Volume 2 • Number 1 • January/March 2016 ISSN 2421-7115
www.aestheticmedicinejournal.org

aesthetic medicine

Official Journal of the International Union of Aesthetic Medicine – UIME

Official UIME English Language Journal of:

Aesthetic and Anti-Aging Medicine Society of South Africa
Aesthetics Medical Society of Uruguay
Aesthetic Medicine Society of Venezuela
Algerian Society of Aesthetic Medicine
American Academy of Aesthetic Medicine
Argentine Society of Aesthetic Medicine
Canadian Association of Aesthetic Medicine
Colombian Association of Aesthetic Medicine
Ecuadorian Society of Aesthetic Medicine
French Society of Aesthetic Medicine
Georgian Society of Aesthetic Medicine
Italian Society of Aesthetic Medicine
Kazakhstan Association of Aesthetic Medicine and Plastic Surgery
Korean Academy of Aesthetic Medicine
Mexican Scientific Society of Aesthetic Medicine
Moroccan Society of Aesthetic Medicine
Polish Society of Aesthetic and Anti-Aging Medicine of Polish Medical Society
Romanian Society for Aesthetic Medicine and Dermatologic Surgery
Society of Aesthetic Medicine in Turkey
Spanish Society of Aesthetic Medicine
Swiss Society of Aesthetic Medicine
Ukrainian Society of Aesthetic Medicine

aesthetic medicine

Official Journal of the International Union of Aesthetic Medicine – UIME

Aesthetic Medicine (registered by the Court of Rome on 28/4/2015 under the number 63/2015) is published 4 times a year (March, June, September, December) by Editrice Salus Internazionale srl, via Giuseppe Ferrari 4 - 00195 Roma, tel. +39 06 36003462 - fax +39 06 37519315, e-mail: salus@editricesalus.it; www.lamedicinaestetica.it.
Subscription Information: All subscriptions inquiries, orders, back issues, claims, and renewals should be addressed to Editrice Salus Internazionale srl. **Free subscription** (Four issues: March, June, September, December).

EPub [15/04/2016]

Guidelines for Authors

The journal, of multidisciplinary aspect, publishes articles concerning topics of Aesthetic Medicine.

All articles in their final version – completed with name, surname, professional qualification, address, phone number and e-mail address – must be sent in word format to the Editorial Committee via e-mail at the following address: salus@editricesalus.it.

All images present within the word file must be numbered progressively and accompanied by the corresponding captions, with precise references in the text. Moreover, the images should be sent separately and in HD (at least 300 Dpi, in TIFF or JPEG format).

Graphs and charts, progressively numbered and accompanied by the corresponding captions, with precise references in the text, must be sent separately, preferably in Excel format.

It is necessary to give the authorization to reproduce already published materials or to use portraits of people, in case they are recognizable. The Authors assume Full, Exclusive and Personal Responsibility and Respect of the rules protecting Privacy, Originality and Content (text, images) of the Articles

The article must be accompanied by the following parts:

- title, short and without abbreviations;
- name and surname of the author/s and the relative professional qualifications;
- summary (15 lines at the most);
- keywords (2-5), using terms of the Index Medicus;
- bibliography according to the AMERICAN MEDICAL ASSOCIATION (AMA) CITATION STYLE.

Structure of the article

In case the article is a review (clinical cases, experiments on instruments etc.) it is sufficient to divide the text in paragraphs and subparagraphs, so that the different parts can be easily identified and the reading is facilitated. In case it is a research, the article must be structured as a scientific work, that is to say:

- Background, it summarizes the current state of knowledge.
- Objectives of the work.
- Materials and methods described in details, in order to let the readers reproduce the results.
- Results, reported accurately with references to charts and/or graphs.
- Discussions and conclusions, focusing on the important and innovative aspects of the case study.
- References must be listed in order of citation within the text and with a progressive Arabian numbering.

The references must be cited according to the AMERICAN MEDICAL ASSOCIATION (AMA) CITATION STYLE. For this reason, they must contain the surname and name's initial of the author(s), original title of the article, title of the journal, year of publication, the number of the volume, the number of first and last page. The footnote references must be written in parenthesis together with the number of the cited resource(s), in order of appearance.

The Editorial Committee will approve the publishing. The authors will receive the corrected drafts, which, after verification, must be resent via e-mail. In case of delay, the Editorial Committee will proceed with the printing. The authors and the organization to which they belong are exclusively responsible for the published articles. The papers cannot be proposed at the same time to other editors, not even published in other journals. The editor will publish the articles with no charge; the author(s) will not receive any compensation. The publishing property belongs to the editor. The printing of the extracts is possible and can be requested and agreed with the Editorial Committee. The journal is under the protection of the International Publishing Laws.

Editorial Office

Editrice Salus Internazionale srl

Via Giuseppe Ferrari 4 - 00195 Roma

Tel. + 39 06 36003462 - Fax +39 06 37519315

E-mail: aemj@aestheticmedicinejournal.org

Website: www.aestheticmedicinejournal.org

Submit your manuscripts at aemj@aestheticmedicinejournal.org

AMERICAN MEDICAL ASSOCIATION (AMA) CITATION STYLE

Rev. 11/1/2012

General rules from the 10th edition

- **Items are listed numerically in the order they are cited in the text**
- **Include up to 6 authors**
- **For more than six, provide the names of the first three authors and then add et al**
- **If there is no author, start with the title**
- **Periodicals (journals, magazines, and newspapers) should have abbreviated titles; to check for the proper abbreviation, search for the Journal Title through LocatorPlus at the National Library of Medicine website**

Citation Type	Example
Journal article – in print – one author	Spencer J. Physician, heal thyself – but not on your own please. *Med Educ.* 2005; 89: 548-549.
Journal article – in print – 2-6 authors	**Salwachter AR, Freischlag JA, Sawyer RG, Sanfey HA.** The training needs and priorities of male and female surgeons and their trainees. *J Am Coll Surg*. 2005; 201: 199-205.
Journal article – in print – more than 6 authors	**Fukushima H, Cureoglu S, Schachern P, et al.** Cochlear changes in patients with type 1 diabetes mellitus. *Otolaryngol Head Neck Surg*. 2005; 133: 100-6.
Journal article – online *if there is no DOI, provide the URL for the specific article	Coppinger T, Jeanes YM, Hardwick J, Reeves S. Body mass, frequency of eating and breakfast consumption in 9-13-year-olds. *J Hum Nutr Diet*. 2012; 25(1): 43-49. **doi: 10.1111/j.1365-277X.2011.01184.x**
Journal article – online from a library database* *there is no specific way to cite articles found in library databases according to the AMA so double check with your professor	Calhoun D, Trimarco T, Meek R, Locasto D. Distinguishing diabetes: Differentiate between type 1 & type 2 DM. *JEMS* **[serial online].** November 2011; 36(11):32-48. **Available from: CINAHL Plus with Full Text, Ipswich, MA. Accessed February 2, 2012.**
Newspaper article – in print *if the city name is not part of the newspaper name, it may be added to the official name for clarity * if an article jumps from one page to a later page write the page numbers like D1, D5	Wolf W. State's mail-order drug plan launched. *Minneapolis Star Tribune*. May 14, 2004:1B.
Newspaper article – online	Pollack A. FDA approves new cystic fibrosis drug. *New York Times*. January 31, 2012. http://www.nytimes.com/2012/02/01/business/fda-approves-cystic-fibrosis-drug.html?ref=health. Accessed February 1, 2012.
Websites	Outbreak notice: Cholera in Haiti. Centers for Disease Control and Prevention Web site. http://wwwnc.cdc.gov/travel/notices/outbreak-notice/haiti-cholera.htm Published October 22, 2010. Updated January 9, 2012. Accessed February 1, 2012.
Entire book – in print	Modlin J, Jenkins P. *Decision Analysis in Planning for a Polio Outbreak in the United States*. San Francisco, CA: Pediatric Academic Societies; 2004.
Book chapter – in print	Solensky R. Drug allergy: desensitization and treatment of reactions to antibiotics and aspirin. In: Lockey P, ed. *Allergens and Allergen Immunotherapy*. 3rd ed. New York, NY: Marcel Dekker; 2004:585-606.

To find more AMA style citations, go checkout the
AMA Manual of Style: A Guide for Authors and Editors. 10th ed. Oxford: Oxford UP.

AMERICAN MEDICAL ASSOCIATION (AMA) CITATION STYLE

Rev. 11/1/2012

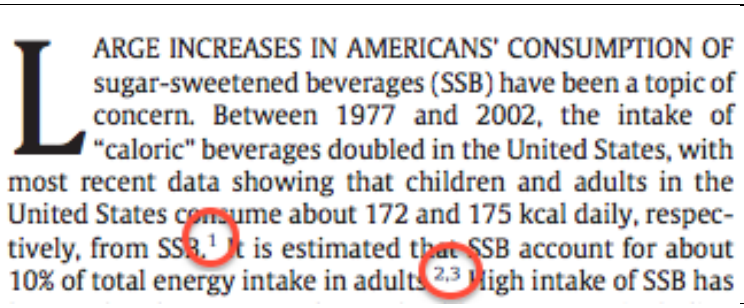
Citing sources within your paper

Unlike APA or MLA, you will not use the author's last name for the in-text citations. Instead, you will number each instance when you are referencing an article. The order of numbering will be contingent on the order in which you use that reference within your paper. In the example below, the first article referenced is given the number one in superscript. In the References section, you will find the matching article listed as number 1.

Example Article

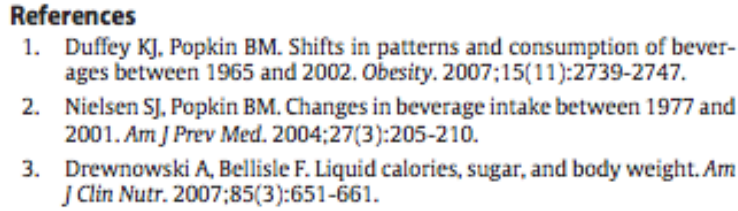
1. Zoellner J, Krzeski E, Harden S, Cook E, Allen K, Estabrooks PA. Qualitative application of the theory of planned behavior to understand beverage consumption behaviors among adults. *J Acad Nutr Diet*. 2012;112(11):1774-1784. doi: 10.1016/j.jand.2012.06.368.

In-Text Citation Example



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 consumption 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.

Use commas to separate multiple citation numbers in text, like you see between references 2 and 3. Unpublished works and personal communications should be cited in the text (and not on the reference list).[1] Superscript numbers are placed outside periods and commas, and inside colons and semicolons. When citing the same source more than once, give the number of the original reference, then include the page number (in parentheses) where the information was found. See pages 41-44 of the *AMA Manual of Style* for more information.

References

Citing AMA guide website. http://libguides.stkate.edu/content.php?pid=99799&sid=749106. Updated April 2011. Accessed October 24, 2012.

To find more AMA style citations, go checkout the
AMA Manual of Style: A Guide for Authors and Editors. 10th ed. Oxford: Oxford UP.

EDITORIAL

In modern years, aesthetics has become quite important in every aspect of everyday life: following the hundreds of journals, magazines, blogs and websites pointing their attention towards this interesting and fascinating topic, the request for aesthetic medicine has increased manifolds.

Aesthetic Medicine is a new field of medicine, in which different specialists share the aim of constructing and reconstructing the physical equilibrium of the individual. Treatment of physical aesthetic alterations and unaesthetic sequel of illnesses or injuries, together with the prevention of aging, are perhaps two of the most iconic areas of intervention for Aesthetic Medicine. However, in order to prevent frailty in the elderly, a program of education is similarly important. Furthermore, the line between health and beauty is extremely thin: psychosomatic disorders resulting from low self-esteem due to aesthetic reasons are frequent and cannot be ignored by a clinician.

It is therefore clear that there is no figure in the field of medicine which is not involved in Aesthetic Medicine: endocrinologists, gynecologists, angiologists, psychologists and psychiatrists, plastic surgeons, dermatologists, dieticians, physiotherapists, orthopedists, physical education instructors, massophysiotherapists, podologists, and rehabilitation therapists are just some of the specialists who are sooner or later going to have to answer their patients' needs for aesthetic interventions. The involvement of all these specialists fits the description of health as defined by the WHO: "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" for which, undeniably, a team of different physicians is required.

The number of patients requiring medical consultation for esthetic reasons is rapidly increasing: in order to be able to provide adequate feedback, medical and paramedical specialists should be trained and, more importantly, should be taught how to work together. Existing Societies of Aesthetic Medicine from different countries share the aim of creating such teams and provide constant updates to the literature: the creation of an international network of specialists from all around the world under the flag of Aesthetic Medicine represents a challenge, but at the same time it is the proof of the widespread interest in this topic.

The first issue of this Journal represents the results of the efforts of the many national Societies and of the *Union Internationale de Médecine Esthétique,* now together as one; it is our hope that in years to come this Journal might improve our knowledge in this field, and provide adequate scientific advancement in the field of Aesthetic Medicine.

Francesco Romanelli, MD
Editor-in-chief
Associate Professor at "Sapienza"
University of Rome

EDITORS' NOTES

Aesthetic Medicine, the booming medical activity

Aesthetic Medicine was born in France 40 years ago. The French Society of Aesthetic Medicine was the first of its kind in the world, followed by Italy, Belgium and Spain. Starts were rather difficult as aesthetic procedures in those early years were only surgical. At that time aesthetic doctors and cosmetic dermatologists had very few real medical procedures to offer to their patients for treating aesthetic problems on face and body.

At the beginning of the '80s, viable medical procedures started to emerge in Europe for aesthetic and cosmetic purposes. Mostly, at that time, they were imported from the United States: those included collagen injections for wrinkles (Zyderm by Dr. Stegman), and chemical peels (phenol by Dr. Baker, TCA by Dr. Obagi). But, subsequently, European research on Aesthetic Medicine gained momentum. Hyaluronic acid appeared on the market, as it was discovered that it could be used as a dermal filler for wrinkles.

During the '90s, the use of lasers offered aesthetic doctors and cosmetic dermatologists new possibilities. The "beam revolution" started with CO2 laser for facial resurfacing. Today, CO2 resurfacing is not used as much anymore, because of the long and difficult post-op. CO2 laser was replaced with the gentler Nd-YAG and Erbium lasers and more recently with non-invasive photonic devices for facial rejuvenation, including IPL, US and radiofrequency. These new technologies allow today's aesthetic doctors and cosmetic dermatologists to offer their patients procedures with low risk of post-op complications.

Then, Botulinum Toxin has "invaded" both sides of the Atlantic Ocean. Today, Botox injections are the most popular treatment for facial expressive wrinkles. Botox injections are now so common everywhere that many cosmetic surgeons have given up their bistouries for syringes.

Last but not least, development in Aesthetic Medicine is shown by mesotherapy and adipolipolysis. About lipolysis, new data and recent publications have explained that radiofrequency, ultrasounds and cryolyse could have positive action to dissolve fat and to improve some unaesthetic disorders like cellulite. These non invasive procedures intend to replace the surgical liposculpture with success.

Nowadays, Aesthetic Medicine has the necessary tools to address all major disorders within the aesthetic field.

After 40 years, Aesthetic Medicine is now active in 27 countries in the world (France, Italy, Spain, Belgium, Morocco, Poland, Russia, Switzerland, Romania, Kazakhstan, Algeria, Brazil, Argentina, Uruguay, Venezuela, Colombia, Chile, Mexico, U.S.A, Canada, South Korea, and recently Ecuador, China, South Africa, Turkey, Ukraine and Georgia). All 27 national Societies are members of the *Union Internationale de Médecine Esthétique* (U.I.M.E.).

Aesthetic Medicine is taught in 8 countries (France, Italy, Spain, Brazil, Argentina, Mexico, Venezuela, Kazakhstan) in universities that deliver UIME's diplomas after 3 to 4 years of studies.

What is the future of Aesthetic Medicine?

In the last few decades, patients' desires to look and feel younge, have fueled Aesthetic Medicine and Cosmetic Dermatology: many different procedures have been developed to satisfy the demands.

As life-span have increased, patients today are not only asking about aesthetic procedures, they are also asking for a way to stay in good physical conditions in the last decades of their lives.

As a direct result, Anti-Aging Medicine, which covers skin aging and general aging, has recently emerged and expanded very quickly.

Anti-Aging Medicine can offer senior patients better nutrition, dietary supplementation with vitamins, minerals, antioxidants, and eventually hormone replacement therapy, but only when needed.

Today, and in the near future, both Aesthetic Medicine and Anti-Aging Medicine will offer to our patients, who now live longer, better wellness with aesthetic treatments for skin aging and anti-aging treatments for general aging.

Aesthetic Medicine is booming, but all medical practitioners should be correctly trained, so its future will be bright.

Jean-Jacques Legrand, MD
General Secretary of UIME

Aesthetic Medicine: a bioethic act

When in 1977 the Italian Society of Aesthetic Medicine published the first issue of the magazine "La Medicina Estetica" Carlo Alberto Bartoletti, the Founder, wrote an editorial in which traced the pathway of the discipline and of the Scientific Society, still valid and projected into the future.

Today from that Editorial Board arise an International Journal, which wants to be indexed, in order to give to the doctors practicing Aestehetic Medicine all around the world a solid basis of shared knowledge.

In the late '60s, what was called in Italy Aesthetic Medicine, moved its first steps thanks to "remise en forme and anti aging projects" imported from the experience the "Institutul de geriatrie Bucuresti", directed by Dr. Ana Aslan.

For this reason,there is the bioethical imperative that the Discipline should be first prevention, then return to physiology and finally correction.

