The Treatment with Fermented Maltodextrin was continued for 3 months fully healing the patient (*Figure 2*).
No side effects of the treatment with Maltodextrin were reported by the patient. They were checked and followed up every week for the first month, and every month for the subsequent three months and every three months by telemedicine for the whole year. Neither relapses nor side effects of treatment were reported during the follow up period.

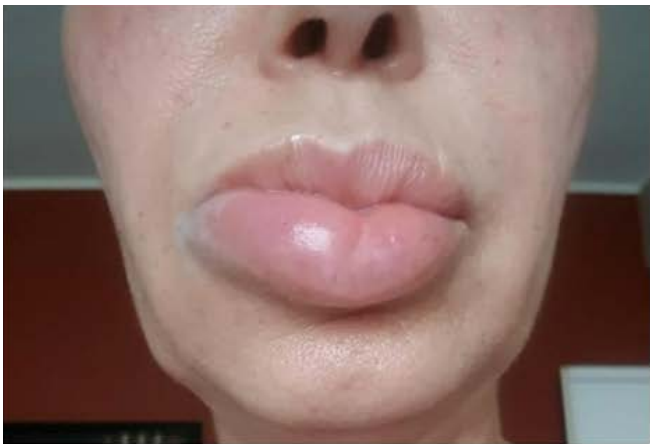

Figure 1 *- Lips oedema, local inflammation and pain 10 days after the last session.*

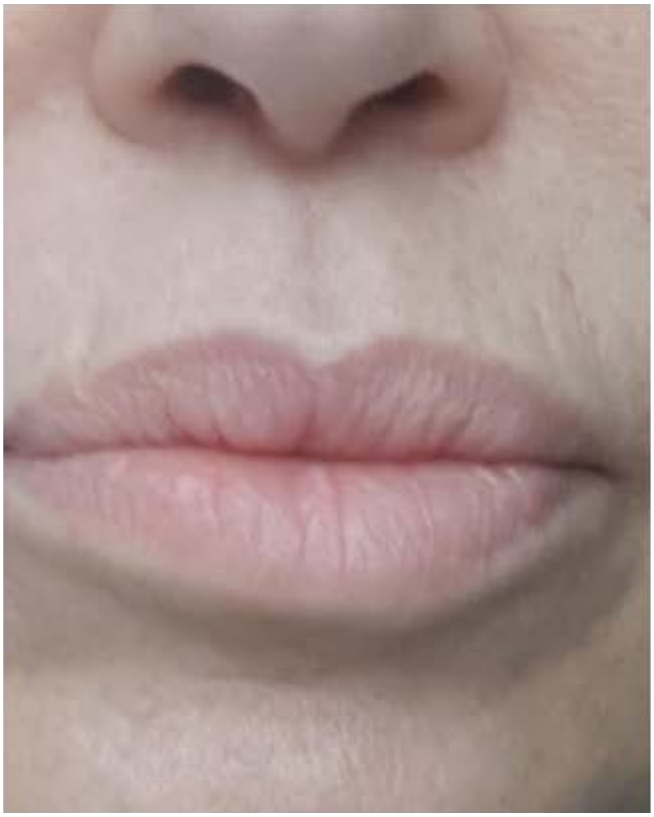

Figure 2 *- Treatment with Fermented Maltodextrin was continued for 3 months fully healing the patient.*

Discussion

Little is known about labial edemas after exposure to radiotherapy, the only studies performed were on patients with breast implants and treated with radiotherapy for breast cancer. It seems to be related to several factors. Radiotherapy has a pro-inflammatory effect because it promotes the production of Reactive Oxygen Species (ROS), pro-inflammatory chemochines, resulting in the recruitment of innate immune cells in the inflammation site leading to tissue damage. In support of this pro-oxidant and pro-inflammatory environment induced by radiotherapy is the fact that non-steroidal anti-inflammatory drugs (NSAIDs), steroids and antioxidants can improve signs of phlogosis in vivo[2] as was seen in our patient.
The type of material used for the implants is also important in causing post-radiation complications.
Lo Torto et al.[3] clearly described how silicone implants, of which the labial implants of our patient were made, undergo greater structure deformation than polyurethane implants that have larger pores and whose structure seems to remain almost intact after radiotherapy.
The therapy of post-radiation oedema mostly relies on conservative methods, the use of NSAIDs, systemic corticosteroids and antibiotics if concomitant infection is suspected. However, prolonged exposure to those medications could lead to steroid-related side effects and antibiotic resistance. Fermented Maltodextrin is a starch derived polysaccharide and used as a prebiotic in intestinal discomfort. Although knowledge about the use of fermented Maltodextrinis is still limited in the medical field, and even more in the field of aesthetic medicine, its beneficial effect is becoming more and more popular. In fact, fermented Maltodexin seems to reduce inflammation by reducing pro-inflammatory cytokines such as interleukin 6 and gamma interferon[4]. Moreover, Maltodextrin seems to improve the patient's response to antibiotics due to the disruption of bacterial biofilm that leads to a better penetration of the antibiotics in the infected site in vitro[5]. In our patient, the administration of fermented Maltodextrin as a support treatment reduced inflammation, extended the relief of symptoms and reduced exposure to steroids and antibiotics in our patient. However, prolonged use of maltodextrin should be avoided because of the risk of gastrointestinal inflammation[6]. In our patient treatment with fermented maltodextrin was stopped 3 months after the appearance of symptoms.

Conclusion

Oedema and local inflammations are common complications of radiotherapy especially in patients with silicone implants. Short supportive treatments with oral fermented Maltodextrin in association with other therapies could be an option to improve symptoms and reduce exposure to steroids and antibiotics as it has good safety profile. To the best of our knowledge this is the first report describing the use of Maltodextrin in post radiation oedema and inflammation in a patient with silicone implants. We strongly encourage reports of such cases in order to increase awareness of potential complications of /and related to aesthetic treatments in order to therefore improve their management.

Acknowledgments

The authors declare that they have no conflict of interest.
The patient gave her written consent for the publication of this case report.

REFERENCES

1. Burleigh A, Beleznay K, Humphrey S. Aesthetic medicine during COVID-19: Patient perspectives and motivations amidst a pandemic. *J Cosmet Dermatol.* 2021; 20(3):711-713.

2. Schaue D, Micewicz ED, Ratikan JA, Xie MW, Cheng G, McBride WH. Radiation and inflammation. *Semin Radiat Oncol.* 2015; 25(1):4-10.

3. Lo Torto F, Relucenti M, Familiari G, et al. The Effect of Postmastectomy Radiation Therapy on Breast Implants: Material Analysis on Silicone and Polyurethane Prosthesis. *Ann Plast Surg.* 2018; 81(2):228-234.

4. Wang S, Zhang S, Huang S, et al. Resistant Maltodextrin Alleviates Dextran Sulfate Sodium-Induced Intestinal Inflammatory Injury by Increasing Butyric Acid to Inhibit Proinflammatory Cytokine Levels. *Biomed Res Int.* 2020; 2020:7694734.

5. Kiamco MM, Atci E, Khan QF, et al. Vancomycin and maltodextrin affect structure and activity of Staphylococcus aureus biofilms. *Biotechnol Bioeng.* 2015; 112(12):2562-70.

6. Arnold AR, Chassaing B. Maltodextrin, Modern Stressor of the Intestinal Environment. *Cell Mol Gastroenterol Hepatol.* 2019; 7(2):475-476.

Review

Effect of Photobiomodulation on Platelet-Rich Plasma: Review Series on New Tools in Regenerative Medicine

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Short title: **Photobiomodulation and Platelet-Rich Plasma**

Abstract

Objective: platelet-rich plasma is one of the blood-derived autologous biological products, that has now become a therapeutic tool. Though its properties have not been fully elucidated yet, the ease of its sample obtention, product processing, and patient application, along with the good results obtained, has extended its application to many medical specialties such as orthopedics, sports, and aesthetic medicine, or gynecology. Lately, photobiomodulation has been presented as an effective PRP activator, resembling what occurs on mesenchymal cells that have been widely studied. This article aims to give a modern view on PRP and its activation through photobiomodulation.
Methods: A review series was carried out in PubMed, Cochrane, and Scopus to find articles about studies done on humans on PRP and photobiomodulation.
Results: a total of five studies with small samples were found. In all of them, the activation with photobiomodulation had positive results.
Conclusion: photobiomodulation showed great potential for PRP activation. However, more studies must be carried out to establish the appropriate protocols with which all potential clinical benefits can be obtained.

Keywords

Photobiomodulation, photoactivation, platelet-rich plasma, platelet, infrared, near-infrared

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Introduction

In the last decade, blood-derived autologous biological products have become useful therapeutic tools for treating several conditions. Below are some medical specialties in which the application of these products is most developed: 1) wound healing, and regenerative medicine, especially for diabetic foot ulcers[1]; 2) orthopedic and sports medicine, where they are used to alleviate pain caused by conditions such as tendinitis, arthritis, ligament sprains, tears, or intervertebral disc degeneration[2-4]; 3) gynecology, where they are used to treat cervical ectopy, vulvar dystrophy, reconstructive surgery for vulvar cancer in urogenital disorders, genital prolapse or urinary incontinence[3]; 4) dermatology and aesthetic medicine, which use them for hair restoration, skin rejuvenation, acne scars, dermal augmentation, and striae distensae, among other conditions[3,5]; 5) cardiac surgery[6]. These types of autologous therapeutic strategies include platelet concentrates (PC), mainly represented by platelet rich-plasma (PRP) and platelet-rich fibrin (PRF), which combine bioactive components derived from plasma/platelets like the cytokines, chemokines, growth factors (GF), and enzymes[7].

PRP is obtained by processing blood as a supra-physiological platelet concentration included in a small volume of plasma, which can be used in the liquid phase or in gel form[8]. Its rationale is based on improving the healing process by increasing the concentration of the platelet-derived growth factor (PDGF), basic fibroblast growth factor (bFGF), transforming growth factor ß (TGF-ß), vascular endothelial growth factor (VEGF), interleukins, hormones, and several hundred other proteins released by platelets[9-11].

Despite the large diversity of protocols for PRP preparation, all of them involve a common sequence: 1) extraction of peripheral blood; 2) centrifugation of the sample; 3) concentration of the platelets; 4) platelet stimulation. Multiple variations can be identified in each of these phases, mainly: 1) volume of drawn blood; 2) type of anticoagulant used; 3) centrifugation parameters; 4) extraction and sample collection materials; 5) the type of platelet-activating agents[12]. All of this results in a highly heterogeneous biological potential[13].

PRP Collection Procedures

There are two basic protocols: those designed based on plasma and those based on the leucocyte layer[8]. Those based on plasma retrieve from 300,000 to 500,000 platelets/µL, employing lower revolutions and less centrifugation time. Alternatively, protocols based on the leucocyte layer, which use buffy-coat systems, apply higher revolution centrifugation cycles for more minutes. The product obtained through these systems is leucocyte-rich PRP (L-PRP). It is characterized by a high concentration of platelets (500,000 to 1,500,000 platelets/µL) and the variable presence of leucocytes and erythrocytes[14].