The worldwide diffusion and the efforts of Industries born on the wave of the phenomenon have often led to choose the fastest route to achieve and maintain the physical aspect in the myth of beauty at all costs, without considering that aesthetic is not synonymous of beauty, but it is a balance between body and mind, and the role of the doctor is to take care of the Person globally and not only focusing on the correction of "a badly accepted blemish".

Faithful to the teaching of my Master had almost 50 years ago, this new journal will have the task of elevating the human resources, aligning and validating methodologies, but above all affirming the *humanitas* of the medical art in its purest sense to pursue the good and the graceful for the person who relies on it.

Fulvio Tomaselli, MD
Honorary President of the Italian
Society of Aesthetic Medicine

Aesthetic Medicine needs science. All over the world.

All Aesthetic Doctors know that science is the basis for safety. Safety is the most important issue in our discipline.

Unfortunately, Aesthetic Medicine is more often surrounded by marketing than by science, despite the hard work done by Scientific Societies all over the World. And, too often doctors working in this field are dealing with sellers that promote products with insufficient scientific studies. However, they sell it anyway. I think that doctors must learn that the first thing to ask about a medical device is the scientific background regarding that product: patients treated, follow up period, adverse events and, most of all, publications.

With this new International Journal completely dedicated to Aesthetic Medicine, proposed by the Italian Society of Aesthetic Medicine, endorsed by UIME and shared by all the National Societies of Aesthetic Medicine belonging to UIME, World Aesthetic Medicine wants to stimulate scientific production in this discipline to increase safety and quality in aesthetic medical procedures.

Another important goal of the Journal is to catalyze the proposal of new protocols and guidelines in Aesthetic Medicine, with the consensus of the entire Aesthetic Medicine Scientific Community.

What this Journal should achieve in the near future is to improve the number and quality of scientific production in Aesthetic Medicine, in order to allow this discipline to grow in the field of evidence based medicine, not only in the rationale field.

I hope this can be the start of a new era for Aesthetic Medicine, with the commitment of all Scientific Societies all over the world.

Emanuele Bartoletti, MD
Managing Editor
President of the Italian
Society of Aesthetic Medicine

INTERNATIONAL SOCIETIES
and NATIONAL SOCIETIES OF AESTHETIC MEDICINE

INTERNATIONAL SOCIETY OF AESTHETIC MEDICINE
154, rue Armand Silvestre - 92400 Courbevoie - France
Honorary Presidents: C.A. BARTOLETTI † (Italy), A. BOURRA (Morocco), M. DELUNE (USA), A. FARIA DE SOUZA (Brazil), J. FONT-RIERA† (Spain), G. MARZULLO (Chile), R. PINTO (Argentine), J. HEBRANT (Belgium), A. ELBAUM (Uruguay)

President:	M. OUGHANEM (Algeria)
Vicepresident:	V. GARCIA GUEVARA (Venezuela)
General Secretary:	J.J. LEGRAND (France)
General Secretary in charge of the American Continent:	R. PINTO (Argentine)
of Africa and Middle East:	A. BOURRA (Morocco)

ALGERIAN SOCIETY OF AESTHETIC MEDICINE
Bt.T1, N°2, Diar Es Saada, El Madania, Algiers – Algeria
oughanem_m@hotmail.com – www.same-dz.com
President: M. OUGHANEM

ARGENTINE SOCIETY OF AESTHETIC MEDICINE
Avenida Santa Fé 3288, 4°A – 1425 Buenos Aires – Argentine
pinto@soarme.com - www.soame.com
President: R. PINTO

BELGIAN SOCIETY OF AESTHETIC MEDICINE
Chaussée de Marche 390 – 5100 Jambes – Belgium
jean.hebrant@skynet.be – www.aesthetic-medicine.be
President: J. HEBRANT

BRASILIAN ASSOCIATION OF AESTHETIC MEDICINE SCIENCES
Avenida Vereador José Diniz – 2480 – Brooklin
Sao Paulo CEP 04604-004
clara_santos@terra.com.br
President: C. SANTOS

CANADIAN ASSOCIATION OF AESTHETIC MEDICINE
c/o CongressWorld Conferences Inc.
220-445 Mountain Highway
North Vancouver, BC, Canada V7J 2L1
drvanaardt@nslaser.com – s.roberts@caam.ca – www.caam.ca
President: R. VAN AARDT

CHILEAN ASSOCIATION OF AESTHETIC MEDICINE
Avda President Riesco 2955, apto 1102, Las Condes Santiago – Chile
docgm@estetic.cl
President: G. MARZULLO

CHINA ACADEMY OF AESTHETIC MEDICINE
Department of Stomatology, General Hospital of PLA 28 Fuxing road, BEIJING 100853 - China
caam01@126.com – www.caamed.com
President: LIU HONG CHENG

COLOMBIAN ASSOCIATION OF AESTHETIC MEDICINE
Calle 4 Sur, n. 43 a 195 - Oficina 141 - Bloque B - Medellin - Colombia
acicme@gmail.com – www.acicme.com.co
President: G. ARROYAVE ESTRADA

ECUADORIAN SOCIETY OF AESTHETIC MEDICINE
Ave de los Shyris 344 y Eloy Alfaro, Edificio Parque Central, Oficina 609 – Quito – Ecuador
seem2008cg@gmail.com – www.seem.com.ec
President: V. TINOCO KIRBY

FRENCH SOCIETY OF AESTHETIC MEDICINE
154, rue Armand Silvestre - 92400 Courbevoie - France
jjlegrand-md@sfme.info – www.sfme.info
President: J.J. LEGRAND

GEORGIAN SOCIETY OF AESTHETIC MEDICINE
I. Abashidze str. 77, Tbilisi 0162 - Georgia
info@gsoam.ge – www.gsoam.ge
President: E. UGREKHELIDZE

ITALIAN SOCIETY OF AESTHETIC MEDICINE
Via Monte Zebio 28 - 00195 Rome - Italy
simei@lamedicinaestetica.it – www.lamedicinaestetica.it
President: E. BARTOLETTI

KAZAKHSTAN ASSOCIATION OF AESTHETIC MEDICINE AND PLASTIC SURGERY
139, Tulebaeva Str. – 480091 Almati , Medeouski
arugulnar@hotmail.com – www.estetic.kz
President: G. ZHUMATOVA

KOREAN ACADEMY OF AESTHETIC MEDICINE
Han-Song B.D. 801, Myeong-dong, Jung-gu, Seoul - Korea
zzang0703@naver.com – www.ons.or.kr
President: J-B. YUN

MEXICAN SCIENTIFIC SOCIETY OF AESTHETIC MEDICINE
Cincinnati 81-307 – Col. Noche Buena – Mexico D.F. 03720 – Mexico
bmillerkobisher@yahoo.com
President: J-B. MILLER KOBISHER

MOROCCAN SOCIETY OF AESTHETIC MEDICINE
19, place du 16 Novembre – 20250 Casablanca – Morocco
drbourra@hotmail.com – www.dermastic.asso.ma
President: A. BOURRA

POLISH SOCIETY OF AESTHETIC AND ANTI-AGING MEDICINE OF POLISH MEDICAL SOCIETY
Ujazdowskie 22, 00-478 Warszawa – Poland
psme@psme.waw.pl; www.ptmeiaa.pl
President: A. IGNACIUK

ROMANIAN SOCIETY FOR AESTHETIC MEDICINE AND DERMATOLOGIC SURGERY
Sevastopol 13-17, Sector 1, Hotel Diplomat, Apt.204 Bucharest – Romania
mihaelaleventer@drleventercentre.com – www.srme.ro
President: M. LEVENTER

RUSSIAN NATIONAL AESTHETIC MEDICINE SOCIETY
12/3 Fotievoi Street, Pol. n.3 – of.512 – 119333 Mosca – Russia
o.panova@rs-am.ru – www.rs-am.ru
President: O. PANOVA

AESTHETIC AND ANTI-AGING MEDICINE SOCIETY OF SOUTH AFRICA
PO Box 1190 – Montana Park 0159 – South Africa
drsmit@ackmain.com
President: R. SMIT

SPANISH SOCIETY OF AESTHETIC MEDICINE
Ronda General Mitre, 210
08006 Barcelona – Spain
secretaria@seme.org – www.seme.org
President: P. VEGA

SWISS SOCIETY OF AESTHETIC MEDICINE
64 avenue de Rumine – 1005 Lausanne – Switzerland
xmartin@worldcom.ch – www.ssme.ch
President: X. MARTIN

SOCIETY OF AESTHETIC MEDICINE IN TURKEY
Rumeli Caddesi Durak Apt N° 2, D.7 – Nisantasi, Istanbul
subasihasanm@superonline.com
www.estetiktipdernegi.org.tr
President: H. SUBASI

UKRAINIAN SOCIETY OF AESTHETIC MEDICINE
Bunina Street, 10 Odessa 65026 – Ukraine
office@virtus.ua
President: V. TSEPKOLENKO

AESTHETIC MEDICINE SOCIETY OF URUGUAY
Ave. Sarmiento, 2470 – 11300 Montevideo – Uruguay
alberto@drelbaum.com – www.sume.com.uy
President: A. ELBAUM

AMERICAN ACADEMY OF AESTHETIC MEDICINE
24671 La Vida Drive – Laguna Niguel, Ca 92677 – USA
mdelune@aol.com – www.aaamed.org
President: M. DELUNE

AESTHETIC MEDICINE SOCIETY OF VENEZUELA
Av. Sucre de Los Dos Caminos, entre 4ta y 5ta transversal,
Res. Centro Parque Boyacà, Edificio Centro, Piso 20, Off. 201 1070 Caracas – Venezuela
fuceme@gmail.com - www.fuceme.org – www.sociveme.org
President: V. GARCIA GUEVARA

Aesthetic Medicine
Volume 2 · Number 1 · January-March 2016

Sarcopenia and testosterone replacement therapy

Francesco Romanelli[1], Andrea Sansone[2], Massimiliano Sansone[3]

[1]MD, Associate Professor - Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Sapienza - University of Rome, viale Regina Elena 324, 00165, Rome, Italy
[2]MD, PhD Student - Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Sapienza - University of Rome, viale Regina Elena 324, 00165, Rome, Italy
[3]MD, Resident - Department of Experimental Medicine, Section of Medical Pathophysiology, Food Science and Endocrinology, Sapienza - University of Rome, viale Regina Elena 324, 00165, Rome, Italy

ABSTRACT

Sarcopenia is an age-related clinical syndrome defined by a reduction in muscle mass and function. This condition is frequently associated with different pathophysiological conditions, such as chronic diseases, cancer, infections, obesity, immobilization, inadequate nutrition, hormonal deficiencies and it negatively affects the quality of life. There's no single mechanism underlying muscle loss in sarcopenia as many factors may be involved in genesis and development of sarcopenia.

A hormonal assessment including serum testosterone should be necessarily performed. Testosterone plays a big role on muscle tissue and low serum level (i.e. hypogonadism) represents a risk factor that should be addressed throughout a replacement therapy.

In the framework of sarcopenia the high-end physiological serum testosterone level range should represent the target to reach. Many formulations that provide steady testosterone level should be considered the best options of treatment and a correct monitoring plan has to be put into practice.

Keywords
Muscle, testosterone, sarcopenia, hormones

Correspondence
Francesco Romanelli
E-mail: francesco.romanelli@uniroma1.it

Accepted for publication 7 January 2016

Introduction

Sarcopenia has been defined as the loss of skeletal muscle mass and strength associated with different clinical conditions, both physiological and pathological; however, a universally accepted clinical definition of sarcopenia is lacking. The European Working Group on Sarcopenia in Older People (EWGSOP) suggested strict diagnostic criteria in order to define accurately such a syndrome. In particular, EWGSOP recommends the presence of both low muscle mass and low muscle function (strength or performance) to diagnose sarcopenia suggesting an easy-to-use algorithm (Figure 1).

The presence of low muscle mass without any reduction in muscle strength or performance characterizes a state of presarcopenia[1]; indeed, the relationship between muscle mass and muscle function is not linear as muscle functions is affected by several factors (i.e. degeneration of motor neurons, fat and connective muscle infiltration, protein degeneration, mitochondrial dysfunction, etc…)[2].

A merely quantitative measure of muscle mass is not sufficient to define how muscle effectively works[3].

Figure 1

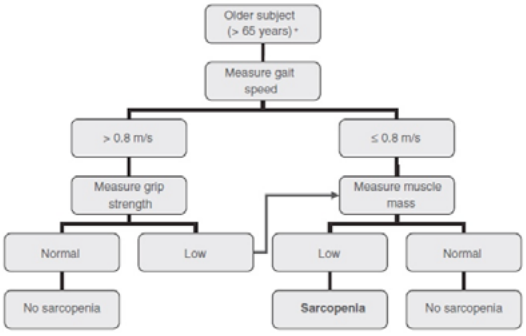


Figure 1 - EWGSOP-suggested algorithm for sarcopenia case finding in older individuals
Source: Sarcopenia: European consensus on definition and diagnosis. Cruz-Jentoft AJ1, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, Martin FC, Michel JP, Rolland Y, Schneider SM, Topinková E, Vandewoude M, Zamboni M; European Working Group on Sarcopenia in Older People. Report of the European Working Group on Sarcopenia in Older People Age Ageing. 2010; 39(4): 412-23

Such a definition is far from being conclusive and it opens the challenge to choose the best measurement techniques to determine muscle mass and muscle strength/performance.

Accuracy and precision should be carefully evaluated, but, in a clinical setting, the low cost and easiness of access to equipment need to be considered.

According to the different techniques used to measure muscle mass and muscle functions, different cut-offs have been proposed[1,4] (Table 1).

Muscle mass	DXA	Skeletal mass (SMI) (appendicular skeletal muscle mass/height^2) Men: 7,26 kg/m^2 Women: 5,5 kg/m^2 (Rosetta Study) Men: 7,23 kg/m^2 Women: 5,67 kg/m^2 (Health ABC Study)
	BIA	SMI using BIA predicted skeletal muscle mass (SM) equation (SM/height^2) Men: 8.87 kg/m^2 Women: 6.42 kg/m^2 SMI using absolute muscle mass not appendicular muscle mass (absolute muscle mass/height^2) Men: Severe sarcopenia ≤8.50 kg/m^2 Moderate sarcopenia 8.51–10.75 kg/m^2 Normal muscle ≥10.76 kg/m2 Women: Severe sarcopenia ≤5.75 kg/m^2 Moderate sarcopenia 5.76–6.75 kg/m^2 Normal muscle ≥6.76 kg/m^2
Physical Performance	Gait Speed	GS < 0,8 m/s in 4 meters course 4,572 meters course Men: Height ≤ 173 cm (GS < 0,65 m/s) Height > 173 (GS < 0,76 m/s) Women: Height ≤ 159 cm (GS < 0,65 m/s) Height > 159 (GS < 0,76 m/s)
	Short Performance Physical Battery (SPPB)	SPPB ≤ 8
Muscle strength	Handgrip Strength (HS)	Men: HS <30 kg Women: HS <20 kg Men: BMI ≤ 24 HS ≤ 29 kg BMI 24.1–26 HS ≤ 30 kg BMI 26.1–28 HS ≤ 30 kg BMI > 28 HS ≤ 32 kg Women: BMI ≤ 23 HS ≤ 17 kg BMI 23.1–26 HS ≤ 17.3 kg BMI 26.1–29 HS ≤ 18 kg BMI > 29 HS ≤ 21 kg

Table 1 - Diagnosis of sarcopenia: measurable variables and cut-off points
Source: Sarcopenia: European consensus on definition and diagnosis. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, Martin FC, Michel JP, Rolland Y, Schneider SM, Topinková E, Vandewoude M, Zamboni M; European Working Group on Sarcopenia in Older People. Report of the European Working Group on Sarcopenia in Older People Age Ageing. 2010 ; 39(4): 412-23

Sarcopenia is a multifactorial process where diseases, nutrition, lifestyle, hormonal factors and aging play important roles. These risk factors often coexist in older adults giving an explanation of high

prevalence of sarcopenia in adults older than 65. According to the published reports, prevalence of sarcopenia ranges from 3% and 52% depending on definition criteria, measurement techniques used to evaluate muscle mass and performance/strength and study populations[2,5,6] (Figure 2).

Figure 2

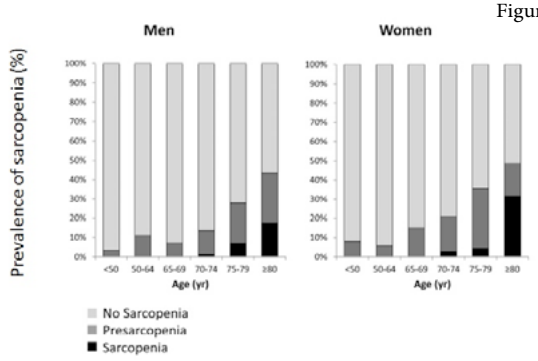


Figure 2 - Prevalence of sarcopenia and presarcopenia in men (left) and women (right) according to age decades.
Source: Volpato S, Bianchi L, Cherubini A, Landi F, Maggio M, Savino E, Bandinelli S, Ceda GP, Guralnik JM, Zuliani G, Ferrucci L. Prevalence and clinical correlates of sarcopenia in community-dwelling older people: application of the EWGSOP definition and diagnostic algorithm. J Gerontol A Biol Sci Med Sci. 2014; 69(4): 438-46

Sarcopenia affects negatively the quality of life and should be carefully evaluated to identify any possible reason in order to recommend a correct therapy. Endocrine changes should be taken into consideration when evaluating sarcopenic subjects; indeed, testosterone, GH, IGF-1, insulin, thyroid hormones, corticosteroids have a big impact on muscle mass and function. The physiological effects of testosterone on muscle and the prevalence of hypogonadism, especially in the elderly, represent the reason why testosterone deserves particular attention in the evaluation of sarcopenia.

Effect of Testosterone on muscle

Physiologically, testosterone administration brings about a significant increase in mean fiber area or diameter and in cross sectional fiber area both in type I and II fiber; furthermore such a change in the cross sectional area was significantly correlated with total and free blood testosterone concentrations[7-10].

The increase in mean fiber area was accompanied by a growth of the myonuclear number as testified by linear relationships between mean nuclear number and mean fiber area[7, 9,10]. As a consequence the number of myonuclei per unit fiber area remained unchanged, suggesting that the nuclear domain remained unmodified in order to sustain the protein synthesis in hypertrophied muscle[10]. As myonuclei in adult muscle fiber are not able to duplicate, it means that testosterone is able to increase in muscle fiber size both by hypertrophy and formation of new fiber. Testosterone administration may have direct effect on proliferation of satellite cells as showed by the evidence that muscle hypertrophy was associated with a significant increase in the number of satellite cells per millimetre of muscle fiber and in satellite cell number, measured by direct counting and expressed as percentage of myonuclear number[11]. Moreover, a significant higher number of fiber expressing embryonic and fetal protein isoforms suggests that hyperplasia is also involved in muscle enlargement of skeletal muscle during testosterone administration[7,9]. Nevertheless, testosterone has no effects on the proportion of muscle fiber type which remains unchanged[7,9,10]. The increase in myonuclei number remains even after the withdrawal of testosterone administration and constitutes a cellular memory facilitating subsequent muscle overload hypertrophy[12].

Hypogonadism: how to diagnose

Hypogonadism represents a clinical and biochemical syndrome associated with age and comorbidities that should be carefully considered in evaluating sarcopenic subjects. From a clinical point of view, the symptoms related to hypogonadism are: reduced sexual desire, decreased spontaneous erections and erectile dysfunction. EMAS study proposed to define hypogonadism in presence of three sexual symptoms in combination with total testosterone less than 11 nmol/L and free testosterone less than 220 pmol/L measured in the morning between 7 a.m. and 11 a.m. and confirmed by a second measurement.

A severe testosterone deficiency requiring therapy is represented by a serum testosterone below 8nmol/L whereas a level between 8nmol/L and 11 nmol/L may not require an immediate therapy. A repeated serum testosterone level between 8 and 11 nmol/L would suggest serum free testosterone measurement by means of equilibrium dialysis or simply by Vermeulen formula considering albumin and SHBG in order to calculate the bioavailable testosterone fraction.

A serum free testosterone below 220 pmol/L suggests the presence of hypogonadism[13] (Figure 3). However, slightly different biochemical cut-offs are present in scientific literature. For instance, clinical guidelines of the Endocrine society recommends to consider a cut-off value of 9,8 nmol/L or 10,4 nmol/L to diagnose hypogonadism[14,15], whereas the International Society of Andrology considers 8 nmol/L as the lower normal limit and suggests to evaluate serum free testosterone if total testosterone is between 8 and 12 nmol/L.

In this case, a free testosterone level below 225 pmol/L can provide supportive evidence for testosterone replacement therapy (TRT)[14,16]. In the diagnostic process of hypogonadism the clinician should consider any possible reason of low serum

Figure 3

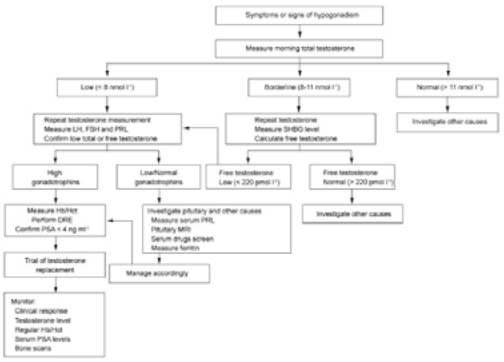


Figure 3 - Algorithm for the diagnosis and treatment of LOH. BMD: bone mineral density; Calc: calculated; DRE: digital rectal examination; Eq. dial: equilibrium dialysis; FSH: follicle-stimulating hormone; Hct: hematocrit; LH: luteinizing hormone; LOH: late-onset hypogonadism; PRL: prolactin; MRI: magnetic resonance imaging; PSA: prostate-specific antigen; T: testosterone
Source: Huhtaniemi I. Late-onset hypogonadism: current concepts and controversies of pathogenesis, diagnosis and treatment. Asian J Androl. 2014; 16(2): 192-202

testosterone and a blood analysis including a complete blood count, LH, prolactin, ferritin, TSH, glycemia, HbA1c, cortisol should be performed.

Hypogonadism is frequently associated with chronic disease (i.e. chronic kidney disease, chronic liver disease, BPCO, congestive heart failure), aging and obesity. Finally, an accurate evaluation of any drug-based therapy should be included to rule out iatrogenic causes (i.e. opioids, glucocorticosteroids, dopamine antagonists, GnRH long acting agonist).

Therapy

Many testosterone preparations are available at the moment and the choice should evaluate the pros and cons of each of formulations, including patient's compliance and cost. Oral preparations are very simple to use but they are no longer employed in clinical settings due to their hepatoxicity. Only oral testosterone undecanoate is still used but should be administered 40/80 mg at meals two or three times a day and, even so, it does not provide a steady serum testosterone level. Indeed, a great variability in its absorption has been observed in the same subjects on different days and among individuals. Injective testosterone esters represent the most common preparation for treating hypogonadism.

They are injected every 20 or 30 days at the dose of 250 mg but their pharmacokinetic profile consists in peaks of two or three days after the injection and in a rapid decline[17]. Intramuscular testosterone undecanoate injected every 12-16 weeks doesn't provide fluctuations in serum testosterone level and a stable value is maintained for a long period. These fluctuations may be not well tolerated by subjects who are prone to hypogonadal symptoms (i.e. low libido, depression, low energy) by the end of dosing intervals and, especially in older men, the supraphysiological serum testosterone level may increase the frequency of adverse effects (i.e. erythrocytosis). Otherwise, transdermal testosterone gel preparations require daily administration at dosage of 2-4 gr containing 40-80 mg of testosterone for 2% gel. They provide stable serum testosterone level resembling the circadian profile. Recently in the USA a new liquid form of testosterone has been approved for hypogonadism and should be applied underarm once a day. Transdermal testosterone patches have a similar pharmacokinetics compared to transdermal gel but dermatitis may represent a potential side effect.

Transdermal buccal and pellet preparations represent less common forms of testosterone replacement therapy. In men requiring fertility, gonadotropins (i.e hCG) represent the treatment of choice, at a dosage of 2000 IU or 5000 IU weekly depending on biochemical response. In secondary hypogonadism, clomiphene citrate (25-50 mg/die) may represent a good alternative to testosterone preparations[15]. Eventually, in presence of gynecomastia or an increase in serum estradiol, oxandrolone, mesterolone or nandrolone may be considered as they are non-aromatizable androgens[18].

In some pathological conditions TRT is not recommended: metastatic breast or prostate cancer, erythrocytosis (haematocrit >54%), severe congestive heart failure, lower urinary tract symptoms (I-PSS score >19), untreated obstructive sleep apnea, desire of fertility and presence of unevaluated prostate nodule or PSA >4.0 ng/ml (3.0 ng/ml in Afro-Americans and subjects who have first-degree relatives with prostate cancer). Therefore, biochemical assessment should always include full-blood count and PSA. A serum PSA increase > 1,4 ng/ml within any 12-month period during TRT or an increase > 0,4ng/ml/year after 6 months from the beginning of TRT require a prostatic biopsy[19].

Monitoring men during TRT is extremely important in order to adjust the dosage and monitor adverse effects. A regular testing including total testosterone, PSA and a full blood count each 3, 6 and 12 months and then annually should be performed. Target serum testosterone should be ranging from 350 ng/dl to 700 ng/dl[20]. In the case of sarcopenic subjects, serum testosterone in the mid-upper range should represent the optimal target; however, these levels may increase the risk of adverse effects, especially in the elderly who have a higher risk, compared to young men, to develop erythrocytosis when treated with injectable testosterone esters[21]. According to the different preparations of TRT, serum testosterone should be evaluated differently. In the case of injectable testosterone esters, serum testosterone levels should be monitored midway and at the end of dosing intervals, whereas injectable testosterone undecanoate requires monitoring testosterone just before the subsequent injections. Transdermal gel testosterone needs to be

evaluated by an assessment of serum testosterone just before the administration, at the very end of the dosing intervals, after at least seven days of treatment.

The use of transdermal patch requires an assessment of testosterone 3h-12h after the application of the patch. Finally, in case of oral undecanoate testosterone, a serum testosterone should be measured 3h-5h after ingestion.

The role of testosterone in sarcopenia

Given the physiological action of testosterone on muscle, it should not represent a surprise the fact that an adequate serum testosterone level is necessary to maintain and measure muscle mass and strength. Complete suppression of endogenous testosterone production with a GnRH long acting analogue brings about a loss in muscle mass, muscle strength, a decrease in whole body protein turnover and protein synthesis and an increase in fat mass[22].

Moreover, low serum testosterone level prevents the physiological muscle adaptations from strength training, a powerful anabolic stimulus, and an increase in fat mass has been observed despite a strength training schedule[23,24]. Indeed, loss of muscle mass is associated with level of serum testosterone below 6.9 nmol/l (2.0 ng/ml)[25]. Similarly, in healthy men, whose endogenous testosterone production had been abolished with a GnRH analogue, a treatment with different doses of weekly intramuscular testosterone esters for 20 weeks produced different effects on muscle mass and strength.

The different doses given were shown to produce a range of serum concentrations from subphysiological to supraphysiological doses. Subphysiological dosing of testosterone produced a gain in fat mass and loss of fat free mass during the study. There were sequential decreases in fat mass and increases in fat free mass with each increase of testosterone dose. These changes in body composition were seen in physiological and supraphysiological treatment doses. With regard to muscle function, the investigators showed dose-dependent increases in leg strength and power with testosterone treatment in young and older men but there was no improvement in fatigability[26-28].

In the evaluation of the effects of testosterone administration on body composition in hypogonadal men or men with borderline low testosterone levels, data from studies show a consistent increase in fat free mass and decrease in fat mass or visceral adiposity with testosterone treatment[29-34]. Less consistent results regarding the effects of testosterone administration on muscle strength are present in literature.

An increase in muscle strength was observed in some studies[30,31] but not in others[32]. Within the same study, the strength of some muscle groups increases whilst others do not[35]. It's likely that such differences are partly due to the methodological variations in assessing strength and to different serum testosterone levels considered as a target. Reference range established as a target for TRT goes from 4.00 ng/ml to 7.00 ng/ml, but when evaluating hypogonadism in sarcopenic subjects, this range should be better characterized in order to maximize the anabolic effects on muscle. Increase in muscle mass and function following testosterone administration has a linear relationship with serum testosterone level which, in turns, depends linearly on the testosterone dose administered[27]. Of course, a supraphysiological dose of testosterone brings about a marked increase in muscle mass but poses serious risk of adverse effects.

Therefore, testosterone replacement dose providing the best trade-off between increase in muscle mass and adverse effects should be established. For instance, in elderly non-hypogonadal men Randall et al. observed that raising serum testosterone level from less than 4,8 ng/ml to 5,0 ng/ml-10 ng/ml, a range similar to that of young men, increase significantly muscle mass and muscle protein synthesis with no training[36]. Similarly, Bhasin et al. observed that both in older and young men, whose testosterone production had been completely suppressed by GnRH long-acting agonist, the best-trade off dose between anabolic effects and adverse effects was 125 mg/week testosterone enanthate corresponding to a serum testosterone level ranging from 5,70 ng/ml to 8,52 ng/ml[26,27].

Of course, this dosage should be carefully evaluated because in these subjects the endogenous production of testosterone had been completely suppressed and a higher dose of testosterone is necessary to reach the serum testosterone level established as target.

In hypogonadal men, whose testosterone production is low but not suppressed, dosage should be titrated in order to maintain a serum testosterone level in mid-upper range. In order to maximize the anabolic effects and minimize adverse effects, it should be considered that testosterone esters may increase the rate of adverse effects because they generate supraphysiological peaks shortly after the injections, especially in older men whose testosterone clearance is diminished[37]. For such a reason, testosterone esters may be not considered the best option of treatment when the target is to maintain serum testosterone level in the high-end range.

Testosterone formulations providing a steady serum testosterone level, such as intramuscular testosterone undecanoate or testosterone gel, seem to be more appropriate. In healthy eugonadal men receiving GnRH long-acting agonist in order to abolish endogenous testosterone production, a dose of 100 mg testosterone gel was necessary to reach the high-end range (i.e. 8,05-9,24 ng/dl)[25]. Indeed, keeping in mind that the testosterone production rates in normal adults ranges from 4 mg to 11,8 mg and considering a bioavailability of 10% for testosterone gel it's easy to establish the dosage of testosterone gel necessary to reach the mid-upper range[38,39].

Conlcusions

The correct assessment of sarcopenia should include an evaluation of hormonal status and the correct functionality of hypothalamic-pituitary-gonadal axis with normal serum testosterone level should be addressed. Indeed, hypogonadism represents a cause for the decline in muscle mass and performance in the elderly and, fortunately, a correct TRT is able to restore adequate serum testosterone level affecting positively muscle tissue. In this context, it's worthy to note that many testosterone formulations are now present but clinicians should consider as treatment of choice those preparations providing steady serum testosterone level.

Therefore, in order to maximize the anabolic effects of TRT, a mid-upper range may be considered as an adequate target; however, in order to decrease the rate of adverse effects, it would be suggested to avoid supraphysiological peaks, especially in elderly men whose clearance of testosterone is reduced. Finally, a correct evaluation of TRT needs to be scheduled in the pursuit of excellence.

References

1 Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing.* 2010; 39(4):412-423.

2 Volpato S, Bianchi L, Cherubini A, et al. Prevalence and clinical correlates of sarcopenia in community-dwelling older people: application of the EWGSOP definition and diagnostic algorithm. *J Gerontol A Biol Sci Med Sci.* 2014; 69(4):438-446.

3 Goodpaster BH, Park SW, Harris TB, et al. The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. *J Gerontol A Biol Sci Med Sci.* 2006; 61(10):1059-1064.

4 Fielding RA, Vellas B, Evans WJ, et al. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. *J Am Med Dir Assoc.* 2011; 12(4):249-256.

5 Cruz-Jentoft AJ, Landi F, Schneider SM, et al. Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). *Age Ageing.* 2014; 43(6):748-759.

6 Lee WJ, Liu LK, Peng LN, Lin MH, Chen LK. Comparisons of sarcopenia defined by IWGS and EWGSOP criteria among older people: results from the I-Lan longitudinal aging study. *J Am Med Dir Assoc.* 2013;14(7): 528.e521-527.

7 Kadi F, Eriksson A, Holmner S, Thornell LE. Effects of anabolic steroids on the muscle cells of strength-trained athletes. *Med Sci Sports Exerc.* 1999; 31(11):1528-1534.

8 Hartgens F, van Straaten H, Fideldij S, Rietjens G, Keizer HA, Kuipers H. Misuse of androgenic-anabolic steroids and human deltoid muscle fibers: differences between polydrug regimens and single drug administration. *Eur J Appl Physiol.* 2002; 86(3):233-239.

9 Eriksson A, Kadi F, Malm C, Thornell LE. Skeletal muscle morphology in power-lifters with and without anabolic steroids. *Histochem Cell Biol.* 2005; 124(2):167-175.

10 Sinha-Hikim I, Artaza J, Woodhouse L, et al. Testosterone-induced increase in muscle size in healthy young men is associated with muscle fiber hypertrophy. *Am J Physiol Endocrinol Metabol.* 2002; 283(1):E154-164.

11 Sinha-Hikim I, Roth SM, Lee MI, Bhasin S. Testosterone-induced muscle hypertrophy is associated with an increase in satellite cell number in healthy, young men. *Am J Physiol Endocrinol Metab.* 2003; 285(1):E197-205.

12 Yu JG, Bonnerud P, Eriksson A, Stal PS, Tegner Y, Malm C. Effects of long term supplementation of anabolic androgen steroids on human skeletal muscle. *PloS One.* 2014; 9(9):e105330.

13 Tajar A, Huhtaniemi IT, O'Neill TW, et al. Characteristics of androgen deficiency in late-onset hypogonadism: results from the European Male Aging Study (EMAS). *J Clin Endocrinol Metab.* 2012; 97(5):1508-1516.

14 Isidori AM, Balercia G, Calogero AE, et al. Outcomes of androgen replacement therapy in adult male hypogonadism: recommendations from the Italian society of endocrinology. *J Endocrinol Invest.* 2015; 38(1):103-112.

15 Bhasin S, Cunningham GR, Hayes FJ, et al. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2010; 95(6):2536-2559.

16 Wang C, Nieschlag E, Swerdloff R, et al. Investigation, treatment and monitoring of late-onset hypogonadism in males: ISA, ISSAM, EAU, EAA and ASA recommendations. *Eur J Endocrinol.* 2008; 159(5):507-514.

17 Di Luigi L, Sgro P, Romanelli F, et al. Urinary and serum hormones profiles after testosterone enanthate administration in male hypogonadism: concerns on the detection of doping with testosterone in treated hypogonadal athletes. *J Endocrinol Invest.* 2009; 32(5):445-453.

18 Corona G, Vignozzi L, Sforza A, Maggi M. Risks and benefits of late onset hypogonadism treatment: an expert opinion. *World J Mens Health.* 2013; 31(2):103-125.