The efficiency of PRP collection procedures could be improved by adjusting some of the process variables and by standardizing protocols[13,15]. Giusti et al. demonstrated that the optimal platelet concentration for angiogenesis induction in human endothelial cells was 1,500,000 platelets/µL; however, excessively high concentrations may inhibit the angiogenic process[16]. In addition, other factors could also influence the final product and should be taken into consideration, such as age, gender, circadian rhythm, or the pharmacological regime[17]. Moreover, it has been shown that its effectiveness can be increased if PRP is combined with other procedures, such as microneedles, dermal fillers, autologous fat grafting, or laser therapies[3]. The effects of PRP photoactivation are currently being studied through light irradiation: photomodulation or photobiomodulation (PBM). The activated PRP results in a product called photoactivated platelet-rich plasma (PA-PRP), of which there are still limited published trials[18].

PRP Chemical Activation Process

The activation of platelets during the preparation of PRP produces the release of the bioactive molecules stored in α–granules and stimulates the development of the matrix through fibrinogen cleavage[19].

The formation of clots traps the GFs generated, allowing bioactive molecules to be released and confined in the injured area. Exogenous or endogenous factors may induce activation. The most common exogenous factors include thrombin, calcium chloride, calcium chloride a thrombin mixture, and calcium gluconate[13,14,20]. Endogenous activation consists of platelet exposure to native collagen or another coagulation factor, such as ADP, thrombospondin, or a platelet-activating factor. Both processes spontaneously induce the formation of clots at the site of the injury, where platelets act[20].

Another exogenous factor that has been suggested as a PRP activator is PBM. In 2020, Irmak et al.[9] described platelet photoactivation in vitro by applying a polychromatic light source in the near-infrared range region and comparing platelets at rest with calcium chloride-activated PRP. This study showed that photoactivation of PRP induced a release of PDGF, FGF, and TGF-beta, which is significantly more significant and more prolonged than that obtained with calcium chloride-mediated activation.

Proposed Mechanism of Action of PBM

Scientific research of PBM started about 50 years ago[21] and, although it is now a promising procedure for treating several diseases, both its intimate mechanism and the wavelengths responsible for triggering its effects remain uncertain[22]. In general, PBM refers to non-invasive, non-toxic phototherapy in the range of 600 to 1000 nm[23]. Its biological effect is attributed to 1) the absorption of light by a photoreceptor of the respiratory chain that would induce mitochondrial activation[23], and to 2) the photons absorbed by mitochondria, which would produce an increase in adenosine triphosphate (ATP)[24]. Another proposed hypothesis associates PBM

with ion channels as the latter would be sensitive to light, thus allowing calcium to enter the cell[25].
Laser light has been shown to stimulate several biological processes, such as cell growth and proliferation[26]. In particular, infrared irradiation affects mammals' bioenergetic balance and mitochondrial biogenesis[27], and can stimulate them[28]. Isolated mitochondrial irradiation induces changes in mitochondrial transcription and translation, increasing the cascade reactions and the number of certain components of the respiratory chain, such as cytochromes, cytochrome oxidase, and flavin dehydrogenase[29]. Lock et al. 2019 suggested that mitochondrial stimulation by PBM could be due to the absorption of light at the metal centers of some molecules of the respiratory chain, which could lead to the stimulation of the cytoplasm and the mitochondrial enzymes[30].
PBM increases complexes I, II, III, IV, and succinate dehydrogenase activity in the electron transfer chain. It has been observed that, following irradiation, some enzymes, such as NADH dehydrogenase or cytochrome C oxidase (CCO), and substrates such as adenine nucleotides, show a significant change in their biochemical properties[31]. Most photostimulation effects could be explained by the absorption of light by cytochrome C oxidase (COX), also known as complex IV, the enzyme that limits the speed of terminal phosphorylation in the mitochondrial respiratory chain9, which seems to be the main photoaceptor. This is supported by 1) increased oxygen consumption during low-level light irradiation, since most of a cell's oxygen consumption is produced at complex IV, in the mitochondria, and 2) the fact that sodium azide (NaN3), a COX inhibitor, cancels out this beneficial effect.
The absorption of photons by COX results in the acceleration of electron transfer reactions and ATP production[26,27]. In addition to increasing ATP and AMPc, PBM also increases the level of nitric oxide (NO), whether from the release of metal complexes into COX (which has two hemes and two copper centers) or due to the regulation of COX activity as a nitrite reductase[32].
There are several devices used for PBM: 1) helium-neon gas lasers (He-Ne), gallium arsenide (GaAs), neodymium-doped yttrium-aluminum garnet (Nd: YAG), aluminum gallium arsenide (GaAlAs), aluminum gallium indium phosphide (InGaAlP), carbon dioxide (CO2); 2) light-emitting diode (LED) matrices; and 3) visible light[23].
It has been well established that the biostimulating effects of the laser depend on parameters such as wavelength, the density of energy, power, frequency, and the duration of the irradiation[33]. Achieving adequate energy dosage to produce the beneficial effects of PBM is a complex task since it not only depends on the parameters of the light applied but also on the correct setting of the source emitting the light energy, the technical application, or the intervals between sessions. Different wavelengths exert different effects on the cells. In stem cells derived from human adipose tissue, for example, it has been observed that red light (660 nm) and near-infrared (810 nm) light stimulate cell proliferation, while blue light (415 nm) and green light (540 nm) inhibit it[34]. To date, the beneficial effects of PBM have been verified both in vivo and in vitro, and in several conditions and physiological processes, such as wound healing, hypoxic injury, and brain degeneration[35], where a decrease in inflammation or stimulation of injury repair have been observed[36]. However, there is still no consensus regarding the molecular, cellular, or tissular mechanisms of action of PBM[37].

PRP Photoactivation

Studies published on PBM and PRP are still scarce. However, many studies on mesenchymal cells have led to promising results, and that could be highly useful to interpret PBM-PRP interactions[38]. Wavelengths between 600 and 1000 nm produce changes in the viability, proliferation, and/or migration of MSCs, predicting an excellent regeneration potential. However, drawing sound conclusions from PBM research on MSCs is no easy task since the multiple devices used and the large variability of parameters applied have caused treatment protocols of varying results[34].
Mandle et al. 2011[39] assessed the viability of platelets and white blood cells, platelet activation, and the release of growth factors and cytokines in the PA-PRP of seven subjects. Cell viability was high in all samples, but the authors concluded that PBM did not activate the platelets. The authors indicate that the treatment effect with this device could be related to white blood cell activation and that experiments are therefore necessary with the PRP produced from whole blood which needs to be compared with paired leucocyte blood samples.
In 2020, Gülseen et al.[40] conducted a study with Gel-MA/PRP hydrogels to assess GF release following the regular application of polychromatic light. They noted that the application of light increased elasticity and decreased the hydrogel radiation rate. The regular application of light resulted in controlled and sustainable GF release, regardless of the number of platelets or GF concentrations, and the protection of PRP bioactivity with high mechanical properties.
In 2021, Ghidini et al.[41] concluded that only a defined amount of energy (fluence 5 J/cm^2 delivered in two minutes and 10 J/cm^2 in four minutes) is most effective to induce cell proliferation and calcium deposition in the presence of platelet-rich plasma.
Considering that platelets also have mitochondria, it could be argued that the effects observed in MSCs following PBM might, to a certain extent, also be observed in platelets: the conditioning of PRP with PBM could provide benefits, such as enhanced regenerative properties[38]. The published studies on PRP conditioning with PBM on humans before application to the patient are summarized below.

In Vivo Research on PRP PBM

A total of five articles were found about the conditioning of human PRP with PBM in vivo: Freitag et al. 2012 and 2013[18,42], Paterson et al. 2016[43], Mohiuddin et al. 2018[44], and Irmak et al. 20209. The parameters and procedures for PRP collection and PBM can be seen in *Table 1 (click here to see Table 1)*.

In 2012 and 2013, Freitag et al.[18] published two clinical cases of two men: a 38-year old with pain in his left knee and a 50-year old with osteoarthritis in the left knee[42]. Both were injected intra-articular PA-PRP. Conditioning was performed at 600-1200 nm. Results showed that the Numerical Pain Rating Scale (NPRS) score improved at 7 weeks and was maintained at 0 until week 15. The Western Ontario and McMaster Universities Arthritis (WOMAC) Index was normalized in both patients between visits 7 and 12, and the patient suffered instability symptoms with entirely resolved osteoarthritis at 15 weeks. In 2016, Paterson et al.[43], conducted a randomized, double-blind study in 19 patients with knee osteoarthritis, Kellgren-Lawrence 2-3. Results of the Osteoarthritis Outcome Score (KOOS) and the Knee Quality of Life 26-item questionnaire (KQoL-26) were measured at 4 and 12 weeks following the PA-PRP injection (n=10). They were compared with a control group (n=9) that received intra-articular hyaluronic acid (HA) injections. The results obtained did not have sufficient statistical power to assess efficacy. Still, preliminary data provided some evidence that the application of PA-PRP in patients with knee arthrosis improved: 1) self-assessed pain, 2) KOOS and KQoL-26 sub-scales, and 3) lower-limb functional capacity tests.
In 2020, Irmak et al.[9], conducted a study in healthy males between 20 and 26 years of age, assessing the level of ATP following the application of polychromatic light to PRP for 10 minutes, after incubation in α-MEM in a CO2 incubator at 37ºC for 24 h (*Table 1*). The study consisted of 2 parts: the first showed a significant increase in ATP following PBM; in the second, platelets were also stimulated with PAC, and there was a significant increase in ATP at 24 h. Mohiuddin et al.[44], in 2018, conducted a study in 232 patients between 40 and 70 years old with knee arthrosis. Patients were treated with PA-PRP (*Table 1*), and, to measure their level of effectiveness, total WOMAC scores were measured at the baseline visit and after treatment. At the end of treatment, 12 months following the PA-PRP injection, the total score was significantly reduced ($p = 0.00$).

Current Barriers of the Effective Implementation of PBM

Cellular conditioning procedures that could help optimize PRP results (and other autologous materials) are well documented. However, this type of protocol requires implementing several successive steps, some of which are not supported by the necessary scientific evidence or are still being developed.