19 Corona G, Rastrelli G, Maggi M. Diagnosis and treatment of late-onset hypogonadism: systematic review and meta-analysis of TRT outcomes. *Best Pract Res Clin Endocrinol Metab.* 2013; 27(4):557-579.
20 Di Luigi L, Sgro P, Aversa A, et al. Concerns about serum androgens monitoring during testosterone replacement treatments in hypogonadal male athletes: a pilot study. *J Sex Med.* 2012; 9(3):873-886.
21 Dimopoulou C, Ceausu I, Depypere H, et al. EMAS position statement: Testosterone replacement therapy in the aging male. *Maturitas.* 2016; 84:94-99.
22 Mauras N, Hayes V, Welch S, et al. Testosterone deficiency in young men: marked alterations in whole body protein kinetics, strength, and adiposity. *J Clin Endocrinol Metab.* 1998; 83(6):1886-1892.
23 Kvorning T, Andersen M, Brixen K, Madsen K. Suppression of endogenous testosterone production attenuates the response to strength training: a randomized, placebo-controlled, and blinded intervention study. *Am J Physiol Endocrinol Metab.* 2006; 291(6):E1325-1332.
24 Sgro P, Romanelli F, Felici F, et al. Testosterone responses to standardized short-term sub-maximal and maximal endurance exercises: issues on the dynamic adaptive role of the hypothalamic-pituitary-testicular axis. *J Endocrinol Invest.* 2014; 37(1):13-24.
25 Finkelstein JS, Yu EW, Burnett-Bowie SA. Gonadal steroids and body composition, strength, and sexual function in men. *The N Engl J Med.* 2013; 369(25):2457.
26 Bhasin S, Woodhouse L, Casaburi R, et al. Older men are as responsive as young men to the anabolic effects of graded doses of testosterone on the skeletal muscle. *J Clin Endocrinol Metab.* 2005; 90(2):678-688.
27 Bhasin S, Woodhouse L, Casaburi R, et al. Testosterone dose-response relationships in healthy young men. *Am J Physiol Endocrinol Metab.* 2001; 281(6):E1172-1181.
28 Storer TW, Magliano L, Woodhouse L, et al. Testosterone dose-dependently increases maximal voluntary strength and leg power, but does not affect fatigability or specific tension. *J Clin Endocrinol Metab.* 2003; 88(4):1478-1485.
29 Isidori AM, Giannetta E, Greco EA, et al. Effects of testosterone on body composition, bone metabolism and serum lipid profile in middle-aged men: a meta-analysis. *Clin Endocrinol (Oxf).* 2005; 63(3):280-293.
30 Page ST, Amory JK, Bowman FD, et al. Exogenous testosterone (T) alone or with finasteride increases physical performance, grip strength, and lean body mass in older men with low serum T. *J Clin Endocrinol Metab.* 2005; 90(3):1502-1510.
31 Ferrando AA, Sheffield-Moore M, Yeckel CW, et al. Testosterone administration to older men improves muscle function: molecular and physiological mechanisms. *Am J Physiol Endocrinol Metab.* 2002; 282(3):E601-607.
32 Snyder PJ, Peachey H, Hannoush P, et al. Effect of testosterone treatment on bone mineral density in men over 65 years of age. *J Clin Endocrinol Metab.* 1999; 84(6):1966-1972.
33 Kenny AM, Prestwood KM, Gruman CA, Marcello KM, Raisz LG. Effects of transdermal testosterone on bone and muscle in older men with low bioavailable testosterone levels. *J Gerontol A Biol Sci Medical Sci.* 2001; 56(5):M266-272.
34 Steidle C, Schwartz S, Jacoby K, Sebree T, Smith T, Bachand R. AA2500 testosterone gel normalizes androgen levels in aging males with improvements in body composition and sexual function. *J Clin Endocrinol Metab.* 2003; 88(6):2673-2681.
35 Ly LP, Jimenez M, Zhuang TN, Celermajer DS, Conway AJ, Handelsman DJ. A double-blind, placebo-controlled, randomized clinical trial of transdermal dihydrotestosterone gel on muscular strength, mobility, and quality of life in older men with partial androgen deficiency. *J Clin Endocrinol Metab.* 2001; 86(9):4078-4088.
36 Urban RJ, Bodenburg YH, Gilkison C, et al. Testosterone administration to elderly men increases skeletal muscle strength and protein synthesis. *Am J Physiol.* 1995; 269(5 Pt 1):E820-826.
37 Yassin AA, Haffejee M. Testosterone depot injection in male hypogonadism: a critical appraisal. Clin Interv Aging. 2007; 2(4):577-590.
38 Korenman SG, Wilson H, Lipsett MB. Testosterone production rates in normal adults. *J Clin Invest.* 1963; 42:1753-1760.
39 Meikle AW, Matthias D, Hoffman AR. Transdermal testosterone gel: pharmacokinetics, efficacy of dosing and application site in hypogonadal men. *BJU Int.* 2004; 93(6):789-795.

Aesthetic Medicine
Volume 2 · Number 1 · January-March 2016

Centripetal approach to facial aesthetic treatments

Paola Rosalba Russo[1], Francesca de Angelis[2], Magda Belmontesi[3], Fernanda Distante[4]

[1]MD, General Surgery Specialist - Xsana s.n.c., Modena,
[2]MD, Plastic Surgery Specialist - Chief at Laser & Plastic Surgery Clinic DE.A. Center - Napoli,
[3]MD, Dermatologist, Vigevano and Milano,
[4]MD, Dermatologist, Medical Advisor & PhVigilance Manager, Galderma Italia S.p.A., Agrate Brianza (MB)

ABSTRACT

Many studies indicate that an oval face shape is a distinctive beauty and youth trait, regardless of ethnicity or other facial anthropometric parameters. In this paper, the main literature data supporting this hypothesis are analysed. We also suggest a new approach to facial examination based on the evaluation of concentric circles, as an alternative to conventional horizontal segments (upper third, middle third and lower third). This approach to facial examination is defined "centripetal approach". This approach, which aims at restoring the facial oval shape, guides the practitioner to administer the fillers starting from the outer zones of the face rather than the inner or central parts. Moreover, this approach helps the practitioner in the selection of the more appropriate dermal filler to inject in each facial area, according to the patient's needs. The Authors describe a series of clinical cases where this approach was tested by using a broad range of hyaluronic acid gels (Restylane and Emervel fillers).

Keywords
Hyaluronic acid, filler, rejuvenation, Non Animal Stabilized Hyaluronic Acid (NASHA), Optimal Balance Technology

Correspondence
Fernanda Distante
Medical Advisor & PhVigilance Manager, Galderma Italia S.p.A., Agrate Brianza (MB)
E-mail: fernanda.distante@galderma.com

Accepted for publication 7 January 2016

Introduction

Facial appearance is a beauty trait of paramount relevance in human species. Many studies in experimental psychology have demonstrated that the female face is the first body part to be watched and evaluated when a subject is put into an empty room[1].

In general, female facial beauty is associated with more gentle curves and smoothness as opposed to the sharp angles and lines that characterize a handsome male face[2].

Two aspects appear to play a relevant role in overall face attractiveness: 1) facial symmetry; 2) facial averageness[3,4].

The importance of symmetry is well known by photographers and it is the main reason why the majority of beauty celebrities only show their "better side" to the camera[2].

Although many studies have been conducted in this field, the geometrical rules underlying "absolute beauty" are still unknown. Because of the relevance it has when it comes to determine female facial beauty, symmetry is a useful starting point in assessing or analysing the facial shape. This can be done by means of geometrical measures comprising the intercanthal distance (ICD), the bizygomatic distance (BZD), the bigonial distance (BGD) and the BZD/ICD and BGD/ICD ratios[2].

The oval shape as a facial beauty indicator

It is common and instinctive knowledge that prominent cheekbones and shaped jawline in an oval facial shape are key attributes of female facial beauty, across different ethnic groups and regions[5]. This oval line should begin at the forehead and curve seamlessly around the outside of the face through the temples, outer cheeks, pre-auricular area, angle of the jaw, jawline, and all the way to the chin[2].

The importance of the facial oval becomes extremely evident when the same face is observed after some years: aging results in altered oval shape and the face not only loses its beauty, but also its young-looking appearance (Figure 1).

Facial aging is a dynamic process that involves facial changes of soft tissue, skeletal support structure and fat compartments. Volume loss and morphological changes occur differentially within these compartments, resulting in facial contour incongruity[6]. The selective deflation of the deep cheek compartment contributes to the decreased projection of the superficial fat pads resulting in excess of skin tissue, illusion of ptosis and uneven facial contour, in contrast with a youthful face, in which there is a smooth transition between compartments, bestowing a defined facial profile (Figure 1)[5,6].

Figure 1

Figure 1 - The facial oval contour as an indicator of aesthetic ideal and youth

In a study led by Goodman[2], 21 photos of beautiful women (actresses, performers, and pageant winners) were analysed to construct an ideal oval shape based on the average of their facial shape dimensions. The study demonstrated that some geometrical relationships are stable, in particular the BZD/ICD and BGD/ICD ratios. The combination of these features resulted in a smooth oval shape, irrespective of other beauty indicators, such as eyes, chin or nose shape. In the study sample, the average BZD:ICD ratio was 4.3 and it was very stable across all subjects, regardless of ethnicity and other facial parameters. The BGD/ICD ratio was very stable as well, with an average of 36. The ideal facial oval constructed from the facial diameters of the 21 subjects had an oval height (forehead-chin distance)/ICD of 6.3.

This study clearly demonstrated that the facial oval is a strong and independent facial beauty indicator. These results, together with similar conclusions from different authors, confirm that the oval is the "ideal female facial shape" and that any variation from it can possibly lead to a loss in "absolute beauty"[2,5,7,8].

The centripetal approach to facial treatments

Facial aesthetic treatments shall ideally aim at preserving, restoring or reshaping the oval facial shape.

Under this perspective, a centripetal approach to facial aesthetic evaluation appears more appropriate and innovative than the traditional approach that divides the face into horizontal segments (upper third, middle third and lower third). The centripetal approach looks at the face as a whole, after sub-dividing it into three concentric circles: external, median and central circle (Figure 2).

Figure 2

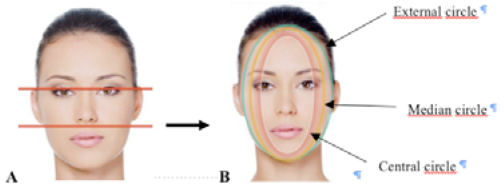


Figure 2 - Switching from a conventional facial assessment based on sub-division into three horizontal segments (A) to a centripetal assessment based on three concentred circles (B)

The final aim of the assessment is the comparison of the face with the ideal oval shape and to individuate any difference in terms of lacking or exceeding tissue.

From a therapeutic perspective, this difference defines the extent of the aesthetic treatments needed to bring the patient's face toward the ideal oval. Moreover, the division into circles allows a more accurate identification of the facial areas that require treatment. In general, the maximum correction should be done first at the outer circle to compensate for bone, volume fat loss and skin excess with the aim to enhance and shape the contour. Moving toward the middle circle, a deep filling aimed at projecting the mid-face and restoring volume loss is required.

Finally, a minimalistic approach should be used in the central circle by filling the naso-labial folds and medium wrinkles, the oral commissures, as well as the lip area[5]. Overall skin quality should be the complementary objective of any facial rejuvenation treatment.

Based on the different possible facial morphological changes the practitioner will be able to choose the most appropriate filler in each area to treat, according to the patient's needs. In this paper we describe a few cases from our experience that show the aesthetic results obtained by using this approach.

Hyaluronic acid gels for different aesthetic purposes

Hyaluronic acid-based fillers (HA fillers) have become the gold standard for full-face rejuvenation[9],[10]. The success of hyaluronic acid in aesthetic medicine relies on its viscoelastic properties, as well as on its biocompatibility and convenience[11].

HA fillers are different in terms of degree of cross-linking, gel calibration (particle sizing), and concentration of HA. Together, these factors determine the two main rheological properties of HA fillers that may be quantified: the complex viscosity (G*) and the elastic modulus (G'). The gel behavior inside the tissue will depend on those rheological features: fillers with higher G′ are relatively firm and can better resist deformation, remaining more targeted into the tissue.

They are more suitable when a more lifting and defined effect is desired. Fillers with lower G′ display a more distributed pattern into the tissue.

They are softer and more suitable when a more restoring and smooth effect is needed[12-14].

Overall, product integration and lifting capacity are the result of gel firmness and particle size.

The physical properties of the fillers may have a big impact on clinical results and overall injection experience, therefore physicians should carefully select the products that are more suitable to individual needs[14].

Since patient's requirements may differ because of different aging patterns and aesthetic preferences, the practitioner will benefit of a palette of gels textures in clinical practice. Fillers based on NASHA technology (Restylane) and Optimal Balance Technology (Emervel) (Q-Med AB, Uppsala, Sweden) all together cover a broad spectrum of viscoelastic G* values[15,16] and have a well-documented efficacy and safety profile[17-26].

All NASHA gels are firm gels that show a unique high resistance to deformation, achieved with a patented technology based on a low level of cross-linking by preserving natural HA entanglements (stabilization with minimal modification). A variable homogeneous particle size, a constant degree of cross-linking and HA concentration (20 mg/ml) characterize the different gels of the NASHA range. The gels of the Emervel family, based on the Optimal Balance Technology, are softer than Restylane fillers.

Different gel properties are achieved by varying both degree of cross-linking and particle size while maintaining a constant HA concentration of 20 mg/ml.

Predictable results with high patient's satisfaction, long duration of effects until 18 months for both ranges and until 36 months after 2 retreatments for Restylane have been shown in extensive randomized clinical trials[17,18,27].

Our 20-years real life clinical practice confirms the satisfactory aesthetic results achievable with Restylane and Emervel fillers. We have selected these two ranges of fillers to test the advantages and clinical results that may be obtained in facial treatments by applying the centripetal approach.

Criteria for filler selection

Fillers for the external circle

The treatment of the outer circle aims at shaping the overall facial oval outline by restoring lost volumes in the temple, cheekbones and the pre-auricular area and by enhancing jawline and chin, according to the individual needs. Our preferential filler choice for restoring lost volumes in the cheekbone is Emervel Volume, that integrates well into the subcutaneous or over-periosteum tissues.

Restylane Perlane or Emervel Deep should be the preferential choice to shape and define the jawline. When bone structure and tissue quality are well represented and a more pronounced effect is desired, Restylane Perlane should be selected for its higher and precise lifting capability.

Emervel Deep displays a more distributed pattern into the tissue, thus it should be selected when

bone and tissue structures are less represented. We usually inject softer gels like Emervel Classic to replace volumes in the delicate pre-auricular and temple areas.

Fillers for the median circle

The treatment of the median circle aims at restoring and projecting the midface area. According to our experience, Restylane Perlane and Emervel Deep are the most suitable gels, because they display a high lifting capability.

They should be selected according to individual needs and tissue characteristics as described for the jaw area. We recommended to inject perpendicularly pillars of small amount of gels (0.2-0.3 ml for each injection point) over the bone, over the periosteal level, or into the deep fat compartments by using a sharp needle. Additionally, in order to provide a more refined result, Restylane or Emervel Classic, selected differentially according to the individual tissue quality and expected results, are injected into the superficial fat compartments in the area through cannula or needle. This technical approach has been described as "dual plane technique" by some Authors[27].

Fillers for the central circle

The treatment of the inner circle aims at correcting minor defects in order to refine residual folds, wrinkles and lines. Vermillion, lip contour and perioral lines are also included in the treatment of the central circle. In general, we recommend small volumes of gel when injecting this facial area in order to obtain harmonious and natural results. According to individual needs and tissue quality characteristics, Restylane or Emervel Classic are the best options for wrinkles and folds of mild to moderate severity. Finally we recommend Emervel Lips for lip enhancement. The small calibration of the gel, together with the great resistance to deformation and the very low rate of swelling make Emervel Lips the ideal gel to inject to shape lips and the vermillion border providing natural and graceful outcome.

Case studies

We describe 5 clinical cases from our broad experience that has included more than 50 patients using this novel centripetal approach to aesthetic treatments. The results are shown through pictures taken before and at different times from treatment (Figures 3-6).

Case #1

A 55 years Caucasian woman presented with Glogau grade III facial aging. Facial examination according to centripetal approach showed changes in the external circle, with moderate volume loss in the zygomatic-temporal and midface areas and an irregular mandibular outline. The median circle resulted altered as well, with evident tear trough, naso-labial folds and laxity in the peri-labial area.

Figure 3

Figure 3 - Case #1 before treatment (left) and after 1 month (right).
Courtesy: Dr. Rosalba Russo

Emervel Volume was injected in the zygomatic and malar areas (1.0 ml/side) while Emervel Deep was injected to enhance the jaws (0.5/side). The loss of tissue in the temporal and pre-auricular areas was restored by injecting Emervel Classic (0.5 ml per side).

Figure 3 shows the significant restoration of the oval facial harmony at 1 month after treatment.

Case #2

Figure 4

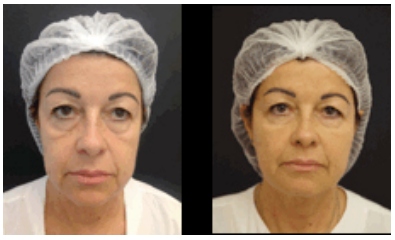


Figure 4 - Case #2 before treatment (left) and after 1 month (right).
Courtesy: Dr. Rosalba Russo

A 53 years Caucasian woman presented Glogau grade III facial aging.