Technical Issues

When deciding the level of effectiveness of PBM for PRP or any other tissue, the following must be considered: 1) control of the energy-emitting source; 2) an understanding of what will happen with the media through which the light will travel; and 3) an understanding of the scope of the obstacles entailed by the media and containers where the PRP will be housed for the application of PBM.
The characteristics of the light energy applied should be accurately known: wavelength, power, and focal distance, among other items. On the other hand, understanding how dispersion, scattering, and other optical phenomena occurring every time light travels through a medium will entail an additional challenge. Finally, it will be essential to study the behavior and properties of PRP as a liquid medium where the target cells will be found to ensure accurate dosage. All these are mainly physical problems.
In general, experimental PBM protocols conducted in PRP or other liquid media-embedded cells placed the target structures in Petri dishes, to which some light-emitting energy source (LEDs or lasers) was applied. These types of setups could have led to some interesting conclusions regarding potential cell responses to light, but in no way could they be used to build therapeutic protocols since they failed to comply with the most basic rule of experimental science: reproducibility. It is necessary to develop a technology or model that will guarantee control of the emitting source and the optical phenomena occurring from the emission of light energy until it impacts the target cell.
In recent years, promising efforts have been undertaken to control the flaws of these types of setups. However, these designs failed since they did not consider the other steps required to obtain an adequate PBM. For example, the study conducted by Mandle et al. in 2011[39], where they applied energy in reproducible conditions but failed to control the container where the target cells were held, lighting the PRP in 10 ml syringes. It cannot be guaranteed that these cells would have received the intended dose since the optical characteristics of the syringe are inadequate and, a setup such as this can cancel out the influence of internal movements or flows of the liquid where the cells are embedded. This is a very sensitive matter, as it means that some of the target cells may have received a higher dosage than planned, while other cells may not have received any energy at all. It becomes apparent that failing to control one or several of these factors may seriously compromise the outcomes and conclusions of any trial. It is necessary to develop a technology or model that consider and control the medium housing the target cells to receive exactly the intended dose since this is the basis for any medical therapeutic procedure.

Biological Issues

The intimate interrelation mechanism between light and the PRP must be understood and agreed upon. Understanding the platelet response changes to the variations in the setup of the source of energy applied will be crucial for the PBM-PRP relationship to change its status from “physical stimulus” to that of a “therapeutic procedure.” Lastly, and perhaps most importantly, we must determine the clinical impact of these changes on cellular responses. In vivo studies in humans are done to understand said clinical impact and the physiological changes that occur after the light energy is absorbed by the PRP target chromophores.

Conclusions

As a renowned therapy with extraordinary regenerative potential, PBM has already embarked upon its transformation journey and will stop being an up-

and-coming tool to become a crucial element in the medical armamentarium. This transformation entails awareness and understanding of all the steps and elements involved through sound evidence. These framework steps can be summarized as follows: 1) Platelets are active quasi-cellular elements, which are fully capable of responding to PBM; 2) Platelet responses are complex, susceptible to modulation, and have extraordinary potential, which can lead to all kinds of clinical improvements; 3) The technology for the useful and effective application of PBM must guarantee the proper cellular stimulus and an accurate dosage; and 4) A larger corpus of evidence must be built, to adequately support and endorse all the steps. This transformation will only be possible to answer the following questions concerning any PBM procedure: 1) What cells should be stimulated? 2) How should they be stimulated to obtain the intended response? And 3) With what clinical goal? All our PBM-related R&D efforts must follow this direction.

Conflict of Interest

The authors have no conflicts of interest or financial ties to disclose.

REFERENCES

1. Driver VR, Hanft J, Fylling CP, Beriou JM. A prospective, randomized, controlled trial of autologous platelet-rich plasma gel for the treatment of diabetic foot ulcers. *Ostomy Wound Manage.* 2006; 52(6):68–70, 72, 74.

2. Melchinger H, Jain K, Tyagi T, Hwa J. Role of Platelet Mitochondria: Life in a Nucleus-Free Zone. *Front Cardiovasc Med.* 2019; 6:153.

3. Emer J. Platelet-Rich Plasma (PRP): Current Applications in Dermatology. *Skin Therapy Lett.* 2019; 24(5):1–6.

4. Mlynarek RA, Kuhn AW, Bedi A. Platelet-Rich Plasma (PRP) in Orthopedic Sports Medicine. *Am J Orthop (Belle Mead NJ).* 2016; 45(5):290–326.

5. Cervelli V, Garcovich S, Bielli A, et al. The effect of autologous activated platelet rich plasma (aa-prp) injection on pattern hair loss: clinical and histomorphometric evaluation. *Biomed Res Int.* 2014; 2014:760709.

6. Gunaydin S, McCusker K, Sari T, et al. Clinical impact and biomaterial evaluation of autologous platelet gel in cardiac surgery. *Perfusion.* 2008; 23(3):179–86.

7. Anitua E, Nurden P, Prado R, Nurden AT, Padilla S. Autologous fibrin scaffolds: When platelet- and plasma-derived biomolecules meet fibrin. *Biomaterials.* 2019; 192:440–60.

8. Mariani E, Pulsatelli L. Platelet concentrates in musculoskeletal medicine. *Int J Mol Sci.* 2020; 21(4):9–12.

9. Irmak G, Demirtaş TT, Gümüşderelioğlu M. Sustained release of growth factors from photoactivated platelet rich plasma (PRP). *Eur J Pharm Biopharm.* 2020; 148:67–76.

10. Golebiewska EM, Poole AW. Secrets of platelet exocytosis - what do we really know about platelet secretion mechanisms? *Br J Haematol.* 2014; 165(2):204–16.

11. Zhu Y, Yuan M, Meng HY, et al. Basic science and clinical application of platelet-rich plasma forcartilage defects and osteoarthritis: a review. *Osteoarthritis Cartilage.* 2013; 21(11):1627–37.

12. Amin I, Gellhorn AC. Platelet-Rich Plasma Use in Musculoskeletal Disorders: Are the Factors Important in Standardization Well Understood? *Phys Med Rehabil Clin N Am.* 2019; 30(2):439–49.

13. Lansdown DA, Fortier LA. Platelet-Rich Plasma: Formulations, Preparations, Constituents, and Their Effects. *Oper Tech Sports Med.* 2017; 25(1):7–12.

14. DeLong JM, Russell RP, Mazzocca AD. Platelet-rich plasma: the PAW classification system. *Arthroscopy.* 2012; 28(7):998–1009.

15. Samadi P, Sheykhhasan M, Khoshinani HM. The Use of Platelet-Rich Plasma in Aesthetic and Regenerative Medicine: A Comprehensive Review. *Aesthetic Plast Surg.* 2019; 43(3):803–14.

16. Giusti I, Rughetti A, D'Ascenzo S, et al. Identification of an optimal concentration of platelet gel for promoting angiogenesis in human endothelial cells. *Transfusion.* 2009; 49(4):771–8.

17. Weibrich G, Kleis WKG, Hafner G, Hitzler WE. Growth factor levels in platelet-rich plasma and correlations with donor age, sex, and platelet count. *J Craniomaxillofac Surg.* 2002; 30(2):97–102.

18. Freitag J, Barnard A, Rotstein A. Photoactivated platelet-rich plasma therapy for a traumatic knee chondral lesion. *BMJ Case Rep.* 2012; 2012:bcr2012006858.

19. Parrish WR, Roides B. Physiology of Blood Components in Wound Healing: an Appreciation of Cellular Co-Operativity in Platelet Rich Plasma Action. *J Exerc Sport Orthop.* 2017; 4(2):1–14.

20. Davis VL, Abukabda AB, Radio NM, et al. Platelet-rich preparations to improve healing. Part II: Platelet activation and enrichment, leukocyte inclusion, and other selection criteria. *J Oral Implantol.* 2014; 40(4):511–21.

21. Heiskanen V, Hamblin MR. Photobiomodulation: lasers: vs. light emitting diodes? *Photochem Photobiol Sci.* 2018; 17(8):1003–17.

22. Greco M, Vacca RA, Moro L, et al. Helium-Neon laser irradiation of hepatocytes can trigger increase of the mitochondrial membrane potential and can stimulate c-fos expression in a Ca2+-dependent manner. *Lasers Surg Med.* 2001; 29(5):433–41.

23. Ahrabi B, Tavirani MR, Khoramgah MS, et al. The effect of photobiomodulation therapy on the differentiation, proliferation, and migration of the mesenchymal stem cell: A review. *J Lasers Med Sci.* 2019; 10(Suppl 1):S96–S103.

24. Han B, Fan J, Liu L, et al. Adipose-derived mesenchymal stem cells treatments for fibroblasts of fibrotic scar via downregulating TGF-β1 and Notch-1 expression enhanced by photobiomodulation therapy. *Lasers Med Sci.* 2019; 34(1):1-10.

25. Fallahnezhad S, Jajarmi V, Shahnavaz S, et al. Improvement in viability and mineralization of osteoporotic bone marrow mesenchymal stem cell through combined application of photobiomodulation therapy and oxytocin. *Lasers Med Sci.* 2019; 35(3):557–66.

26. Karu TI. Multiple roles of cytochrome c oxidase in mammalian cells under action of red and IR-A radiation. *IUBMB Life.* 2010; 62(8):607–10.

27. Hamblin MR. Mechanisms and Mitochondrial Redox Signaling in Photobiomodulation. *Photochem Photobiol.* 2018; 94(2):199–212.

28. Benedicenti S, Pepe IM, Angiero F, Benedicenti A. Intracellular ATP level increases in lymphocytes irradiated with infrared laser light of wavelength 904 nm. *Photomed Laser Surg.* 2008; 26(5):451–3.

29. Bortoletto R, Silva NS, Zângaro RA, Pacheco MTT, Da Matta RA, Pacheco-Soares C. Mitochondrial membrane potential after low-power laser irradiation. *Lasers Med Sci.* 2004;18(4):204–6.

30. Silveira PCL, Ferreira GK, Zaccaron RP, et al. Effects of photobiomodulation on mitochondria of brain, muscle, and C6 astroglioma cells. *Med Eng Phys.* 2019; 71:108–13.

31. Yu W, Naim JO, McGowan M, Ippolito K, Lanzafame RJ. Photomodulation of oxidative metabolism and electron chain enzymes in rat liver mitochondria. *Photochem Photobiol.* 1997; 66(6):866–71.

32. De Freitas LF, Hamblin MR. Proposed Mechanisms of Photobiomodulation or Low-Level Light Therapy. *IEEE J Sel Top Quantum Electron.* 2016; 22(3):7000417.

33. El Gammal ZH, Zaher AM, El-Badri N. Effect of low-level laser-treated mesenchymal stem cells on myocardial infarction. *Lasers Med Sci.* 2017; 32(7):1637–46.

34. Wang Y, Huang YY, Wang Y, Lyu P, Hamblin MR. Red (660 nm) or near-infrared (810 nm) photobiomodulation stimulates, while blue (415 nm), green (540 nm) light inhibits proliferation in human adipose-derived stem cells. *Sci Rep.* 2017; 7(1):1–10.

35. Kim K, Lee J, Jang H, et al. Photobiomodulation enhances the angiogenic effect of mesenchymal stem cells to mitigate radiation-induced enteropathy. *Int J Mol Sci.* 2019; 20(5):1131.

36. Kouhkheil R, Fridoni M, Abdollhifar MA, et al. Impact of Photobiomodulation and Condition Medium on Mast Cell Counts, Degranulation, and Wound Strength in Infected Skin Wound Healing of Diabetic Rats. *Photobiomodul Photomed Laser Surg.* 2019; 37(11):706–14.

37. De Freitas LF, Hamblin MR. Proposed Mechanisms of Photobiomodulation or Low-Level Light Therapy. *IEEE J Sel Top Quantum Electron.* 2016; 22(3):7000417.

38. Pinto H, Goñi Oliver P, Sánchez-Vizcaíno Mengual E. The Effect of Photobiomodulation on Human Mesenchymal Cells: A Literature Review. *Aesthetic Plast Surg.* 2021; 45(4):1826-1842.

39. Mandle R, Kevy S, Jacobson M. AdiLight-1: PRP study. 2011 (click here).

40. Gülseren I, Gumusderelioglu M. Photoactivated platelet rich plasma (PRP) based patient-specific bio-inkfor cartilage tissue engineering. *Biomed Mater.* 2020 Jun 18.

41. Ghidini G, Mori D, Pulcini S, Vescovi P, Sala R. Photobiomodulation with a 645 nm Diode Laser of Saos-2 Cells and Platelet-Rich Plasma: The Potential for a New Mechanism of Action. *Photobiomodulation, Photomedicine, Laser Surg.* 2021; 39(2):86–93.

42. Freitag JB, Barnard A. To evaluate the effect of combining photo-activation therapy with platelet-rich plasma injections for the novel treatment of osteoarthritis. *BMJ Case Rep.* 2013; 2013:bcr2012007463.

43. Paterson KL, Nicholls M, Bennell KL, Bates D. Intra-articular injection of photo-activated platelet-rich plasma in patients with knee osteoarthritis: A double-blind, randomized controlled pilot study. *BMC Musculoskelet Disord.* 2016; 17:67.

44. Akm M, P L, Choudhury KN, BU S. Clinical outcome of photoactivated platelet-rich plasma in the treatment of knee osteoarthritis. *Rheumatol Orthop Med.* 2018; 4(1):1-4.

aesthetic medicine

Letter to the Editor

Microneedling Therapy for Post-Acne Atrophic Facial Scars: A Cost-effective Solution

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Abstract

Background: acne scar treatment remains a challenge to the clinician despite the availability of an array of treatment modalities. Microneedling therapy or collagen induction therapy is a minimally-invasive non-surgical modality for facial rejuvenation. Controlled skin injury is inflicted using a microneedling device which triggers the body to fill these micro-wounds by producing new collagen and elastin in the papillary dermis. This leads to a reduction of scars, improved skin texture, firmness and, hydration, with minimal damage to the skin.
Aim and objectives: the study aimed to evaluate the efficacy of microneedling therapy in atrophic post-acne facial scars. The objectives of the study were to analyze the changes seen in the scars and skin texture after a minimum of three sessions of microneedling therapy.
Materials and method: 10 patients with facial acne scarring, underwent three sessions of microneedling therapy using Dermaroller. Subjective and objective evaluations were performed using questionnaires and photographs respectively and the results were statistically analyzed.
Results: all patients were satisfied with the treatment outcome. The outcome was rated by the observers as excellent in 3 patients and good in 7 patients. The total time taken for treatment completion was 1.5-2 months.
Conclusion: microneedling is a cost effective therapy for treating post-acne atrophic facial scars.

Keywords

Microneedling therapy, collagen induction therapy, percutaneous collagen induction therapy, dermaroller, acne scars, atrophic facial scars

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Introduction

Symmetry, balance, and proportion are the basics of facial beauty and the perception of facial aesthetics markedly determines subject attitudes and social behavior[1]. Scars are areas of fibrous tissue that replace normal skin after injury as part of the biological process of wound repair in the skin[2,3]. Severe scarring caused by acne is associated with substantial physical and psychological distress and low self-esteem, particularly in adolescents[4]. Acne is a disease of the pilosebaceous unit involving abnormalities in sebum production, follicular epithelial desquamation, bacterial proliferation, and inflammation[5]. The disease is characterized by a great variety of clinical lesions which could be non-inflammatory such as open and closed comedones or inflammatory which vary from small papules with an inflammatory areola to pustules and large, fluctuant and tender nodules. Scarring frequently results from severe inflammatory nodulocystic acne but may also result from more superficial inflamed lesions or self-manipulation[4]. Scarring occurs early in all types of acne, not just in nodulocystic diseases, but does vary with the severity and delay in seeking treatment[4]. There are two general types of acne scars: hypertrophic (keloid) scars and atrophic (icepick, rolling and boxcar) scars[6]. Scar treatment aims at giving the skin a better physical appearance. Resurfacing techniques destroy the epidermis and allow for re-epithelialization with collagen remodeling. They include chemical peels, dermabrasion, lasers, selective photothermolysis, cryotherapy, and electrosurgery[7].

Surgical methods include excision, punch elevation, and subcision[8]. Acne scars can be treated with dermal fillers which are quite a safe method, with a low risk of inflammatory reactions[6]. Scars may be filled with collagen injections, artificial dermal filler, or autologous fat transfer. Dermal fillers have a variable duration of effect (6-12 months)[6,9]. Topical retinoids are a good adjunct to resurfacing techniques as they increase the synthesis of mucopolysaccharides, collagen, and fibronectin and decrease collagenase production[7]. They also shorten the healing time after invasive cosmetic procedures[10]. However majority of the treatment options suffer from limitations and considerable morbidity and may interfere with the daily activities of patients in the post-treatment period. Newer treatments and techniques are being considered in recent years; one being microneedling, which has shown favorable clinical and histopathological responses in skin post treatment[11]. Microneedling using dermaroller is a new technique for scar treatment, particularly acne scars, stretch marks, wrinkles, and facial rejuvenation. It is a simple and affordable modality that also can be employed for transdermal drug delivery[12].

The concept of microneedling gained popularity in 2004-2005 following the invention and commercialization of the dermaroller. The term microneedling describes a dynamic process when microneedles arranged on a drum-shaped instrument, are passed (rolled) through the skin. The effectiveness of microneedling therapy is based on two mechanisms: first, the surgical release of the skin from its attachment to deeper tissues causing skin elevation, and second, the introduction of controlled trauma which promotes wound healing, augmenting the depressed site by connective tissue formation[13]. The study aimed to evaluate the effectiveness of microneedling therapy in atrophic acne scarring of the face.

Aim and objectives

The study aimed to objectively evaluate the efficacy of microneedling treatment in atrophic post acne facial scars.

The objectives were:

1. To analyze the changes seen in atrophic post acne facial scars by using microneedling therapy.
2. To analyze changes in skin texture after a minimum of three sessions of microneedling therapy.

Materials and methods

Following ethical clearance from the Yenepoya University Ethics Committee, 10 subjects with post-acne scarring on the face including the cheek and forehead region, reporting to the Department of Oral and Maxillofacial Surgery, Yenepoya Dental College, Mangalore from 2012-2014, were included in the study. Inclusion criteria included male and female patients with facial scars due to acne in the age group of 20-40 years with no systemic illnesses. Medically compromised patients, patients with active acne/active infection on the face, facial scars due to other causes such as burns or trauma, patients with keloidal tendency, patients on systemic medications for acne, and patients with unrealistic expectations were excluded from the study.

Pre-operative evaluation

Informed consent was obtained from all the patients and case history was recorded. Patient's skin was analyzed carefully for any active acne and pre-operative photographs were taken in the profile view (*Figures 1a* and *2a*). Patients were informed regarding a possible erythema following the procedure, lasting for about 48-72 hours. Patients were instructed to wash their face with soap and water prior to starting the treatment.

Procedure: Eutectic mixture of lignocaine 2% and prilocaine 2% (EMLA cream) was applied under occlusion for 1 hour to the affected areas and wiped using a gauze (*Figure 1b*). Dermaroller is a plastic device with a 12-cm handle that holds a drum-shaped cylinder at the end which is 2 cm in diameter and 2 cm in width. 192 medical grade stainless steel needles are arranged in eight rows on the cylinder surface. Each needle is 1.5 mm long and has a diameter of 0.25 mm. Needles are arranged radially at 15° to the roller center. The dermaroller was rolled on to the skin with minimal pressure using one hand, while stretching the skin with the other hand so that the base of the scars could be reached. Lateral pressure was avoided during rolling of the instrument on the skin to prevent scarring.

The instrument was moved backward and forward 6–10 times in four directions; horizontally, vertically, and

diagonally right and left to cover an area of roughly 2×2 inches until uniform pinpoint bleeding was seen (*Figure 1c*). This uniform pinpoint bleeding was taken as the end point. The serous ooze was wiped and the area was cleansed with a moist gauze. Microneedling was performed once every 2 weeks for a total of three sessions in all the patients. Post microneedling: Ice packs were applied on the area for 10-15 minutes. Patients were advised to avoid direct sun exposure for a minimum of 10 days and to use medicated sunscreen with a sun protection factor (SPF) of 30 for two weeks. Patients were asked not to apply any ointments apart from sunscreen and soaps on the treated area for 3 days after the session.

Post-operative evaluation

Digital color facial photographs were taken using a Sony Cyber-shot digital camera (DSC-W50, Sony Corp, Tokyo, Japan). Frontal, Left and Right profile views were obtained at baseline, during follow-up at each visit and at the end of follow-up 4 weeks after the last session (*Figures 1d and 2b*).

Patients were given a questionnaire to evaluate the post-operative changes in the skin texture and scars in the treated area (*Annexure I*). Three randomly selected, blinded observers were shown the pre and post-operative photographs of the patients and asked to evaluate the changes in size, shape, colour and overall satisfaction on a scale of 1 to 10. The assessment was done 3 weeks following the completion of the third sitting. The results were analyzed statistically using Kendall's W and Cochrane Q analysis.

Results

The atrophic facial scars were classified as icepick, box-shaped, rolling and hypertrophic types of scars. All 10 patients were classified as phototype IV according to the Flitzpatrick classification. Among the 10 patients, 8 patients were female and 2 were male. The most common type of scarring seen was the icepick type.

The total time period for the treatment was 8-10 minutes. The patients could resume their routine immediately after the procedure. Despite the application of EMLA cream on the area of scarring for 45minutes-1 hour, 60% of patients found the procedure painful. Other common adverse events noted were redness (n=9) and bleeding (n=3). There was hardly any change in pigmentation after three sittings (p=0.71) but significant improvement of the scars was noted in terms of number and depth (p=0.039). In the self-evaluation, patients considered the outcome of the treatment as good.

All three independent observers evaluated the cases separately to avoid inter-observer bias. The results of 3 patients were graded as "excellent outcome" and rest were graded as "good outcome". Though the Inter-observer agreement with respect to post-op assessment was low, the difference was not significant statistically (p=0.254). The correlation co-efficient between observer 1 and 2, 1 and 3 and 3 and 2 was -0.227, 0.175 and 0.557 respectively. The values are insignificant due to the small sample size and larger grading scale.