The lower third appeared hypertrophic, with imbalanced volumes if compared with the other two thirds, due to previous aesthetic treatments carried out only in the lower third by other practitioners.

A significant deflation of the midface area with severe evidence of the tear trough and naso-labial folds was observed at the clinical evaluation. The mandibular outline was poorly defined.

The zygomatic and pre-auricular areas and the mandibular outline were treated with Emervel Volume (1.0 ml/side). Afterwards, an injection with Emervel Deep (1.0 ml/ side) was performed in the malar area and in the tear trough.

After one month, an excellent balance between the

upper and lower face was achieved, with an oval shape restoration and a significant refreshed and younger appearance (Figure 4).

Case #3

Figure 5

Figure 5 - Case #3 before treatment (left) and after 1 month (right).
Courtesy: Dr. Rosalba Russo

A 53 years Caucasian man presented with Glogau grade III facial aging. The patient displayed a moderate deflation in the left zygomatic-malar area subsequent to a previous trauma due to a car accident. He had successfully completed a dietetic regime, with significant weight loss also involving the facial adipose panniculus.

The asymmetry in the zygomatic-malar area was successfully balanced by injecting Emervel Volume (0.5 ml per side). The jawline and the mandibular angle were injected with Restylane Perlane (1.0 ml per side).

After one month, the patient regained satisfactory facial symmetry and subcutaneous volume. The face appeared refreshed and relaxed (Figure 5).

Case #4

Figure 6

Figure 6 - Case #4 before treatment (left) and after 6 months (right).
Courtesy: Dr. Francesca de Angelis

A 43 years Caucasian woman presented with Glogau grade III facial aging. Skin color appeared inhomogeneous and skin texture thickened. The overall oval facial contour was uneven, in particular the temple area was flat and the jawline showed sagging skin and an excess of envelop. Volume deflation in the midface made the tear trough more evident and gave a tired look.

A treatment plan based on 3 alternative monthly session with Restylane Skinboosters and non ablative laser was the first step in order to improve skin condition. Then, a centripetal approach was applied for treating with fillers.

Emervel Classic (0.5 ml/side) was injected in the temple area through cannula; since bone structure and tissue quality were well represented, Restylane Perlane (0.3 ml/side) was injected into the deep fat compartment of the midface and to define the jawline and the mandibular angle (0.5 ml/side). Emervel Lips (0.8 ml) was injected into the lips to enhance vermillion shape. Improvement of parotid area and marionette lines was obtained by Emervel Classic and residual fine lines around the perioral area were treated with Emervel Touch. Naso-labial folds were not injected at all.

Figure 6 shows the dramatic improvement of overall facial appearance after 6 months. The oval face appeared restored, skin quality significantly improved in color, luminosity and tissue compactness.

A refreshed an harmonious look was achieved with a global effect of facial rejuvenation and high patient's satisfaction.

Case #5

Figure 7

Figure 7 - Case #5 before treatment (left) and after 6 months (right).
Courtesy: Dr. Francesca de Angelis

A 48 years Caucasian woman presented with Glogau grade IV facial aging. Dynamic wrinkles of moderate severity were evident at rest. The oval facial contour was altered by a flat temporal area and poor definition of mandibular angle and jawline. Volume deflation in the midface and parotid area were also evident providing a senescent looking appearance.

A treatment plan based on 3 monthly session with Restylane Skinboosters was followed by one session of ablative laser to improve skin condition. After 1 month from the laser treatment, fillers were injected to recover the three-dimensional oval contour by approaching centripetally. Emervel Classic (0.5 ml/side) was injected in the temporal area to restore volume loss. Emervel Deep was injected to restore volume in the parotid area and to define the jawline (0.5 ml/side). The deep medial zygomatic compartment was projected by injecting Emervel Deep (0.5 ml/side). In this patient Emervel Deep was preferred to Restylane Perlane, since the bone structure was poorly represented. Emervel Lips (1.0 ml) was injected into the lips and lip contour to enhance vermillion shape. Naso-labial folds were not injected at all. Figure 7 shows the significant facial rejuvenation obtained and still lasting at 6 months.

Skin condition and fine lines improvement

Whenever an aesthetic treatment is carried out, the practitioner should always examine skin condition and set up strategies to improve and prevent skin aging signs, such as fine lines, elasticity, roughness and other skin defects, i.e. acne scars (Figures 8a and 8b)[28-30].

In our experience we complement any filler treatment with Restylane Skinboosters, a softer form of NASHA gel specifically designed to progressively improve skin condition. We inject microdroplets of skinboosters into the deep dermis all over the sun exposed skin areas (face, neck and décolletage, as well as dorsal hands). A treatment plan based on 3 monthly sessions, starting 1-2 months before filler treatments, is recommended. Finally, Emervel Touch is the best option to refine residual fine lines all over the face, such as periocular, forehead and perioral lines.

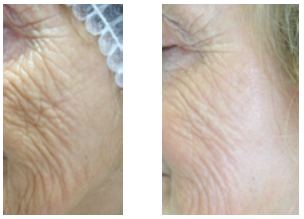


Figure 8a

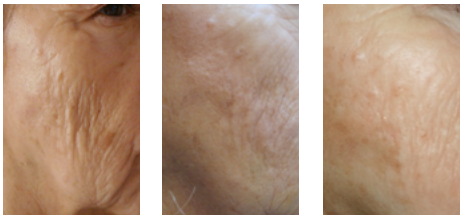


Figure 8b

Figures 8a and 8b - Skin condition improvement achieved after 3 monthly sessions of Restylane Skinboosters (2 ml/session) in two female patients affected by severe skin facial aging. The pictures are taken 30 days after the 3rd session. Courtesy of Dr. Magda Belmontesi

Discussion and Conclusions

Basing on this approach, the face is sub-divided into concentric circles during the diagnostic evaluation. This approach is ideal for better identifying the most suitable fillers for treating different facial areas, according to individual needs and tissue characteristics[9,15].

The amount of gel used in each session was moderate, in fact an average of 3.5 ml was adequate to reach optimal results. In our experience, 98% of patients reported from high to moderate satisfaction level. In particular, 80% of them considered the outcome more harmonious and natural compared to previous aesthetic treatments. Only 1 out of 50 treated patients reported unchanged satisfactory results compared to other past treatments.

Authors' recommendations when following this approach is the knowledge of anatomy, with particular reference to the areas of temples (external circle) and other advanced treatment areas (tear trough). No serious adverse events were reported in our experience. Only 2 patients reported monolateral recurrent swelling and pain in the infraorbital area for one month.

The availability of a broad spectrum of different viscoelastic properties as displayed for NASHA and Optimal Balance Technologies gels make possible to balance the three dimensional facial harmony by injecting them at both superficial and deep levels, with predictable and long lasting results[10,17-27].

This significant versatility opened the way to an innovative approach to aesthetic facial treatments, which we have called "centripetal approach".

The basis of the centripetal approach is the concept that facial beauty is associated with an ideal oval shape and specific geometrical characteristics[2].

In conclusion, the centripetal approach should become a useful tool in helping practitioners to assess the patient's face, enhance options for discussion with patients and promote indications for logical aesthetic treatments. The availability of a broad range of HA textures together with a well characterized efficacy and safety profile are key factors to predictable and satisfactory results.

References

1. Sands NB, Adamson PA. Global facial beauty: approaching a unified aesthetic ideal. *Facial Plast Surg.* 2014; 30(2):93-100.
2. Goodman GJ. The oval female facial shape- A study in beauty. *Dermatol Surg.* 2015; 41(12):1375-83.
3. Baudouin JY, Tiberghien G. Symmetry, averageness, and feature size in the facial attractiveness of women. *Acta Psychol (Amst).* 2004; 117(3):313-32.
4. Komori M, Kawamura S, Ishihara S. Averageness or symmetry: which is more important for facial attractiveness? *Acta Psychol (Amst).* 2009; 131(2):136-42.
5. Shetty R. Outer Circle Versus Inner Circle: Special Considerations While Rejuvenating an Indian Face Using Fillers. *J Cutan Aesthet Surg.* 2015; 8(3):169-172.
6. Ramanadham SR, Rohrich RJ. Newer understanding of specific anatomic targets in the aging face as applied to injectables: superficial and deep facial fat compartments – an evolving target for site-specific facial augmentation. *Plast Reconstr Surg.* 2015; 136(5 Suppl):49S-55S.
7. Milutinovic J, Zelic K, Nedeljkovic N. Evaluation of facial beauty using anthropometric proportions. *ScientificWorldJournal.* 2014; 2014:428250.
8. Pallett PM, Link S, Lee K. New "golden" ratios for facial beauty. *Vision Res.* 2010; 50(2):149-54.

9. Fahri D, Essayagh E, Brunet H, et al. Sélectionner un acide hyaluronique injectable pour chaque zone du visage: un consensus d'experts. *J Méd Esth et Chir Derm.* 2015; 167(42):185-194.
10. Cohen JL, Dayan SH, Brandt FS, et al. Systematic review of clinical trials of small- and large-gel-particle hyaluronic acid injectable fillers for aesthetic soft tissue augmentation. *Dermatol Surg.* 2013; 39(2):205-31.
11. Smith KC. Reversible vs. nonreversible fillers in facial aesthetics: concerns and considerations. *Dermatol Online J.* 2008; 14(8):3.
12. Rzany B, Cartier H, Kestemont P, et al. Full-face rejuvenation using a range of hyaluronic acid fillers: efficacy, safety, and patient satisfaction over 6 months. *Dermatol Surg.* 2012; 38 (7 Pt 2): 1153-61.
13. Sundaram H, Cassuto D. Biophysical characteristics of hyaluronic acid soft-tissue fillers and their relevance to aesthetic applications. *Plast Reconstr Surg.* 2013; 132(4 Suppl 2):5S-21S.
14. Salles AG. Discussion: juvéderm volbella with lidocaine for lip and perioral enhancement: a prospective, randomized, controlled trial. *Plastic Reconstr Surg Global Open.* 2015; 3:e322.
15. Segura S, Anthonioz L, Fuchez F, Herbage B. A complete range of hyaluronic acid filler with distinctive physical properties specifically designed for optimal tissue adaptation. *J Drugs Dermatol.* 2012; 11(1 Suppl):s5-8.
16. Edsman K, Nord LI, Ohrlund A, Lärkner H, Kenne AH. Gel Properties of Hyaluronic Acid Dermal Fillers. *Dermatol Surg.* 2012; 38(7 Pt 2):1170-1179.
17. Narins R, Dayan S, Brandt F, Baldwin E. Persistance and improvement of naso-labial fold correction with non animal-stabilized hyaluronic acid 100,000 gel particles/mL filler on two retreatment schedules:results up to 18 months on two retreatment schedules. *Dermatol Surg.* 2008; 34 Suppl 1:S2-S8.
18. Narins RS, Brandt FS, Dayan SH, Hornfeldt C. Persistence of nasolabial fold correction with a hyaluronic acid dermal filler with retreatment: results of an 18-month extension study. *Dermatol Surg.* 2011; 37(5): 644-650.
19. Brandt F, Bank D, Cross SL, Weiss R. A lidocaine-containing formulation of large-gel particle hyaluronic acid alleviates pain. *Dermatol Surg.* 2010; 36 Suppl 3:1876-85.
20. Taylor SC, Burgess CM, Callender VD. Safety of nonanimal stabilized hyaluronic acid dermal fillers in patients with skin of color: a randomized, evaluator-blinded comparative trial. *Dermatol Surg.* 2009; 35 Suppl 2:1653-60.
21. Hamilton RG, Strobos J, Adkinson NF. Immunogenicity studies of cosmetically administered nonanimal-stabilized hyaluronic acid particles. *Dermatol Surg.* 2007; 33 Suppl 2:S176-85.
22. Glogau RG, Kane MA. Effect of injection techniques on the rate of local adverse events in patients implanted with nonanimal hyaluronic acid gel dermal fillers. *Dermatol Surg.* 2008; 34 Suppl 1:S105-9.
23. Dover JS, Rubin MG, Bhatia AC. Review of the efficacy, durability, and safety data of two nonanimal stabilized hyaluronic acid fillers from a prospective, randomized, comparative, multicenter study. *Dermatol Surg.* 2009; 35 Suppl 1:322-30.
24. Rzany Bayerl C, Bodokh I, et al. Efficacy and safety of a new hyaluronic acid dermal filler in the treatment of moderate nasolabial folds: 6-month interim results of a randomized, evaluator-blinded, intra-individual comparison study. *J Cosmet Laser Ther.* 2011; 13(3):107-12.
25. Ascher B, Bayerl C, Brun P, et al. Efficacy and safety of a new hyaluronic acid dermal filler in the treatment of severe nasolabial lines - 6-month interim results of a randomized, evaluator-blinded, intra-individual comparison study. *J Cosmet Dermatol.* 2011;10(2):94-8.
26. Talarico S, Meski AP, Buratini L, et al. High patient satisfaction of a hyaluronic acid filler producing enduring full-facial volume restoration: an 18-month open multicenter study. *Dermatol Surg.* 2015; 41(12):1361-1369.
27. Salti G, Rauso R. Facial rejuvenation with fillers: the dual plane technique. *J Cutan Aesthet Surg.* 2015; 8(3): 127-133.
28. Kerscher M Bayrhammer J, Reuther T. Rejuvenating influence of a stabilized hyaluronic acidi-based gel of nonanimal origin on facial skin aging. *Dermatol Surg.* 2008; 34(5):720-6.
29. Williams S, Tamburic S, Stensvik H, Weber M. Changes in skin physiology and clinical appearance after microdloplet placement of hyaluronic acid in aging hands. *J Cosmet Dermatol.* 2009; 8(3): 216-25.
30. Gubanova EI, Starovatova PA, Rodina MY. 12-month Effects of Stabilized Hyaluronic Acid Gel Compared With Saline for Rejuvenation of Aging Hands. *J Drugs Dermatol.* 2015;14 (3): 288-295.

Aesthetic Medicine
Volume 2 · Number 1 · January-March 2016

New technologies for the prevention and treatment of empty nose syndrome: minimally invasive and regenerative surgery with PRL

Lino Di Rienzo Businco[1], Alessia Di Mario[2], Mario Tombolini[2], Salvatore Laurino[3], Domenico Crescenzi[3], Marco Radici[4]

[1]ORL Service, S. Spirito Hospital, Casa di cura Santo Volto, Rome, Italy
[2]ORL Service, Policlinico Umberto I, Sapienza, Università degli studi di Roma, Italy
[3]ORL Service, Carcassonne Hospital, Tolouse, France
[4]ORL Service, Fatebenefratelli Hospital, Rome, Italy

ABSTRACT

Background: Empty nose syndrome (ENS) is a devastating complication of turbinate surgery. The management of ENS is challenging and the evidence base for most treatment modalities remains low. In the present study we propose a safe and effective surgical reconstruction treatment based on the use of Platelet Rich Lipotransfert (PRL). The PRL is a preparation rich in stem cells and growth factors, taken from the same patient, that has the potential capability to regenerate the volume of the turbinate and to restore the functionality of the mucosa.

Methodology: 46 patients randomly divided in two groups: one group treated with PRL and the other one with medical treatment alone. The aim of the study was to compare the safety and efficacy of the PRL for the treatment of ENS in comparison with medical treatment alone.

Results: Both procedures had no collateral effects but only patients treated with PRL showed a statistically significant improvement ($p<0.05$) in the subjective nasal symptoms and the endoscopic nasal objectivity after surgery.

Conclusions: Turbinate reconstruction with PRL is a safe, simple and effective procedure characterized by a very low invasiveness with easy availability to autologous biological tissue and no collateral effects.

Keywords
Empty nose syndrome, turbinate, stem cells, atrophic rhinitis, Platelet Rich Lipotransfert (PRL)

Disclosure information
the authors state to have no actual or potential conflict of interest in relation to this paper. They didn't receive funds (grants, consulted fees, honorarium, travel reimbursements, medicines, equipment, or administrative support) from a third party to support the work (such as government granting agency, charitable foundation or commercial sponsor).

Correspondence
Lino Di Rienzo Businco
E-mail: ldirienzo@businco.net

Accepted for publication 7 January 2016

Introduction

Surgery for turbinate hypertrophy is very common and represents the eighth most frequent procedure employed in the otolaryngological field[1].

Over years numerous surgery techniques for the treatment of inferior turbinate hypertrophy have been proposed, in which the principle problem was to increase the nasal airflow preserving the functions of the mucosal lining, location of important protective activity and of pharmaceutical drug absorption useful in the long term postoperative treatment of submucosal membrane inflammation (turbinectomy, submucosal membrane extraction with or without debrider, cryocoagulation, mono or bipolar electrocauterization, Laser CO_2 and diode, radiofrequencies, coblator, molecular quantum resonance)[1,2].

Before the diffusion of turbinate shrinkage mini-invasive techniques without thermal damage, many of the former techniques (in particular those using high temperatures with electrosurgical knife and those extremely demolitive with scissors with partial or complete amputations of the turbinate, though they guaranteed an apparent increase of the nasal airflow and a reduction of air resistance to rhinomanometry) were accompanied by a loss of nasal sensitiveness and by the paradoxical reduction of the perception of the air passage with the damage of the mucosal nervous receptors of intranasal anatomy and of the mucosa itself, and by the production of aerial vortices with secondary atrophic rhinitis leading to real Empty Nose Syndromes (ENS) with crusting, bleeding and synechiae, with a strong negative impact on the quality of the patient's life[1,3,4]. ENS, described for the first time by Kern and Stenkvist in 1994, is a rare and highly debilitating pathology, and fortunately not all patients subjected to demolitive surgical intervention on turbinates (inferior or middle) develop this syndrome[5,6]. However, when ENS occurs (this may happen after months or years from demolition surgery), its symptoms strongly reduce the quality of life, and they can be summarized in: intranasal mucosal dryness, paradoxical nasal breathing obstruction (notwithstanding the large intranasal airspace), facial pains, cephalea, crusting and altered nasal discharge, with a variability of clinical manifestations which differ according to patient[5,7].