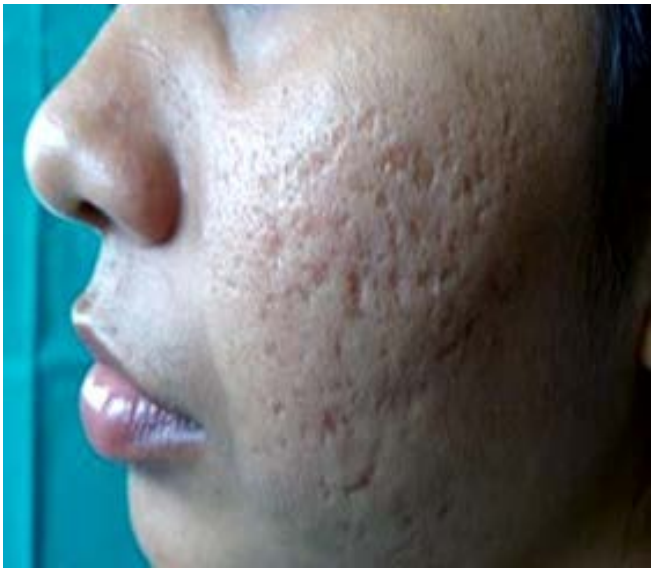

***Figure 1a** - Pre-operative photograph in profile view.*

***Figure 1b** - Application of EMLA local anesthetic cream and occlusal dressing.*

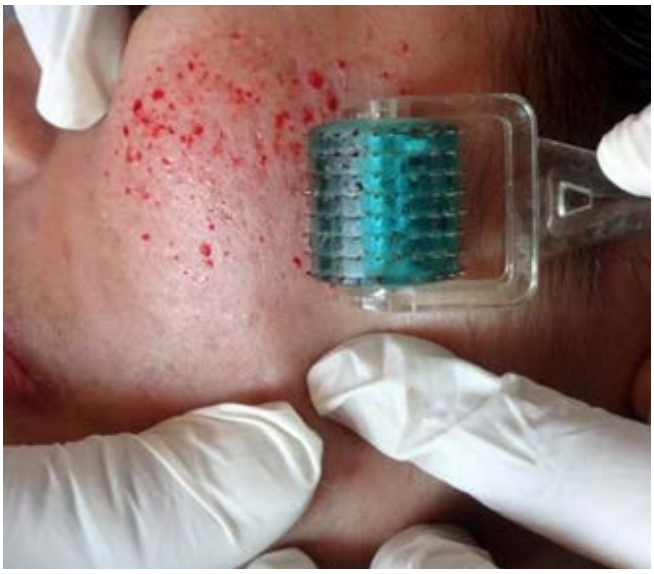

***Figure 1c** - Microneedling procedure using Dermaroller.*

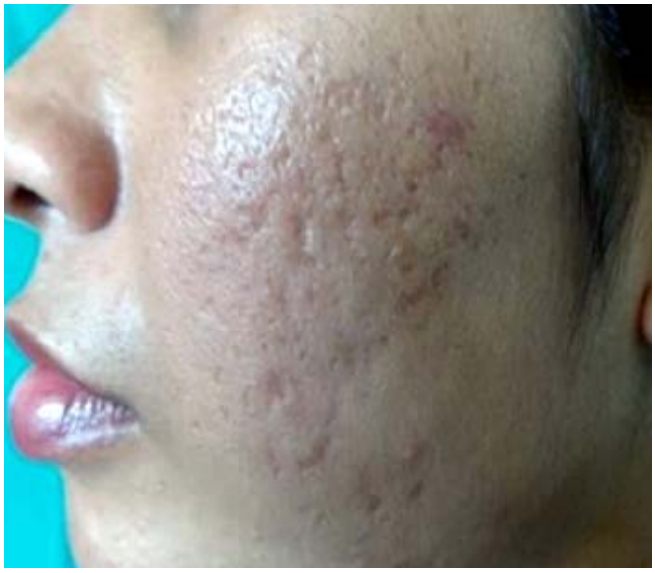

Figure 1d *- Post-operative profile view after 3 sessions of treatment.*

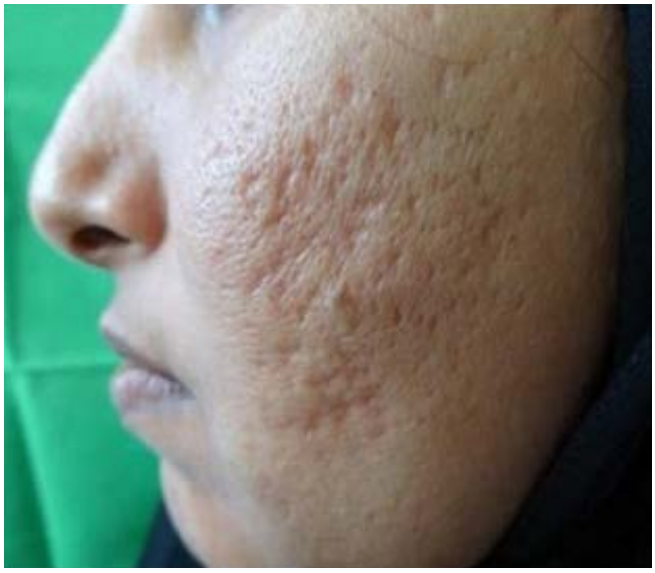

Figure 2a *- Pre-operative photograph in profile view.*

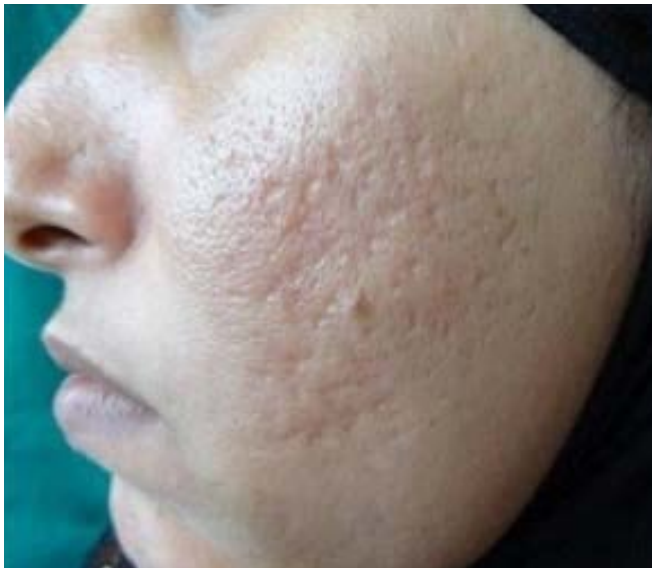

Figure 2b *- Post-operative profile view after 3 sessions of treatment.*

Discussion

Severe inflammatory acne can destroy the epidermis, dermis and the underlying fat and hence treating acne scars is one of the most difficult cosmetic surgery procedures[14]. The main treatment goal is to obtain as much improvement as possible rather than perfection[14]. As acne scarring can lead to significant psychological distress and low self-esteem, it is of utmost importance to have effective and satisfying treatments in the physician's armamentarium[9]. The best treatment for acne scarring is prevention through early treatment of active acne. Once scarring has developed, treatment should be personalized to suit the needs of the individual. Irrespective of the approach, patients must be counseled regarding possible options and realistic expectations must be set[6].

Our study aimed at evaluating the efficacy of collagen induction therapy in atrophic facial scars. Microneedling therapy, also known as collagen induction therapy is a recent addition to the treatment armamentarium for managing post-acne scars[11]. The treatment is performed as an office procedure after application of a local anesthetic cream, by means of an instrument known as a dermaroller[11]. Both surgical and non-surgical treatment options have been reported with complications and post-op sequelae[15]. As shown by Fernandes and Signorini, microneedling has advantages compared with conventional methods for the treatment of scars. The most important is that the epidermis remains intact because it is not damaged, eliminating most of the risks and side effects of chemical peeling or laser resurfacing[16].

Histological studies have shown that the skin was indistinguishable from normal skin and that the epidermis showed more dermal papillae. Skin becomes thicker with greatly increased collagen deposition and significantly more elastin[17]. Fabbrocini et al., (2009) showed that microneedling does not cause any damage to the stratum corneum, other layers of the epidermis or the basal membrane and there is no dermabrasive reduction of epidermal thickness evident 24 hours after the procedure. The number of melanocytes neither increased nor decreased in any of the groups[18]. This explains why microneedling can be repeated safely in dark skin and is also suited to areas where laser treatments and deep peels cannot be performed[19]. Most of our patients were dark skinned individuals and these studies supported our case selection.

In this study we used Jacob's classification of atrophic acne scars encompassing icepick, box scars and rolling scars and unifying the literature terminology. The Flitzpatrick scale was used to evaluate the skin type. All our patients belonged to the Flitzpatrick Type IV. A total number of 10 patients were a part of this study and all of them completed three sessions of the procedure.

The main result of this study showed that PCI (microneedling therapy) appears to be a simple and encouraging method for treating acne scars. It is cost effective with few or no side effects. The treatment was painful at times despite the application of local anesthesia owing to increased depth of the scars. The post-operative complications were pain, erythema and swelling lasting for a few hours after the procedure.

The tram line effect[19] was not reported in any of our patients. Immediately after the treatment, the skin showed uniform minimal pinpoint bleeding with a small ooze of serum that stops immediately. Fernandes (2005), recommends soaking the skin with saline swabs for an hour or two and then cleaning the skin thoroughly with a Tea Tree Oil–cleanser. He also suggests that the patient should avoid direct sun exposure for at least 10 days if possible and use a broad-brimmed hat or scarf to protect the facial skin[20].

Most of the studies so far have considered subjective assessments by the patients and health professionals by comparing the pre and post–operative photographs. There are no standardized parameters for assessing the post-operative changes. Jordan et al., (2000), assessed the effectiveness of laser resurfacing treatment for facial acne scars and concluded that there is a need for "good quality randomized controlled trials with standardized scarring scales" in order to compare treatment results among different articles[21]. Although the treatment efficacy evaluations classified the outcomes as excellent or good improvement in all of our patients, the results cannot be compared with the literature because of the lack of a standardized and worldwide accepted acne scar classification. The progress of the treatment was gradual and required follow-ups at regular intervals. This was in agreement with Fabbrocini et al., (2009), who showed that the severity of the acne scars in all patients was greatly reduced after only two sessions with an 8-week interval, without any side effects apart from redness and swelling, which disappeared in 2 to 3 days[18]. In our study the patients underwent three sittings and the results were more satisfactory after the third sitting. The overall treatment period for the patients was 3 months with an interval of 2 weeks between the two sittings. The follow-up period for all the patients was four weeks from the last sitting. The patients could resume their daily activities immediately after the treatment. It is difficult to satisfy the patient with high expectations since the treatment does not completely erase the scars but helps decrease their severity. We found that the patients who were self-motivated accepted the treatment and were satisfied with their results. All the observers more or less agreed on the result outcome. In our study we observed that icepick and box scars responded better than the rolling type of scars. In box scars the change in size and depth is appreciable. However Sharad (2011), reported no significant change in deep icepick scars after using the microneedling therapy[22]. For the optimization of acne scar treatment, there is no general guideline available. There are several combined management options utilizing medical, surgical and laser devices that are useful in obtaining significant improvement. Further research such as randomized controlled trials, are needed to quantify the benefits and to establish the duration of the effects, the cost-effectiveness of different treatments, psychological benefit and improvement of quality of life of these patients. Lastly, it is important to realize that a typical patient has scars of different morphological types and grades and it is difficult to treat all these scar types satisfactorily with a single treatment option and multiple treatment modalities may be required.

Conclusion

Acne scarring is a source of great stress and concern for the younger population and should not be dismissed by the clinician. The armamentarium for acne treatment is broad and evolving.

The conclusions of our study are:

a) Microneedling therapy is a simple, effective, minimally invasive, and economical procedure to improve atrophic post-acne scarring on the face.

b) Despite no antibiotic coverage, patients did not develop any infection.

c) The procedure was well tolerated by the patients with minimum post-operative complications.

d) A minimum of three sittings was essential for good results.

e) Further randomized clinical trials may be required to attain a more suggestive and definite inference.

Declarations

Funding: Nil
Conflict of interest: Nil
Ethical approval: Obtained from Yenepoya Ethics Committee (YUEC175/11/12/12)
Informed consent: Obtained from all participants prior to the treatment.

ANNEXURE I
PATIENT QUESTIONNAIRE

Please tick the correct response

During the procedure

1) Was the procedure painful? If yes, how long did the pain last?:	YES NO
2) Was there bleeding few hours after the procedure? If yes, for how long did the bleeding last?	YES NO
3) Was there any redness after the procedure?	YES NO
4) Was there any swelling?	YES NO

After 1st sitting

1) Was there any reduction in number of scars?	YES NO
2) Pigmentation:	Increased/ Decreased /Same
3) Was there any reduction in the depth of the scar?	YES NO
Has the skin texture improved?	YES NO

After 2nd sitting

1) Was there any reduction in number of scars?	YES NO
2) Pigmentation:	Increased/ Decreased /Same
3) Was there any reduction in the depth of the scar?	YES NO
4) Has the skin texture improved?	YES NO

After 3rd sitting

1) Was there any reduction in no. of scars?	YES NO
2) Pigmentation:	Increased/ Decreased /Same
3) Was there any reduction in the depth of the scar?	YES NO
4) Has the skin texture improved?	YES NO

1 month post-op follow up

Are you satisfied with the treatment?	YES NO
Rate the outcome of the treatment on a scale of 10	

REFERENCES

1. Dion KK, Berscheid E, Walster E. What is beautiful is good. *J Personal Soc Psychol.* 1972; 24:285-290.

2. Viera MH, Amini S, Valins W, Berman B. Innovative therapies in the treatment of keloids and hypertrophic scars. *J Clin Aesthet Dermatol.* 2010; 3(5):20-26.

3. Alster TS, West TB. Resurfacing of atrophic facial acne scars with a high-energy, pulsed carbon dioxide laser. *Dermatol Surg.* 1996; 22(2):151-155.

4. Fabbrocini G, Annunziata MC, D'Arco V, et al. Acne scars: pathogenesis, classification and treatment. *Dermatol Res Pract.* 2020; 2010/893080.

5. Leyden JJ. A review of the use of combination therapies for the treatment of acne vulgaris. *J Am Acad Dermatol.* 2003; 49(3 Suppl):S200-10.

6. Goodman GJ. Management of post-acne scarring. What are the options for treatment? *Am J Clin Dermatol.* 2000; 1(1):3-17.

7. Basta-Juzbašić A. Current therapeutic approach to acne scars. *Acta Dermatovenerol Croat.* 2010; 18(3):171-5.

8. Bhargava S, Kumar U, Varma K. Subcision and Microneedling as an Inexpensive and Safe Combination to Treat Atrophic Acne Scars in Dark Skin: A Prospective Study of 45 Patients at a Tertiary Care Center. *J Clin Aesthet Dermatol.* 2019; 12(8):18-22.

9. Levy LL, Zeichner JA. Management of acne scarring, part II: a comparative review of non-laser-based, minimally invasive approaches. *Am J Clin Dermatol.* 2012; 13(5):331-40.

10. Hein R, Mensing H, Muller PK, Braun-Falco O, Krieg T. Effect of vitamin A and its derivatives on collagen production and chemotactic response of fibroblasts. *Br J Dermatol.* 1984; 111(1):37-44.

11. El-Domyati M, Barakat M, Awad S, Medhat W, El-Fakahany H, Farag H. Microneedling Therapy for Atrophic Acne Scars: An Objective Evaluation. *J Clin Aesthet Dermatol.* 2015; 8(7):36-42.

12. Doddaballapur S. Microneedling with dermaroller. *J Cutan Aesthet Surg.* 2009; 2(2):110-111.

13. Singh A, Yadav S. Microneedling: Advances and widening horizons. *Indian Dermatol Online J.* 2016; 7(4):244-254.

14. Kadunc BV, Trindade de Almeida AR. Surgical treatment of facial acne scars based on morphologic classification: a Brazilian experience. *Dermatol Surg.* 2003; 29(12):1200-9.

15. Gupta A, Kaur M, Patra S, Khunger N, Gupta S. Evidence-based Surgical Management of Post-acne Scarring in Skin of Color. *J Cutan Aesthet Surg.* 2020; 13(2):124-141.

16. Fernandes D, Signorini M. Combating photoaging with percutaneous collagen induction. *Clin Dermatol.* 2008; 26(2):192-9.

17. Fulton JE Jr, Silverton K. Resurfacing the acne-scarred face. *Dermatol Surg.* 1999; 25(5):353-9.

18. Fabbrocini G, Fardella N, Monfrecola A, Proietti I, Innocenzi D. Acne scarring treatment using skin needling. *Clin Exp Dermatol.* 2009; 34(8):874-9.

19. Pahwa M, Pahwa P, Zaheer A. "Tram track effect" after treatment of acne scars using a microneedling device. *Dermatol Surg.* 2012; 38(7 Pt 1):1107-8.

20. Fernandes D. Minimally invasive percutaneous collagen induction. *Oral Maxillofac Surg Clin North Am.* 2005; 17(1):51-63.

21. Jordan R, Cummins C, Burls A. Laser resurfacing of the skin for the improvement of facial acne scarring: a systematic review of the evidence. *Br J Dermatol.* 2000; 142(3):413-23.

22. Sharad J (2011) Combination of microneedling and glycolic acid peels for the treatment of acne scars in dark skin. *J Cosmet Dermatol.* 2011; 10(4):317-23.

aesthetic medicine

Narrative Review

Influencer marketing by healthcare providers - Ethics and the law

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Abstract

In some professional settings, social media platforms are accepted as gold-standard marketing mechanisms. Many businesses have a vast social-media presence, backed-up by marketing agency support and digital analytics that measure the impact of marketing strategies. Many healthcare professionals have embraced this trend, especially in the fields of aesthetic medicine, plastic and reconstructive surgery and aesthetic dentistry where 'influencer marketing' has gained traction to promote one's practice.

There is very little academic literature about the use of influencer marketing in the healthcare context internationally and no South African publications on this topic. However, anecdotal experience suggests that influencer marketing is widely used by health practitioners, with little to no guidance on its ethical acceptability or legal permissibility.

Addressing this gap, and providing practical guidance, is urgent and the purpose of this article, which presents a detailed ethical-legal analysis of influencer marketing use by healthcare professionals. The analysis draws on international ethical standards, South African legislation, ethical guidelines for health professionals and principles of advertising regulation.

The article concludes that whilst influencer marketing may be legally permissible - with certain conditions and caveats – it is ethically questionable, and as such may be best avoided in the healthcare setting, or should be utilised with extreme caution. Recommendations for the use of influencer marketing within the confines of the law and ethical best practice are provided.

Keywords

Ethics, ethics professional, ethics clinical, legislation, social media

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Introduction

In some professional settings, social media platforms are accepted as gold-standard marketing mechanisms[1,2].
Many businesses have a vast social-media presence, backed-up by marketing agency support and digital analytics that measure the impact of marketing strategies. Many healthcare professionals (HCPs), including some in South Africa (SA) have embraced this trend, especially in the fields of aesthetic medicine, plastic and reconstructive surgery and aesthetic dentistry where "influencer marketing" has gained traction to promote one's practice.
There is very little academic literature about the use of influencer marketing in the healthcare context internationally and we could find no SA publications on this topic. However, our anecdotal experience is that influencer marketing is widely used by HCPs, with little to no guidance on its ethical acceptability or legal permissibility. Addressing this gap, and providing practical guidance, is urgent and the purpose of this article. Through a detailed ethico-legal analysis, we conclude that influencer marketing is legally permissible - with certain conditions and caveats - but ethically questionable, and as such may be best avoided in the healthcare setting, or should be utilised with extreme caution.

Influencer marketing 101

An influencer is broadly defined as a person able to influence potential buyers of a product or service by promoting or recommending it on social media platforms like WhatsApp, Twitter, SnapChat, Tiktok, YouTube and others. A recent case in the United Kingdom[3] suggested that anyone with > 30,000 followers on social media is considered an influencer, though this would differ by jurisdiction.
Brand owners and service providers pay influencers for marketing, either directly in the form of cash, or indirectly through discounts or free services (freebies). Interestingly, a recent German study found that the public are not as "influenced" by the communications of influencers as we may have believed. More research is required to establish whether influencer marketing plays a major role in customer choice of HCP or procedure[4]. Social media endorsement is closely linked to the wider milieu of celebrity endorsement of brands, which is significant business. Unlike an influencer, a brand ambassador is normally in a formalised contractual relationship with the service provider or brand owner[5].

What makes healthcare different?

Unlike many other industries, healthcare hinges on the relationship of trust between HCP and patient[6], with the general premise that any action that could be considered coercive - such as offering an incentive or promoting a certain product or professional over others - may impact on the autonomous decision-making of the patient[7]. This could result in an erosion of public trust, the upshot of which is that the public may be increasingly unwilling to approach HCPs for care.Protecting the "fiduciary relationship" is the cornerstone of much medical legislation, its attendant regulations and ethical guidelines[8]. There are few other professions that protect the relationship between parties so vociferously, perhaps the closest being law. Hence there is an additional burden on HCPs to be especially judicious in all their dealings with the public.
In SA, HCPs registered with the Health Professions Council of South Africa (HPCSA) are obliged to practice according to the legal mandates of the Health Professions Act No 56 of 1974 as amended[9], National Health Act No 61 of 2003[10], the Medicines and Related Substances Act 101 of 1965 as amended[11] and other pertinent health legislation. HPCSA registration also calls on HCPs to follow the HPCSA Ethical Rules - a series of booklets addressing a wide gamut of topics. Moreover, as with all other business areas, health professionals are expected to comply with legislation like the Protection of Personal Information Act No 4 of 2013[12], the Promotion of Access to Information Act No 2 of 2000[13] and the Consumer Protection Act no 68 of 2008[14].