In these cases of iatrogenic damage with ENS and secondary atrophic rhinitis, the medical therapy (antihistamines, steroids, specific nasal immunotherapy, nasal wash solutions) prove themselves invariably insufficient to resolve the symptoms of nasal obstruction and inflammations of the patient, with the quality of life considerably reduced and with few possibilities on the doctor's part to improve the local nasal clinical history casefile[8,9].

Even the usual examination tools employed for the evaluation of nasal patency (rhinomanometry, acoustic rhinometry, peak nasal inspiratory flow) are unable to correlate with the clinical symptoms of patients as they do not investigate the physiological mechanisms of the subjective perception of the intranasal airflow (the activation of TRPM8 receptors determines the perception of the passage of air from the nose)[9,10].

Various world specialists have tried to identify a reconstructive surgical technique capable of improving the symptoms of ENS, with encouraging yet partial results; Rice and Di Rienzo Businco with the use of hyaluronic acid[11,12], Yong with inferolateral endonasal cartilage implants[13], and Papay with his fibromuscular temporalis graft implantation[14], but these techniques reveal problems with the reabsorption of the substance used in reconstruction over time. Those problems have been overcome by Jiang with Medpor's implants which is resolute regarding the volume loss but with scarce effectiveness on the recovery of mucosal functionality[15] and by Modrznski with submucosal injections of hydroxyapatite on the turbinate and septum[16]. Also, the studies of AlloDerm (acellular dermal matrix) was proposed by Saafan as having a greater efficacy with respect to silastic implants, yet with partial results when compared with a relatively invasive surgical technique[17].

For some years, plasma enriched with platelets, Platelet Rich Plasma (PRP) have been extensively employed in medicine and surgery for their properties to stimulate an efficient regeneration of both soft tissue and bone tissue (better scar healing and with a reduction in postoperative infections, pain and blood loss) leading these blood components to be routinely used in various branches of surgery and medicine[18,19]. The widespread use of platelet derivatives has certainly proved favourable in their efficacy, combined with an extreme easiness of use and not least in the absence of adverse reactions.

Adipose tissue has likewise been the object of great attention these years, for its regenerative potential (above all Stromal Vascular Fraction SVF, Adipose Stem Cells ASC), developed to return volume and functionality, especially in plastic surgery[20,21,22,23]. Based on these assumptions, our aim was to verify the efficacy and safety of a new and simple endoscopic infiltrative technique for the reconstruction in patients affected with ENS, of atrophic turbinates and partially amputated, in that they had been coagulated or resected by previous nasal surgery, in addition to a topical medical treatment based on thermal water cleansing and a humidifying vitamin unguent. Such a reconstructive endoscopic surgical technique, different from other methodologies as described in previously published literature which entail intranasal cutting and more invasive implants, is based on the simple injective proceedings in locations of resected turbinates, of PRP mixed with autologous fat[21] taken from a periumbilical extraction (Platelet Rich Lipotransfert - PRL). The fat was purified utilizing Coleman's technique[24,25], and the mixture of PRL thus attained was injected

endoscopically into a group of ENS affected patients, comparing the functional results with a group checked with ENS undergoing sole medical therapy.

Our aim was to compare the variations of clinical-instrumental parameters and symptoms from the beginning to the end of the treatments - dividing patients into two groups of study, the first (group A), with sole medical pharmaceutical therapy and the second (group B) with the same medical therapy to which was added an endoscopic treatment with PRL on inferior turbinate regions previously amputated.

Materials and methods

For the study, 46 patients (39 male) with an age of above 18 years were enrolled consecutively (table 1), following a complete ORL evaluation with physical clinical examination, endoscopy, ConeBeam CT scan of paranasal sinuses, allergy evaluation and SNOT-22 questionnaire, undergoing more than 3 years of treatment in other centres, to turbinectomy or electrocauterization operations of the inferior turbinates owing to their hypertrophy with consequent ENS results (ENS-IT according to the Houser classification)[5]. The ENS diagnosis was supported by the Houser test, which consisted in positioning a pledget soaked in a saline solution in the nasal cavity of patients for 20-30 minutes, revealing their subjective improvement from obstructive symptoms[5].

The criteria for patient inclusion in the study were: failure in every precedent medical test carried out, obstructive nasal symptoms to the VAS greater than 5 (min. 0 – max. 10), and documented resection of the inferior turbinates for a surface equal to or greater than 50% of the endoscopic examination and CT. For the evaluation of damage from inferior turbinate resections our compartmental turbinate classification was utilized so as to objectively quantify the location and the amputated section (Figures 1,2)[1]. Patients with a previous history of cocaine abuse, coagulopathy, grave systemic or infective diseases and neoplastic pathologies were excluded from the study. All patients signed the informed consent and the study received approval from the local ethics committee.

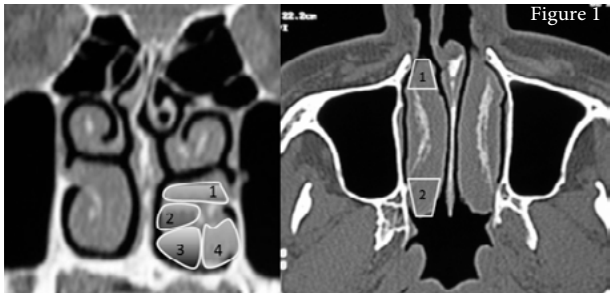


Figure 1 - Compartmental classification of the inferior turbinates. On the right: 1 Superior, 2 Middle, 3 Inferior, 4 Infero-lateral. On the left: 1 Anterior, 2 Posterior

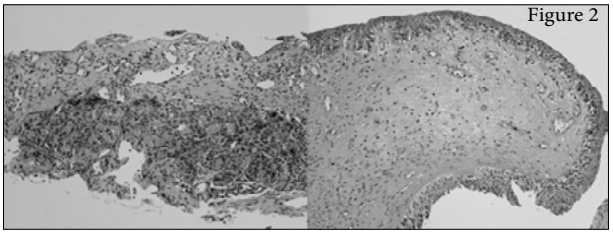


Figure 2 - On the right: Turbinate mucosa after turbinectomy (Ematossilina-Eosina). On the left: Turbinate mucosa after PRL (Ematossilina-Eosina)

Study design

The patients were assigned alternately to two groups, A and B (A: checkup, medical therapy only; B: medical therapy and surgical reconstruction treatment) with each containing 23 patients. The assigning of patients to be subjected to treatment A or B was obtained by a random sequence of computer generated numbers. The medical treatment was based on the administration of an intranasal spray with a solution of salt-bromine-iodine thermal water (3 spurts per nostril 3 times daily) together with the nightly application of a nasal unguent based on vitamins (vitamins E, A, D-panthenol). Group B patients, before medical therapy, were subjected to an endoscopic reconstruction of inferior turbinates with PRP mixed with autologous fat (PRL). Both groups were requested to note any collateral effect that presented itself during the course of the study.

Preparation of PRP

The preparation process consisted of 3 phases: hemal extraction, centrifugation to obtain a concentrated platelet and activation[26]. Following hemal extraction from a peripheral vein, some sodium citrate as an anticoagulant was added to the blood (system of RegenLab, Le Mon-sur-Lausanne, Switzerland). The method of manual PRP preparation consists in a calibrated centrifugation of 1500 rpm for a total of 10 minutes which allowed the platelet to remain in suspension with the plasma while the leucocytes and erythrocytes settled on the bottom of the test tube. After the centrifugation the platelet and leukocyte buffy coat were extracted with 9ml of plasma[21]. Calcium chloride was added to the PRP as thus obtained to activate the platelet and stimulate the secretions of growth factors with emiocytosis of alpha granules. The quantity of calcium chloride added is equal to the 10% of the amounts of PRP produced.

Preparation of fat

The purified fat was obtained after the transumbilical extraction with lipoaspiration microtubes (1.5mm in diameter) via centrifugation for 3 minutes at 3000 rpm (Coleman's technique) and

inserted aseptically into a syringe of 1ml mixed with PRP. This procedure allowed a purified fat preserving the adipocytes in their entirety to be obtained, while separating the fluid components from those serosanguineous[24,25].

Procedure

Group B patients undergoing treatment were prepared 15 minutes before the reconstruction of turbinates with local anesthesia for mucosal contact with a cotton substance soaked in Lidocaine located along the full length of the inferior meatus. A nasal endoscope of 3mm 0° (Karl Storz, Tuttlingen, Germany) was used for a selective infiltration of turbinate compartments under endoscopic guidance. The PRL solution was injected, after their endoscopic identification, in the sites of previous cauterization regions or amputations of the previously tested turbinates with the positioning of pledgets soaked in a saline solution (Houser's test), via a syringe of 5ml with a spinal needle of 22G of 90mm. The procedure did not determine significant bleeding, with exceptions made for a modest quantity from the injection site (drops), which never required either nasal tamponing or suspension of the procedure.

Clinical evaluation

At the beginning of the study (T_0), every patient was requested to indicate the seriousness of subjective nasal symptoms on a VAS scale (0 min. -10 max.) (nasal obstruction, nasal discharge, sneezing, itching, pain). All patients were required to complete the SNOT-22 questionnaire before and after the treatment and the results were confirmed with regard to the five most important questions. All patients underwent a basal anterior rhinomanometry (AAR) to evaluate their nasal resistance (Rhinomanometer Labat srl, Treviso, Italy) during the day. In accordance with the International Committee on Standardization of Rhinomanometry, the nasal airflow resistance was measured using a standard pressure (150 Pa) and the total nasal resistance was calculated by rhinomanometric monolateral registrations[27]. The AAR measuring was not carried out in the case the patient was affected by a common acute cold or a nasal allergy crisis, postponing the measuring to the end of the acute phase. The AAR measuring was performed on a seated patient after a 15-minute period of room acclimatization, in standard conditions of temperature and humidity.

Each patient was assigned a rhinoendoscopic score with a 1-4 increasing gravity after at least one month of abstinence from medical therapy, carried out at the beginning and at the end of the study based on the evaluation (performed by the same examiner) of the volume of the nasal crusting in relation to the respiratory obstacle (from 1: flat crusting on the mucosal surface, minimally obstructing the respiratory lumen, to 4: bridge crusting between the nasal wall and completely obstructing septum). In order to obtain a functional piece of data on the nasal mucosal state in both groups under study, the Mucociliary Transport Time (MCTt) was calculated, before and after the treatment. All patients were subjected to MCTt nasal evaluation, using a vegetable carbon powder and saccharin mixture of 3%. The MCTt was calculated as the time interval between the moment in which the powder was positioned on the head of the inferior turbinate (anterior compartment) up to when a stripe of the same powder appeared in the oropharynx during the direct pharyngoscopic examination[28]. The clearance time for saccharin was instead calculated by taking the end of the test into consideration when the patient detected a sweet taste in the mouth. All evaluations and tests were repeated and compared with those basal ones after 12 months of treatment for both groups in the study. It was possible after more than 1 year of treatment in 3 patients from group B, to carry out a biopsy for histologic examinations of the region of the turbinate reconstructed with PRL in the course of other operations carried out for different reasons other than those of the nose. The sections of the turbinate mucosa of 5µm were prepared according to standard procedure after the inclusion of paraffin and after being stained with hematoxylin-eosin.

Statistical analysis

The value P (Student test, with statistical significance for $p < 0.05$) was utilized for all subjective and objective parameters. The statistical analysis was undertaken with SPSS (software package for statistical analysis) version 17.0 (Chicago, IL, USA).

Results

The study included 46 patients aged between 32-67 (Tables 1,2). The medical therapy did not determine any collateral effects in any of the patients from either group in the study. Patients from group B did not report pain during or after the procedure, with the exception made for few sporadic cases of nasal burns and minimal discharge mixed with blood after nose-blowing, for which paracetamol when required (500mg tablets) was prescribed in the postoperative period without any adverse consequences reported.

In particular, no cases of epistaxis, nor any general or local complications in the nasal sites treated with PRL (synechiae, crusting formation) were found.

The area of umbilical fat removal was healed without residue and the stitching (nylon 5-0) was removed in 5-7 postoperative days. With regard to the subjective nasal symptoms and the endoscopic nasal objectivity (Figures 3a-b, 4a-b), when compared with the after treatment, a statistically significant

improvement in group B ($p<0.05$) was noted (Table 3). Concerning the objective rhinomanometric evaluation when compared to post-treatment, a trend similar to what had been observed in subjective nasal symptoms was noted, with an improvement in favour of group B that had been treated with PRL ($p<0.05$) (Table 4).

The comparative results between the two groups A and B of MCTt have shown a statistically notable variation revealing a greater efficacy of the treatment with PRL compared with that sole medical one in the improvement in the mucociliary function (Table 4). The comparison between groups A and B before and after treatment according to the SNOT-22 questionnaire with regard to the most important 5 questions, showed an improvement for both groups under study but with more favourable efficacy results for group B (Table 5).

	Group A (n=23)	Group B (n=23)	p-Value
Age (years)	39.3 ±2.02	42.5 ±2.08	p-0.05
Sex			
Male	18(82.6%)	20(86.9%)	p-0.05
Female	5(17.4%)	3(13.1%)	

Table 1 - Patients demographics data

	Group A (n=23)	Group B (n=23)	p-Value
Nasal Obstruction (Mean ± SD)	9.19 ± 0.75	9.43 ± 0.71	P>0.05
Itch	7.19 ± 1.15	8.11 ± 0.98	p>0.05
Rhinorrhea	9.32 ± 1.10	9.45 ± 0.93	p>0.05
Sneezing	7.21 ± 1.12	7.50 ± 1.21	p>0.05
Pain	7.91 ± 1.11	7.60 ± 1.31	p>0.05
Clinic/Rhino-endoscopic Score			
1	0	0	p>0.05
2	3(13.1%)	3(13.2%)	
3	9(39.1%)	10(43.4%)	
4	11(47.8%)	10(43.4%)	

Table 2 - Comparison between VAS and rhinoendoscopic score before treatment

	Control A (n=23)	Treatment B (n=23)	p-Value
Nasal Obstruction (Mean ± SD)	7.15 ± 0.65	4.49 ± 0.61	P<0.05
Itch	6.11 ± 1.10	5.10 ± 0.78	p<0.05
Rhinorrhea	7.82 ± 0.60	5.35 ± 0.43	p<0.05
Sneezing	6.10 ± 1.11	5.20 ± 1.11	p<0.05
Pain	6.11 ± 1.10	4.90 ± 1.11	p<0.05
Clinic/Rhino-endoscopic Score			
1	0	10(43.4%)	p<0.05
2	4(17.4%)	13(56.6%)	
3	15(65.2%)	0	
4	4(17.4%)	0	

Table 3 - Comparison of the results after treatment

	Gr A	Gr B
AAR	1.23 ± 0.04 Pa/cc3/sec	1.11 ± 0.05 Pa/cc3/sec
MCTt	20.9 ± 2 min	21.45 ± 2 min
Pre-treatment		
	Gr A	Gr B
AAR	1.08 ± 0.06 Pa/cc3/sec	0.57 ± 0.03 Pa/cc3/sec
MCTt	17.56 ± 2 min	14.5 ± 2 min
Post-treatment (difference between groups p<0.05)		

Table 4 - Comparison between AAR and MCTt pre and post-treatment

	Gr A	Gr B
5 most important questions (mean)	24.2	23.3
Pre-treatment		
	Gr A	Gr B
5 most important questions (mean)	16.2	10.8
Post-treatment (difference between groups p<0.05)		

Table 5 - Comparison of SNOT-22 for the 5 most important questions pre an post-treatment (mean)

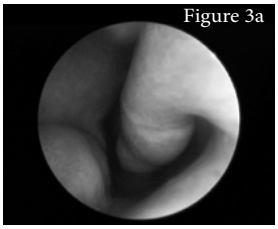


Figure 3a - Pre-treatment

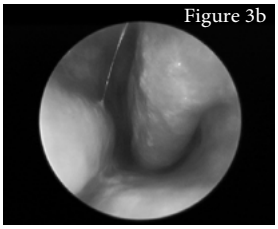


Figure 3b - Post-PRL

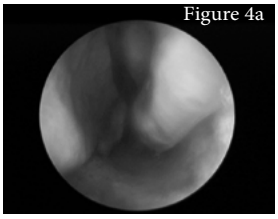


Figure 4a - Pre-treatment

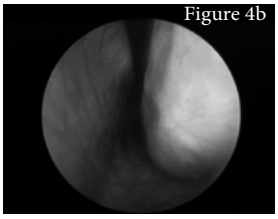


Figure 4b - Post-PRL

Histologic evaluations

According to the results of previous histologic experiences of the efficacy of PRP in animal and human studies, in the samples of our examined patients we have observed a satisfactory reconstruction of the mucosa and submucosa of the turbinate after 12 months from the treatment with PRL compared with the preoperative checkup (Figures 5,6)[29,30].

Particularly the almost complete reepithelialization of the mucosal surface of the turbinate and the reduction of the inflammatory part of the submucosa have been observed in the areas subjected to a reconstruction with PRL.