The rise and rise of the influencer

Although there is no published literature on influencer marketing in healthcare in SA, the fact that it is so widely used is perhaps unsurprising. The very nature of the influencer is that they are expected to document their every move, making their daily lives a sellable product[15]. This means that many influencers post about their experiences in seeking medical care, often without any pre-engagement with the HCP in question and without compensation from the HCP. This poses its own set of ethical, legal and reputational challenges for HCPs, as it requires regular monitoring of ones online reputation and a robust system for managing posts that name or implicate the HCP on social media. Discussing these is beyond the scope of this article.
We are aware of many instances where HCPs have been approached by influencers, who offer to post about their medical treatment in exchange for a discount or freebie. Anecdotally, HCPs - especially in aesthetic medical practices - have expressed concern that influencers feel entitled to freebies, and suggest that influencers may be rude or inconsiderate if their offer to post is turned down.

What are the ethical implications?

Ethical healthcare practice in South Africa is governed by the HPCSA, which has published several guidelines based on international ethical principles. These guidelines address aspects like privacy, confidentiality, informed consent, disclosure, the fiduciary relationship, ethical research and management of children[9]. The HPCSA's 17 booklets detailing Ethical Guidelines for Good Practice have a quasi-legal standing, as they are mandated in the Health Professions Act[9], and the HPCSA has sweeping judicial powers to discipline any practitioner in breach by bringing a charge of misconduct. We have undertaken a thorough evaluation of these guidelines and synthesised their recommendations regarding advertising, marketing, canvassing, touting and other relevant aspects. We conclude that the guidelines offer no definitive recommendation on whether the use of influencer marketing is ethical, however appreciating

the nuance of the guidelines suggests that it would not be viewed favourably by the HPCSA.

Booklet 11 of the guidelines states that:
"A practitioner shall be allowed to advertise his or her services or permit, sanction or acquiesce to such advertisement: Provided that the advertisement is not unprofessional, untruthful, deceptive or misleading…"

Advertising of any "…health related product or **health related service**" is widely defined as[17]:

"… any written, pictorial, visual or other descriptive matter or verbal statement or reference in respect thereof:
- *Appearing in any newspaper, magazine, pamphlet or other publication; or*
- *Distributed to members of the public; or*
- *Brought to the notice of members of the public in any manner whatsoever,*

That is intended to promote the sale of that … health related product or to attract patients to any particular health establishment or health related service."

So far so good. We have established that health practitioners are permitted to advertise their services within reason, and that advertising involves publishing one's services in such a manner as to promote their sale. However, the line between acceptable and unacceptable advertising is extremely fine., with Booklet 11[17] stating that:

"Health care practitioners shall not advertise or endorse or encourage the use of any health establishment … health related product or health related service in a manner that unfairly promotes the practice of a particular health care practitioner or a health care facility for the purpose of financial gain or other valuable consideration."

Moreover, the Social Media guidelines[18] state that:
"When using social media, even if via personal or anonymous blogs, health care practitioners must comply with the HPCSA rules on advertising practice, (including not engaging in active or passive touting and canvassing or allowing others to do so on their behalf)" (Section 9.2)

The Social Media guidelines[18] specifically warn practitioners against utilising social media for canvassing and touting, and the limits of social media as an advertising platform for health professionals.
- Canvassing is: "… the promotion of one's professional goods and services by drawing attention to one's personal qualities, superior knowledge, quality of service, professional guarantees, or best practice. An example of canvassing is a health care practitioner declaring on social media or posting patient reviews that state he or she is 'the best health care practitioner in the country'" (Section 9.5).
- "Touting involves drawing attention to one's professional goods or services by offering guarantees or benefits that fall outside one's scope of practice. An example is advertising free WiFi services to patients while waiting for their consultations." (Section 9.4)

Amalgamating these, we can make some important ethical inferences.
- Influencer marketing that crosses the line of canvassing or touting is ethically problematic, but it is not clear whether influencer marketing that avoids these aspects is acceptable, because it might still be perceived as unfairly promoting the practice or professional who has sanctioned it.
- The statement that "A practitioner shall not … allow canvassing or touting to be done for patients on his or her behalf" (Section 3.2) suggests that any post by an influencer that claims the HCP is superior to others may be ethically problematic, but no remedy is suggested. This is challenging as HCPs would, by these standards, be implicated in canvassing and touting that they had nothing to do with. We argue that it seems unreasonable to imagine that an HCP may be seen to have brought the profession into disrepute if an influencer posts a review of their treatment online without the HCP having any prior knowledge[19]. However it would take a case being brought against an HCP to clarity this.

This analysis suggests that when it is solicited, influencer marketing may be ethically acceptable provided it does not constitute unfair advertising, canvassing or touting. However we need to consider the ethical implications of actively engaging influencers to provide advertising though the lens of coercion and perverse incentives too.

Coercive use of services

A central tenet of the HCP-patient relationship is that HCPs must not act towards patients in a way that coerces that patient into utilising their services, or undergoing a procedure without consideration of the alternatives. This is enshrined in patient-centred care and realised through the process of information giving and informed consent[20]. Engaging an influencer to undergo a treatment at ones practice, and providing this treatment at a discount, may be coercive in that the patient will feel they have no choice - because the discount will make this treatment substantially cheaper than anywhere else.

Let's consider what could happen when influencer marketing goes wrong. The tragic death of Bodybuilder and influencer Odalis Santos Mina[21] - who suffered a cardiac arrest during a non-surgical aesthetic procedure she was promoting online (*Box 1*) - raises some of the main contentions. These are that Mina was coerced into undergoing the treatment, and that her autonomy was violated. Moreover, the reputational fallout suffered by the clinic who sanctioned Mina and performed the procedure has been devastating - and we don't believe it is worth the risk.

Perhaps, because they are larger than life, we sometimes forget that 'influencers are people too'. In the healthcare context, they are our patients, and we are expected to treat them according to the same standards as we do anyone else. The Patients' Rights Charter[22] states that patients should be free to choose an HCP where possible, and they are entitled to confidentiality and informed consent. One of the main tenets of informed consent is voluntariness – that a person is in no way coerced or induced to undergo medical treatment or examination[20]. Any action that proposes to compromise

the voluntariness of a treatment decision may thus be unethical, and possibly illegal.

Of course, it can be argued that the influencer is simply exercising their autonomy by accepting an incentive to undergo a treatment and post about it, and that influencers are entitled to earn a living as everyone else is. This argument will likely stand until a procedure goes wrong, and an influencer starts seeking damages from the HCP. Here, if the HCP has sanctioned the influencer to market services, they are particularly vulnerable because it could easily be painted as coercion, even if this was not the case. We must also remember that the court of public opinion is a formidable foe[23], and influencers play in this arena daily. If a procedure involving an influencer, solicited by an HCP, goes wrong, the HCP could suffer major reputational damage in the court of public opinion long before the facts are ascertained in a court of law or arbitration. Undoing this damage can be a near-impossible task, and it could put an end to a promising medical career.

Box 1 - Fitness influencer dies in procedure she was promoting

On July 7th, 2021, Mena presented at a Mexican aesthetic clinic to undergo an FDA-approved anti-sweating procedure known as miraDry®. As an influencer, Mena had previously been paid by the clinic to promote miraDry® - so it made sense that she would choose the clinic for her treatment. However, whilst undergoing local anaesthesia prior to the procedure, Mena suffered a cardia arrest and staff at the clinic were unable to revive her. Although the cause of death is under investigation, the clinic claims that Mena was taking a steroid-based medication known as Clenbuterol, which interacted with the local anaesthetic causing the cardiac arrest. The clinic claims that Mena did not inform them that she was on any medication or supplements. However, Mena's family have laid a charge of negligence against the clinic, claiming that the anaesthesia was administered by non-professionals and that Mena was anesthetized by an employee who had never trained as an anaesthetist. The facts have yet to be established, and the case is now under formal investigation.

Is it legal?

There is no case law to clarify the way in which an SA court might interpret legislation in a case involving influencer marketing in healthcare. We argue that it would be most distressing to be the 'test case' in this scenario - for instance the HCP who is sued by an influencer because their discounted anti-wrinkle injections resulted in a droopy eyelid the week before a star-studded public appearance. The influencer post related to this scenario is unlikely to be a glowing review of the HCP.

Presently, SA does not have laws specific to influencer marketing. However, we can likely turn to the Consumer Protection Act (CPA) 68 of 2008[24] and the Advertising Regulatory Board (ARB) Regulations and Code of Advertising Practice[25] to understand how influencer marketing would be dealt with legally. These sources should be read in conjunction with specific industry or profession related laws, regulations and guidelines - some self-regulatory and others legally binding.

Declaration of advertising as a legal obligation

Influencer marketing in SA gained legal traction following an ARB case involving Volvo in 2019 (*Box 2*)[26]. This complaint elucidated certain legal provisions of the ARB Code that many may be unaware of.

This includes the fact that service providers across the span of industry - and influencers alike - may be held accountable for non-disclosure of the nature of their relationship.

Box 2 – Volvo, Amanda du Preez, Kandy Kane

The complainant (Ms Amanda du Preez) objected to an Instagram post by a certain Kandy Kane (@kandykanemakeup) who has around 23000 followers on Instagram, and around 14000 subscribers to her YouTube channel. The complaint was essentially that Kandy Kane had said nice things in her post about the Volvo she was driving, but she hadn't really explained her relationship with the company. Certainly, the post had not been identified as advertising. In their response, Volvo said that the relationship between themselves and Kandy Kane was "not one of financial investment" but rather a "trade exchange". "The ARB agreed that Volvo and Kandy Kane were in contravention of its rules, and required that the post be amended to reflect the nature of the relationship."

It is a legal requirement that solicited influencer marketing posts clearly indicate that they are advertisements. Clause 3.2 of Appendix K to the ARB Code25 (which is related to Declaration of Advertising and designed to ensure transparency) stipulates that: "… advertisers are required to disclose if content is part of a Social Media Advertising campaign as opposed to purely Organic Social Media." Framed within the proceeding discussion, a Social Media Advertising Campaign would constitute influencer marketing solicited by an HCP, whereas Organic Social Media would refer to unsolicited posts. Clause 3.2 continues by stating that:

… where Paid Advertising may reasonably appear to the consumer to be the unsolicited opinion of the influencer or platform, then the material must be clearly identified as Paid Advertising through the use of supported Social Media identifiers.

Supported Social Media identifiers include… "#AD" … "#Advertisement' …'#Sponsored".