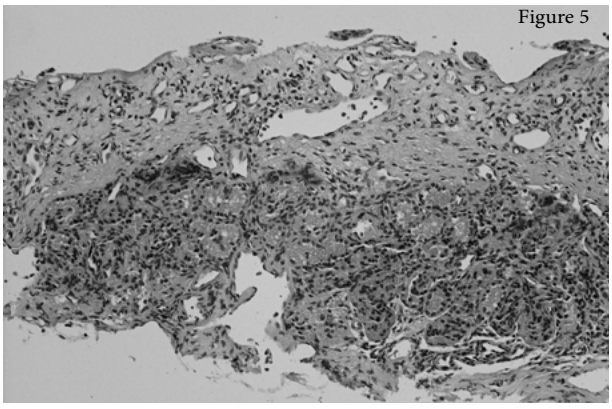


Figure 5 - Turbinate mucosa after turbinectomy (Ematossilina-Eosina)

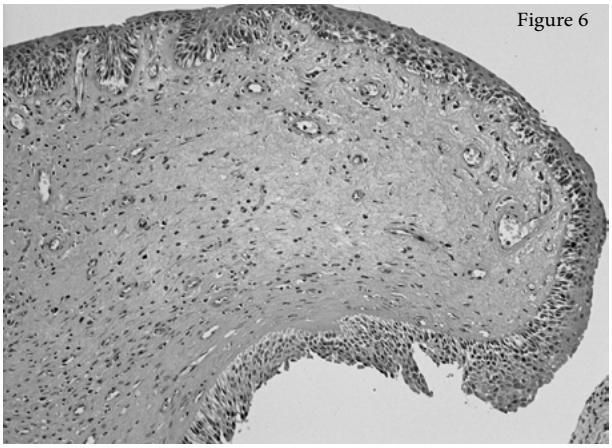


Figure 6 - Turbinate mucosa after PRL (Ematossilina-Eosina)

Conclusions

The results allow us to conclude a greater efficacy of both medical therapy and infiltrative treatment with PRL, compared to the sole medical therapy in order to check the signs and symptoms of ENS-IT with the subtotal amputation of the inferior turbinates. With regard to the nasal symptoms VAS evaluated, a greater efficacy has been shown in the checkup of the group of patients following treatment B. In particular the patients who received the treatment with PRL showed better objective parameters (RAA, endoscopic score) and with the SNOT-22, when compared to the group following the sole medical therapy. The improvement (at RAA) of group B, appears to be due to the smaller quantity of intranasal crusting and consequently better air canalization in the patients treated with PRL. The results of the evaluation of MCTt document an improvement of the function of the mucosal surfaces of the turbinate after the reconstruction with PRL, which is very notable in a category of patients affected by ENS where the damage of the mucociliary clearance together with the mucosal atrophy represents the main invalidating pathogenic moment of the quality of life owing to the continuous formation and crusting stasis in the nasal cavity. In our experience, the association of PRL has resulted in being one of the key points to the efficacy of the reconstructive treatment in terms of restoring functionality, since the mixed components together contributed to the recovery both of the volume and the specific-site functionalities of the damaged or amputated nasal regions. It is possible to hypothesize that on the basis of the favourable results obtained there is a restoration of regional neovascularization where there has been a volumetric site-specific increase, which together with the regenerative powers of platelet growth factors (GF) have led to an objective

and symptomatological improvement[31,32,33]. The surgical technique also showed itself to be extremely simple both rhinosurgically and for the extraction of the periumbilical fat, but above all, in accordance with previously published literature, without the collateral effects[34] and discomfort for the patient. The surgical approach we have described, with endoscopic technique and compartmental evaluation of the treated turbinate undersurface, allows a greater homogeneity of the classification of ENS-IT damage, together with a better evaluation of the obtained results after a certain period, with the presupposed essential sharing of clinical data among different centres and in order to guarantee the reproducibility of the methodology. Such a repair operation has been characterized by a very low invasiveness with a rapid postoperative period (day surgery) with easy availability to autologous biological tissue without the necessity of using other tissue from other anatomic sites as reported by other authors using different methodologies (nasal mucosa, muscular band, osteo-cartilaginous flaps, etc), and, above all, with no collateral effects. The basis of this regenerative surgery is represented by 3 elements: growth factors contained in a platelet gel, stem cells taken from adipose tissue (mixed with the PRP to obtain the PRL) and the biomaterials of synthesis (hyaluronic acid, collagen). The hematostatic capacity of platelets and their complex action mechanism (more than 300 proteins) is well-known, but only recently, owing to the progress of molecular biology could we minutely understand the different mechanisms which induced growth factors. Once activated, platelets release the growth factors contained in the alpha granules which are able to perform specific functions in the cell regeneration and in the development of the tissue where they have been liberated. The PRP contains different typologies of GF (isomers of the platelet GF transforming GF β1 and β2, GF insulin α and β, vascular endothelial GF) able to promote bone regeneration and to induce the differentiation of pluripotent cells. The GFs act as activation signals to attract stem cells to the damage site and are contemporarily able to induce their proliferation. The action of GF on the osteoblasts is, for example, able to induce mitosis and to stimulate the migration of the mesenchymal cell progenitors. A notable aspect for its practical implication, is how the chemotactic and mitogenic stimulus of PRP on mesenchymal stem cells is able to determine the best reconstitution and regeneration of the damaged tissue in a directly proportional way with the platelet concentration (dose-dependent efficacy)[18,29,30,23]. The clinical effects of the PRP[35,36] on the implanted tissue can be summarized in a biostimulation with:

- cellular proliferation
- bioreparative and regenerative processes
- angiogenesis and revascularization of tissue
- proliferation of mesenchymal cells
- production of fibroblasts
- production of collagen

The clinical experience in the field of regenerative nasal surgery has shown a greater efficacy in the processes of the mucosal regeneration and its functionality with the activation of cellular proliferation and gain of volume. The reconstruction of the inferior turbinates with PRL associated with the topical medical therapies of washing and of using an emollient, has proved to be better in a statistically notable way, compared to the group receiving only medication,improving the subjective nasal symptoms and objective rhinoendoscopic observations in a group of patients affected by ENS, particularly noting an improvement in the quality of the patient's life concerning the nasal complaints measured by using SNOT-22.

In conclusion, regenerative surgery in the nasal districts aims towards the more promising possibility of mini-invasive solutions of many problems linked to the defective functionality of the nose, particularly after previous demolitive operations (ENS or atrophic rhinitis), but also for the excessive use of inhaled stupefacient substances (cocaine) thanks to the capacity of the new mixture to help in rebuilding both the shape and the function of damaged anatomic areas. Our studies are evaluating possible further functional improvements in ENS after repeated sittings of infiltrations of PRL in the same treated undersurface areas from 6 and 12 months from the first infiltration[37] and the stability during the time of the results obtained.

References

1. Di Rienzo Businco L, Di Rienzo Businco A, Lauriello M. Comparative study on the effectiveness of Coblation-assisted turbinoplasty in allergic rhinitis. *Rhinology.* 2010; 48(2):174-8.
2. Di Rienzo Businco L, Laurino S, Di Rienzo Businco A, Ventura L, Lauriello M. Turbinoplasty with quantic molecular Resonance in the treatment of persistent moderate-severe allergic rhinitis: comparative analysis of efficacy. *Am J Rhinol Allergy.* 2014; 28(2): 164-8.
3. Lauriello M, Micera A, Muzi P, Di Rienzo Businco L, Bonini S. TLR4 and TLR9 Expression in Different Phenotypes of Rhinitis. *Int J Otolaryngol.* 2012; 2012:925164.
4. Addolorato G, Ancona C, Capristo E, et al. State and trait anxiety in women affected by allergic and vasomotor rhinitis. *J Psychosom Res.* 1999; 46(3):283-9.
5. Houser SM. Surgical treatment for empty nose

syndrome. *Arch Otolaryngol Head Neck Surg.* 2007; 133:858-863.
6. Sozansky J, Houser SM. Pathophysiology of Empty Nose Syndrome. *Laryngoscope.* 2015; 125(1):70-74.
7. Baraniuk JN. Subjective nasal fullness and objective congestion. *Proc Am Thorac Soc.* 2011; 8(1):62-69.
8. Scheithauer MO. Surgery of the turbinates and "empty nose" syndrome. GMS Curr Top *Otorhinolaryngol Head Neck Surg.* 2010; 9:Doc03.
9. Eccles R, Morris S, Tolley NS. The effects of nasal anesthesia upon nasal sensation of airflow. *Acta Otolaryngol.* 1988; 106(1-2):152-155.
10. Zhao K, Jiang J, Blacker K, et al. Regional peak mucosal cooling predicts the perception of nasal patency. *Laryngoscope.* 2014; 124(3):589-595.
11. ModrzynskiM. Hyaluronic acid gel in the treatment of empty nose syndrome. *Am J Rhinol Allergy.* 2011; 25(2):103-6.
12. Di Rienzo Businco L, Lauriello M, Marsico C, Corbisiero A, Cipriani O, Tirelli GC. Psychological aspects and treatment of patients with nasal septal perforation due to cocaine inhalation. *Acta Otorhinolaryngol Ital.* 2008; 28(5):247-51.
13. Jung JH, Baguindali MA, Park JT, Jang YJ. Costal cartilage is a superior implant material than conchal cartilage in the treatment of empty nose syndrome. *Otolaryngol Head Neck Surg.* 2013; 149(3):500-5.
14. Papay FA, Eliachar I, Risica R. Fibromuscular temporalis graft implantation for rhinitis sicca. *Ear Nose Throat J.* 1991; 70(6):381-4.
15. Jiang C, Shi R, Sun Y. Study of inferior turbinate reconstruction with medpor for the treatment of Empty Nose Syndrome. *Laryngoscope.* 2013; 123(5):1106-1111.
16. Rice DH. Rebuilding the inferior turbinate with hydroxyapatite cement. *Ear Nose Throat J.* 2000; 79(4):276-7.
17. Saafan ME. Acellular dermal (alloderm) grafts versus silastic sheets implants for management of empty nose syndrome. *Eur Arch Otorhinolaryngol.* 2013; 270(2):527-33.
18. Anitua E, Andia I, Ardanza B, Nurden P, Nurden AT. Autologous platelets as a source of proteins for healing and tissue regeneration. *Tromb Haemost.* 2004; 91(1):4-15.
19. Cervelli V, Gentile P, Scioli MG, et al. Application of platelet-rich plasma in plastic surgery: clinical and in vitro evaluation. *Tissue Eng Part C Methods.* 2009; 15(4):625-634.
20. Lane MD, Tang QQ. From multipotent stem cell to adipocyte. *Birth Defects Res A Clin Mol Teratol.* 2005; 73(/):476-477.
21. Cervelli V, Gentile P, Grimaldi M. Regenerative surgery: use of fat grafting combined with platelet-rich plasma for chronic lower-extremity ulcers. *Aesthetic Plast Surg.* 2009; 33:340-345.
22. Cervelli V, Gentile P. Use of cell fat mixed with platelet gel in progressive hemifacial atrophy. *Aesthetic Plast Surg.* 2009; 33(1):22-27.
23. Cervelli V, Gentile P, De Angelis B, et al. Application of enhanced stromal vascular fraction and fat grafting mixed with PRP in posttraumatic lower extremity ulcers. *Stem Cell Res.* 2011; 6(2):103-111.
24. Coleman SR. Facial recontouring with lipostructure. *Clin Plast Surg.* 1997; 24(2):347-367.
25. Coleman SR. Long-term survival of fat transplants: Controlled demonstrations. *Aesthetic Plast Surg.* 1995; 19:421-425.
26. Kevy SV, Jacobson MS. Comparison of methods for point of care preparation of autologous platelet gel. *J Extra Corpor Technol.* 2004; 36(1):28-35.
27. Clement PAR, Godts F; Standardisation Committee on Objective Assessment of the Nasal Airway, IRS, and ERS. Consensus report on acoustic rhinometry and rhinomanometry. *Rhinology.* 2005; 43(3):169-79.
28. Passàli D, Mezzedimi C, Passàli GC, Nuti D, Bellussi L. The role of rhinomanometry, acoustic rhinometry, and mucociliary transport-time in the assesment of nasal patency. *Ear Nose Throat J.* 2000; 79:397-400.
29. Pieri F, Lucareli E, Corinaldesi G, et al. Mesenchymal stem cells and platelet-rich plasma enhance bone formation in sinus grafting: a histomorphometric study in minipigs. *J Clin Periodontol.* 2008; 35:539-546.
30. Warnke PH, Springer IN, Wiltfang J, et al. Growth and transplantation of a custom vascularized bone graft in a man. *Lancet.* 2004; 364(9436):766-770.
31. Prunet-Marcassus B, Cousin B, Caton D, André M, Pénicaud L, Casteilla L. From heterogeneity to plasticity in adipose tissues: site-specific differences. *Exp Cell Res.* 2006; 312(6):727-736.
32. Cao Y, Sun Z, Liao L, Meng Y, Han Q, Zhao RC. Human adipose tissue-derived stem cells differentiate into endothelial cells in vitro and improve postnatal neovascularization in vivo. *Biochem Biophys Res Commun.* 2005; 332(2):370-379.
33. Matsumoto D, Sato K, Gonda K et al. Cellassisted lipotransfer: Supportive use of human adipose-derived cells for soft tissue augmentation with lipoinjection. *Tissue Eng.* 2006; 12(12):3375-3382.
34. Gutowski KA; ASPS Fat Graft Task Force. Current applications and safety of autologous fat grafts: A report of the ASPS fat graft task force. *Plast Reconstr Surg.* 2009; 124(1):272-280.
35. Man D, Plosker H, Winland-Brown JE. The use of autologous platelet-rich plasma (platelet gel) and autologous platelet-poor plasma (fibrin glue) in cosmetic surgery. *Plast Reconstr Surg.* 2001; 107(1):229-37.
36. Marlovits S, Mousavi M, Gäbler C, Erdös J, Vécsei V. A new simplified technique for producing platelet-rich plasma: A short technical note. *Eur Spine J.* 2004; 13 Suppl:S102-S6.
37. Zhu M, Zhou Z, Chen Y et al. Supplementation of fat grafts with adipose-derived regenerative cells improves long-term graft retention. *Ann Plast Surg.* 2010; 64(2):222-228.

Aesthetic Medicine
Volume 2 · Number 1 · January-March 2016

Fat grafts calibration

Sebastian Torres

MD, Plastic and Maxillofacial surgery, private practice - Rome, Italy

ABSTRACT

Fat grafting technique has become particularly popular in the last years, among physicians and patients, due to its permanent volumetric potential and regenerative capacity. Nevertheless an open debate is currently ongoing regarding the optimal viscosity, adipocytes size, cytoarchitecture and adipose stem cells quantity within the grafts. The author has proposed recently a new concept related to a differential harvesting and grafting technique that provides different grafts parameters depending on the intended use. A new device that allows closed washing of the lipoaspirates is introduced and the cytological and histological characteristics of the grafts obtained are presented and discussed.

Keywords
Differential harvesting, differential grafting, viscosity, calibration

Correspondence
Sebastian Torres
E-mail. info@sebastiantorresmd.com

Accepted for publication 7 January 2016

Introduction

Fat tissue is commonly believed to have deposit and structural functions and to be a rather homogeneous and inert compartment. Differences in cellular types in morphology and quantity have been found in different body areas. Moreover different cellular aspirates can be obtained when the depth of the aspirating cannula is varied within the same area or when the size of the aspiration cannula ports is modified. All of the above has raised the introduction of a new concept, differential harvesting and grafting depending on the cellular population and the clinical use intended for the grafts.

The term Differential fat harvesting stands for fat harvesting through different cannulas (port sizes or diameter) based on the placement area, technique to be used, or intended cellular population. The first one allows to target the grafts according to the expected receptor site and benefits, and gives specific characteristics to each type of graft, regarding all aspects of the technique.

A new closed washing system is introduced and cytological and histological properties of the grafts obtained are presented and discussed.

Materials and methods

Aesthetic private patients with request of fat grafting procedure were recruited on a first come basis between May 2013 and October 2015.

One hundred and twenty one (121) private patients (35 males and 86 females), were treated between October 2013 and May 2015 for fat grafting procedures. Thirty seven (37) patients undergone body fat grafting and eighty (80) facial fat grafting. Four (4) patients received both corporal and facial fat grafts.

Exclusion criteria included BMI<18,5, tobacco use, connective tissue diseases, current chemo or radiotherapy and all general contraindications for aesthetic surgery.

Torres fat grafts records, (a special assessment sheet specially created to standardize fat grafting technique; harvesting, anesthesia, processing, enhancing and infiltration steps) were used to establish approximate volumes and desired grafts characteristics.

Local anesthesia (mepivacain regional blocks) and minor sedation (midazolam ev) were available for the procedures.

Harvesting was performed according to the pre-established forms. The harvesting area is defined pre operatory and registered. Furthermore, the physician predicts the volume quantity and quality to be transplanted, by comparing old and actual pictures of the patients. This is registered per area to have a pre operatory volumetric map prediction.

Following the record, the differential harvesting concept was applied, where fat was extracted in 2 different manners, obtaining 2 grafts viscosities. Thin fat parcels are used to fill critical areas of the face (periocular, lips, temporal, nasal) and for superficial placement through needles. Thick fat parcels are used to be placed through cannulas for volumetric purposes on the rest of the face. Thin fat parcels were extracted with a 6 port (0.8 mm each) Tulip Tonnard harvesting 2 mm width × 15 cm length cannula (Tulip medical, San Diego, CA) coupled to biplane luer lock handle attached to a 100 mL Tissu-Trans Filtron Unit (Shippert Medical, Denver, CO) linked to a surgical aspirator.

Thick fat parcels are automatically extracted with a Shippert 4 port (5 mm × 2 mm each) harvesting 3 mm width × 15 cm length cannula (Shippert medical, Denver, CO) connected to a biplane luer lock handle attached to a separate 250 mL Tissu-Trans Filtron Unit (Shippert Medical, Denver, CO) linked to a surgical aspirator.