The Consumer Protection Act (CPA) confers similar legal

obligations and defines "advertisement" as:
… any direct or indirect visual or oral communication transmitted by any medium, by means of which a person seeks to bring the attention of the public to the existence of any goods or services or promote the supply of any goods or services.
This means that sponsored content, like influencer marketing, is considered advertising, and the CPA applies. Section 29 of the CPA states that a producer, retailer or service provider must not market goods or services in a way that is misleading, fraudulent or deceptive. Section 41 of the CPA stipulates that the supplier must not fail to correct an apparent misapprehension on the part of the consumer.
So, when a social media influencer fails to disclose that posted content has been sponsored, they are in blatant violation of the CPA as is, arguably, the service provider or brand owner[24].
Furthermore, the CPA requires that advertising must take place in a fair and reasonable manner and that goods or services must not be marketed in a way that is false or misleading. Could an argument be made that a paid-for advertisement which is not clearly labelled as one is misleading? Probably. After all, a consumer is far more likely to be induced to purchase a product that has been given a rave review by a person they admire.
Therefore, as with the ARB, in terms of the CPA ensure that all posts contain an indication that they are advertisements.

Declaration of a relationship of exchange as a legal obligation

Both the CPA[24] and the ARB[25] impose a legal requirement to declare any kind of "Trade Exchange" (*Box 2*) or other mutually beneficial relationship in advertising. Appendix K, Clause 4 of the ARB code provides as follows:
To ensure full transparency publishers and influencers are required to disclose if they were provided (permanently or on loan) with goods or services in return for media coverage (whether this is expressly stated or not). … influencers are expected to disclose their relationship whether it is money or goods that have been exchanged.
According to the CPA, any form of compensation or inducement, whether in monetary terms or some other form will likely trigger the need to disclose the relationship with the advertiser or service provider. This recommendation applies to all types of influencer-brand relationships, regardless of whether the influencer receives money or free products and perks.

Advertising regulations and medical legislation

Both influencers and HCPs additionally need to be aware of wider advertising regulations specific to healthcare. Section 18 of the Medicines and Related Substances Act 1965 (as amended)[11] notes that Schedule 2-6 medicines may not be advertised to the public and the prices of these medicines may not be listed on social media. Moreover, trade names may not be mentioned on social media. Regulations relating to Medical Devices, published in the Government Gazette No. 40480 on the 09 December 2016[27], state that Class C and D Medical Devices may not be advertised to the public.
The penalties for contravening these regulations may be more serious than those imposed by the ARB and the CPA. In certain instances, there may even be criminal liability. Ignorance of the law will not suffice as a legal defence in this case by a service provider.

Core principles of medicine

Core principles of healthcare are compassion, integrity, respectfulness, trustworthiness, benevolence and discernment[28].
These apply equally when we use influencer marketing and HCPs need to ensure that such marketing is aligned with these core values. Is the influencer acting with integrity? Are they honest and authentic? Most importantly is it in the best interest of the patient? HCPs will be judged on how and why they use social media. It should be used with benevolence to educate, inform and positively impact healthcare. It should not be for self-aggrandisement, internet fame or financial reward. Moreover, HCPs needs to protect their integrity and professional image. A major risk associated with the use of influencer marketing is the posting of unprofessional content that reflects badly on the HCP. It follows that HCPs who don't practice wisdom and discretion in deciding what content to post online may also be incapable of exercising sound professional judgment in providing care[29].
Regarding discernment, a doctor has the competency to analyse scientific literature, backing social media posts with evidence and references where appropriate. However, an influencer might give inaccurate information and advice, lacking quality and reliability, thus misleading the public. While evidence-based medicine de-emphasizes anecdotal reports, social media tends to promote them[30]. Doctors need to keep advice and information factual and based on scientific evidence when communicating on social media, and this is very difficult to manage when marketing is in the hands of an influencer.

The final verdict

The ethical and legal analysis above demonstrates that influencer marketing as utilised by HCPs is legally acceptable provided it does not fall foul of an extensive range of legislation and legally binding guidelines. However, it is unclear whether influencer marketing in healthcare is ethically acceptable, and for this reason practitioners are advised to utilise maximum caution when employing this strategy, or better yet, to avoid using influencer marketing altogether. For those who still insist, *Box 3* provides some guidelines, however this does not constitute legal advice.
The upshot is that both practitioners and the influencers they solicit for marketing bear legal responsibility for the content that is posted, however the HCP alone is obliged to act in an ethical manner, and the HCP alone will be subject to ethical censure if something goes wrong.

Box 3 - Guidelines for HCPs utilising influencer marketing

- Content solicited by the HCP must always be marked as an advertisement with a social media identifier
- The nature of the relationship between influencer and HCP must always be declared, as well as the exchange or compensation provided for the post
- The content of the post should not constitute canvassing or touting
- The content must not constitute illegal advertising or pricing of scheduled substances or devices
- Ideally the legal and ethical parameters of what acceptable influencer marketing is should be attested by both parties, preferably in a legally binding contract.'
- A professional medical marketing compan can assist in ensuring appropriate posts. A good medical marketing company will consult with lawyers and be fully aware of the latest laws and ethical requirements in SA
- Ensure that informed consent is sought for all procedures involving influencers, with the necessary disclaimers that the influencer is undergoing the procedure as part of their business, and voluntarily in this context
- Ensure that influencers understand that by posting about their medical treatment, they are making information that would generally be considered confidential publicly available
- Keep advice and information factual and based on scientific evidence when communicating on social media

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REFERENCES

1. Appel G, Grewal L, Hadi R, Stephen AT. The future of social media in marketing. *J Acad Mark Sci.* 2020;48(1):79-95.

2. Tuten TL. Social Media Marketing (4e). *London, United Kingdom: Sage.* 2020.

3. MacDonald S. This Mama Life influencer Sarah Willox Knott breached rules with sleeping pills advert. The Times [Internet]. 2019. Available from: LINK [Accessed 6 September 2021].

4. Krisam M, Altendorfer L-M. Influencer Marketing in Healthcare: A Review. *Gesundheitswesen.* 2021. Online ahead of print. DOI: 10.1055/a-1377-6478.

5. Jarrar Y, Awobamise AO, Aderibigbe AA. Effectiveness of Influencer Marketing vs Social Media Sponsored Advertising. *Utopia y Praxis Latinoamericana.* 2020; 25(12): 40-54.

6. Ward P. Trust and communication in a doctor-patient relationship: A literature review. *J Healthc Commun.* 2018;3(3):36.

7. Kilbride MK, Joffe S. The new age of patient autonomy: Implications for the patient-physician relationship. *JAMA.* 2018; 320(19): 1973-4.

8. Health Professions Council of South Africa. Guidelines for good practice in the Health Care Professions. *Pretoria, South Africa;* 2016.

9. Health Professions Act No 56 of 1974. Government of the Republic of South Africa. Available from: LINK [Accessed 6 September 2021]

10. National Health Act No 61 of 2003. Government of the Republic of South Africa. Available from: LINK [Accessed 6 September 2021]

11. Medicines and Related Substances Act No 101 of 1965. Government of the Republic of South Africa. Available from: LINK [Accessed 6 September 2021]

12. Proection of Personal Infomation Act No 4 of 2013. Government of the Republic of South Africa. Available from: LINK [Accessed 6 September 2021]

13. Promotion of Access to Information Act No 2 of 2000. Government of the Republic of South Africa. Available from: LINK [Accessed 6 September 2021]

14. Consumer Protection Act No 68 of 2008. Government of the Republic of South Africa. Available from: LINK [Accessed 6 September 2021]

15. Jin SV, Muqaddam A, Ryu E. Instafamous and social media influencer marketing. *Mark Intell Plan.* 2019; 37(5): 567 – 579.

16. Health Professions Council of South Africa. 2016. Booklet 2 - Ethical and professional rules of the Health Professions Council of South Africa. Available from: LINK [Accessed 6 September 2021]

17. Health Professions Coubncil of South Africa. 2016. Booklet 11: Guidelines on over servicing, perverse incentives and related matters. Available from: LINK [Accessed 6 September 2021]

18. Health Professions Council of South Africa. 2019. Booklet 16 - Ethical Guidelines On Social Media. Available from: LINK [Accessed 6 September 2021]

19. Dobson H. 2015. Facebook Hosts and Third Party Posts: Defamation In The Internet Age. University of Otago, New Zealand. Available from: LINK [Accessed 6 September 2021].

20. Nelson RM, Beauchamp T, Miller VA, Reynolds W, Ittenbach RF, Luce MF. The concept of voluntary consent. *Am J Bioeth.* 2011; 11(8):6-16.

21. Zitser J. Fitness influencer dies after getting botched procedure for underarm sweating at a Mexican clinic, reports say. 2021. Available from: LINK [Accessed 6 September 2021]

22. Government of the Republic of South Africa. 2016. The Patients' Rights Charter. Available from: LINK [Accessed 6 setpember 2021]

23. Kim S, Krishna A, Plowman KD. Winning in the court of public opinion: Exploring public relations–legal collaboration during organizational crisis. *Corp Commun.* 2018; 24(1):96-114.

24. Consumer Protection Act No 68 of 2008. Government of the Republic of South Africa. Available from: LINK [Accessed 6 September 2021]

25. Advertising Review Board. 2021. Appendix K - Social Media Code. Available from: LINK [Accessed 6 September 2021]

26. Advertising Regulatory Board. 2019. Volvo – Amanda du Preez. Available from: LINK [accessed 6 September 2021]

27. Department of Health, Government of the Republic of South Africa. 2016. Regulations Relating to Medical Devices and In Vitro Diagnostic Medical Devices (IVDs). Available from: LINK [Accessed 6 September 2021]

28. Rawbone R. Principles of Biomedical Ethics. *Occup Med.* 2015; 65(1):88-9.

29. Ventola CL. Social media and health care professionals: *Benefits, risks, and best practices. P.T.* 2014;39(7):491.

30. Singh SP, Rai A, Wal A, Tiwari G, Tiwari R, Parveen A. Effect of Social Media in health care: Uses, risks, and barriers. *WJPPS.* 2016;5(7): 282-303.

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French Society of Aesthetic Medicine
Palais des Congrès de Paris
President: J.J. Legrand
Email: info@sfme.info
Web: www.sfme.info

8 - 9 October - Montreux (Switzerland)
17th Congress of the Swiss Society of Aesthetic Medicine
Hotel Suisse Majestic, Montreux
President: V. Parzin
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Web: www.ssme.ch

28 - 30 October - Pretoria (South Africa)
AMCSA 2021
Aesthetic Medicine Congress South Africa
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6 November - Online Event
XXI Jornada Anual de la Sociedad Uruguaya de Medicina Estetica
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Web: www.sume.com.uy

6 - 7 November - Online Event
CAAM 2021 Virtual Conference
Canadian Association of Aesthetic Medicine
President: J. Carroll
Email: info@caam.ca
Web: www.caam.ca/conference-education-

9 - 11 December - Cascais, Lisbon (Portugal)
V National Congress of Aesthetic Medicine
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