Aspiration pressure was set to less than 500mmHg to avoid cellular breakdown[1].

Grafts processing was done through simultaneous differential closed system washing with the aid of Filtron Tissu-Trans (Shippert Medical, Denver, CO, USA). Two sizes of mesh were used within the filters 800 micron for macro grafts and 300 micron for micro graft.

Platelet Rich Plasma (PRP) at 10% of total fat volume was used to enhance the grafts[2].

The fat volume to be injected was predicted and accordingly blood samples were taken to obtain PRP.

Disposable clinical used test tubes were use to obtain 8ml cc patients blood samples and centrifugated at (3100rpm-1500g /5min), to obtain 5ml PRP[3]. Prior to infiltration fat- PRP mix was adequately emulsified through luer lock female-female adaptor with at least 10 passages to guarantee adequate viscosity and even dispersion of the compounds.

Differential infiltration was performed depending on intended effect and graft characteristics.

The thin fat parcels infiltration was carried out through 0.9 mm × 5 cm Tulip injector cannula (Tulip medical, San Diego, CA) in facial critical areas (temples, periorbital, lips, and nasal) or with needles; 23 G × 30 mm in SNIF or 27 G × 4 mm in Mesofat technique[4-5].

The needle was placed in superficial wrinkles and lines, to enhance corrections at an intradermal plane for deep folds, and in cases of strong photo and chrono-aging (Mesofat). In body fat grafting, the needle placement was favored in the breast around the nipple to enhance volumetric result, and skin tonicity and in buttocks as a complementary procedure to treat cellulite dimples, concomitant to Subcision[6].

Thick fat parcels were infiltrated using a 1.2 mm × 7 cm Tulip cannula in all the other parts of the face. 2mm x 10 cm and 2mm x 15cm cannulas were used for body grafting. This placement was favored whenever the primary goal was volumetric enhancement and

when soft tissue envelope was thick.

Cytological and histological random samples were taken and analyzed. Specific markers (CD 31 and CD 34) were tested to determine specific cellular lines.

A 5 point self-assessment scale was applied to the patients at 3-6-12 months.

The scale range for results evaluation included; dissatisfied (worse than before), poor (almost like before), moderate satisfaction (slightly better), good (better), excellent (much better).

Results

Mean aspirated volume for corporal grafts was 598,9ml *(Standard error 49,77; Median 480; Mode 450; SD 318,715; Minimum 300; Maximum 1500)*, mean aspirated volume for facial grafts patients was 135,36 ml *(Standard error 5,31; Median 150; Mode 150; SD 48,65; Minimum 30; Maximum 250)*. The average duration of the procedure was 105 minutes (range 60-180 minutes). Infiltrations were performed according to the Torres grafts forms pre-established. The details are shown in figures 1-4.

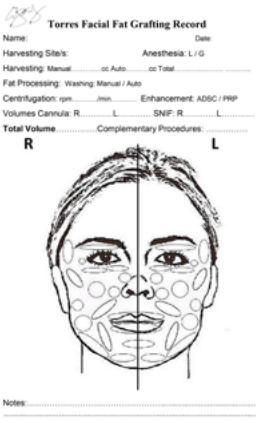


Figure 1 - Torres Facial Fat Grafting Record

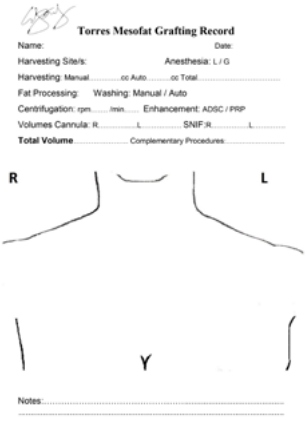


Figure 2 - Torres MesoFat Transfer Record

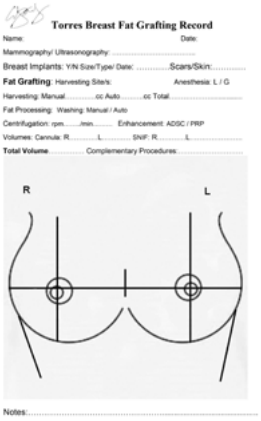


Figure 3 - Torres Breast Fat Grafting Record

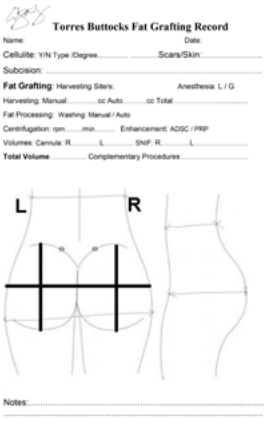


Figure 4 - Torres Buttocks Fat Grafting Record

Mean volumes of infiltrations were *44,68cc for the face (Standard error 0,9; median 48; Mode 50; SD 8,25; Minimum 20; Maximum 55), 276,5cc for each breast (Standard error 12,38; Median 300; Mode 300; SD 55,37; Minimum 180; maximum 360) and 747,86cc for both buttocks (Standard error 47,5; Median 690; Mode 700; SD 217,66; Minimum 500; Maximum 1500)*.

Follow up was completed for up 17 months (range 3-17 months).

Self-assessment scale was rated as good or excellent by the majority at 3, 6 and 12 months (Figures 5, 6, 7, 8, 9).

Figure 5

Figure 6

Figure 7

Figure 8

Figure 9

Cytological and histological random samples (first patient treated each month was analyzed for all the duration of the study) showed normal adipocytes cytoarchitecture, no inflammatory response, and abundant vascular stromal fraction and adipose stem cells, the latter especially in the 300 micron net filter aspirate. The net content of ASC was 20% more on the smaller net. The lipoaspirate retained 10% of saline, according to decanting in lab. Anesthetic solution measurements were non-significant in the grafts.

Discussion and Conclusions

Fat tissue is commonly believed to have deposit and structural functions and to be a rather homogeneous and inert compartment. Differences in cellular types in morphology and quantity have been found in different body areas[7-8]. According to cellular type we classified fat in monolobular (white) and multilobar (brown). The former serves as energetic storage and regulation of liposynthesis and lipolysis. Moreover it controls hunger, gives mechanical protection in some areas, provides thermic Isolation, and represents a secondary sexual character.

The latter is principally important for neonates and it is responsible for thermogenesis.

White fat is further divided according to its function in storage, structural and fibrous. The main differences between these subtypes relay on adipocytes sizes, intercellular space, collagen stromal component and related staminal niches.

A greater understanding of fat metabolism has shifted and improved fat grafting techniques, nevertheless a standardization of the method has proven to be quite challenging[9].

Moreover, different cellular aspirates can be obtained when the depth of the aspirating cannula is varied within the same area[10] or when the size of the aspiration cannula ports is modified[11-13]. The author has previously published how by harvesting fat in the superficial subcutaneous layer (close to the dermal vascular plexus) the amount of ASC obtained from lipoaspirates can be substantially higher than those obtained from lipoaspirates harvested in the deep subcutaneous layer (next to the muscular fascia)[10].

Cannulas port affect the disruption of the tissues and adipocyte integrity. The smaller the cannula port, the higher the adipocyte stress, lysis and oil production in the harvested tissue, resulting in less viable adipose cells, with greater necessity of fat processing (washing or centrifugation). Cannulas port size affects directly the adipocytes. The larger the aspiration cannula, the greater the viscosity, retention and quality of the graft.

On the other hand, the smaller the cannula size, the lesser the viscosity, and higher tissue disruption, oil content and amount of ASC within the graft (Figure 10).

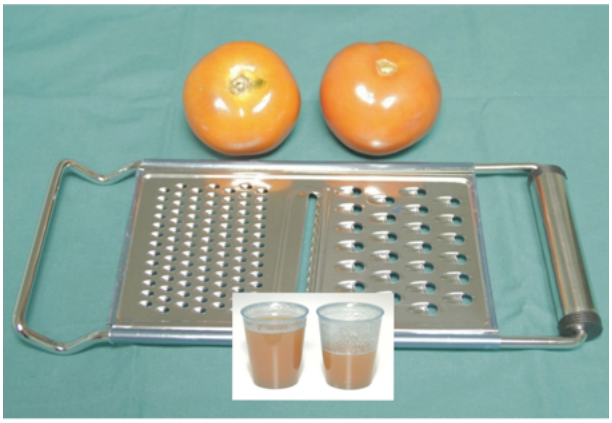


Figure 10 - Differential harvesting concept

A fluid grafts allows needle or fine cannula placement and avoids irregularities in critical areas.

The higher tissue disruption, the more ASC released into the lipoaspirate. This comes to its maximum, when laser lipolysis aspirates are analyzed, revealing

no viable adipocytes but a high content of ASC to be cultured and expanded in lab (expert empirical experience). An example of the former is provided in Figure 6.

All of the above has raised the introduction of a new concept, differential harvesting and grafting depending on the cellular population and the clinical use intended for the grafts[14].

The term Differential fat harvesting stands for fat harvesting through different cannulas (port sizes or diameter) based on the placement area, technique to be used, or intended cellular population.

This technique allows to obtain different sizes of fat parcels and to perform a differential fat grafting, in order to gain as much as possible from each individual treatment goal, volume restoration and skin regeneration, for greater patient and surgeon satisfaction.

The benefits of the differential harvesting are versatility of fat, more precise corrections, and achieving homogeneous results[14].

It improves fat survival in critical spots and reduces the overall fat oil content resulting in reduced inflammation and downtime for patients[14].

Furthermore it may reduce the potential complications, and speed up the whole process[14] a critical aspect when deciding as a surgeon to alter the surgical technique.

Moreover it allows us to obtain different extraction samples to be processed or enhanced in different ways.

This is the first time a differential closed system washing processing is described. By modifying the nets holes dimension within the filters canisters we were able to select the size of the adipocytes and the amount of ASC that will come from our lipoaspirate.

It is like fishing through different nets in open sea, where the size of the nets will determine the type of fish that will remain attached to them. Excellent biological characteristics of the cellular types were encountered showing that viable grafts are obtained through this methodology.

On this manner we can manage grafts viscosity, and cellular characteristics, to customize or target the treatments according to the area or goal intended.

In areas of great muscular mechanical stress, a fact known as an important factor determining early absorption of fillers[15], it allows multiplane corrections (intradermal, subcutaneous, and supraperiosteal) permitting to obtain a better volumetric survival, because we do not overcorrect on one plane, we expand all of them so that the transplanted cells may establish new circulatory connections and posterior survival.

The other important factor is the dead space created in the infiltrative phase. The bigger the cannulas, the more important the trauma becomes as the dead space to be filled with serum on the scarring tissue will interfere in cells integration. By having different adipose parcels sizes, small cannulas and needles can be used for delivery, reducing the trauma and dead space in the healing phase. The lesser the inflammation, the closer the transplanted cells will be to the vessels.

It is well known that whatever the ASC do, it relies mainly in the cellular niche or immediate micro ambient surrounding[16]. Cellular niche is different in the intradermal, subcutaneous and supra periosteal plane, so we can expect different actions from this cells depending on the plane transplanted. Differential fat harvesting and posterior differential grafting is a valid alternative, to expand the repertoire of fat use, allow a more homogeneous effect, reduce the potential complications, speed up the process, improve graft survival, and to enhance overall aesthetic outcome.

Local factors have commanded the research for grafts integration. Nevertheless many systemic factors have risen interest recently to allow an overall improvement of the technique[17]. The mastery of this technical modifications, which affect our graft, together with the understanding of recipient site[17-21] and systemic factors, will allow us to get long lasting and reproducible results for the benefit of our patients.

References

1. Shippert RD, Vacuum Pressures during Autologous Fat Transfer: A study of the closed syringe types and other types of aspirator pressures. *Am J Cosmet Surg.* 2009; 26(4):230-235.
2. Li J, Shi X, Chen W. Influence of repeatedly injecting platelet-rich plasma on survival and quality of fat grafts in nude mice. *Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi.* 2013; 27(4):454-9.
3. Cho JM, Lee YH, Baek RM, Lee SW. Effect of platelet-rich plasma on ultraviolet b-induced skin wrinkles in nude mice. *J Plast Reconstr Aesthet Surg.* 2011; 64(2):e31-e39.
4. Zeltzer AA, Tonnard PL, Verpaele AM. Sharp-needle intradermal fat grafting (SNIF). *Aesthet Surg J.* 2012; 32(5):554-61.
5. Torres Farr S. SNIF & Mesofat for neck and décolleté rejuvenation. Presented at the World Congress of Facial Plastic Surgery, 2012, Rome, Italy.
6. Hexsel DM, Mazzuco R. Subcision: a treatment for cellulite. *Int J Dermatol.* 2000; 39(7): 539-44.
7. Sbarbati A, Accorsi D, Benati D, et al. Subcutaneous adipose tissue classification. *Eur J Histochem.* 2010; 54(4):e48.
8. Chon SH, Pappas A. Differentiation and characterization of human facial subcutaneous adipocytes. *Adipocyte.* 2014; 4(1):13-21.
9. Strong AL, Cederna PS, Rubin JP, Coleman SR, Levi B. The Current State of Fat Grafting: A Review of Harvesting, Processing, and Injection Techniques. *Plast Reconstr Surg.* 2015; 136(4):897-912.

10. Trivisonno A, Di Rocco G, Cannistra C, et al. Harvest of superficial layers of fat with a microcannula and isolation of adipose tissue-derived stromal and vascular cells. *Aesthet Surg J.* 2014; 34(4):601-13.
11. Kirkham JC, Lee JH, Austen WG. Fat graft survival: physics matters: invited commentary to "The impact of liposuction cannula size on adipocyte viability". *Ann Plast Surg.* 2014; 73(3):359.
12. Tambasco D, Arena V, Finocchi V, Grussu F, Cervelli D. The impact of liposuction cannula size on adipocyte viability. *Ann Plast Surg.* 2014; 73(2):249-51.
13. Kirkham JC, Lee JH, Medina MA, 3rd, McCormack MC, Randolph MA, Austen WG, Jr. The impact of liposuction cannula size on adipocyte viability. *Ann Plast Surg.* 2012; 69(4):479-81.
14. Torres Farr S, Trivisonno A. Differential Fat Harvesting. *Plast Aesthet Res.* 2014; 1(3):103-107.
15. Torres Farr S. Injectable skin fillers adverse effects. *La Medicina Estetica.* 2009; 33(3):395-420.
16. Chen S, Lewallen M, Xie T. Adhesion in the stem cell niche: biological roles and regulation. *Development.* 2013; 140(2):255-65.
17. Zhang D, Yan B, Yu S, et al. Coenzyme Q10 inhibits the aging of mesenchymal stem cells induced by D-galactose through Akt/mTOR signaling. *Oxid Med Cell Longev.* 2015; 2015:867293.
18. Kakagia D, Pallua N. Autologous fat grafting: in search of the optimal technique. *Surg Innov.* 2014; 21(3):327-36.
19. Kato H, Mineda K, Eto H, et al. Degeneration, regeneration, and cicatrization after fat grafting: dynamic total tissue remodeling during the first 3 months. *Plast Reconstr Surg.* 2014; 133(3):303e-13e.
20. Baek RM, Park SO, Jeong EC, et al. The effect of botulinum toxin A on fat graft survival. *Aesthetic Plast Surg.* 2012; 36(3):680-6.
21. Sezgin B, Ozmen S, Bulam H, et al. Improving fat graft survival through preconditioning of the recipient site with microneedling. *J Plast Reconstr Aesthet Surg.* 2014; 67(5):712-20.

Courses and Congresses

2016

January – Caracas (Venezuela)
Degree course in Corporal Aesthetic
16 hours of University Credits
Degree Course in Facial Aesthetic
18 hours of University Credits
Degree Course in Metabolism, Nutrition and integral management of obesity
10 hours of University Credits
Tel. 00 58 416 6219974
www.fuceme.org
fuceme@gmail.com

18-20 February – Malaga (Spain)
31st National Congress of Aesthetic Medicine
Spanish Society of Aesthetic Medicine
Ronda General Mitre, 210, 08006 Barcelona (Spain)
President: Petra Vega
Web: www.seme.org
E-mail: secretaria@seme.org

3-5 March – Mexico City (Mexico)
XI Pan American Congress of Aesthetic Medicine
XIII Mexican Congress of Aesthetic and Anti-Aging Medicine
XIII Venezuelan Congress of Aesthetic Medicine
Mexican Scientific Society of Aesthetic Medicine
Aesthetic Medicine Society of Venezuela
Venue: Pepsi Center, WTC México
Calle Dakota S/N, Nápoles, 03810
Presidents: Blanca Miller Kobisher – Victor Garcia Guevara
info@ippcvtas.com
www.congresodemedicinaestetica.com

25-27 March - Casablanca (Morocco)
International Congress of Dermastic
Moroccan Association of Surgical Dermatology – Cosmetic Aesthetic Medicine – Anti-Aging Medicine
President: Ahmed Bourra
www.dermastic.asso.ma
dermastic.asso@hotmail.com

31 March - 2 April - Buenos Aires (Argentina)
26th Argentinian Congress of Aesthetic Medicine
Argentinian Society of Aesthetic Medicine
SOARME
President: Prof. Dr. Raúl Pinto
info@soarme.com
www.soarme.com

13-15 May – Rome (Italy)
11th European Congress of Aesthetic Medicine
37th National Congress of the Italian Society of Aesthetic Medicine
11th National Congress of the Italian Academy of Aesthetic Medicine
Venue: Congress Centre Rome Cavalieri
President: Emanuele Bartoletti
sime@lamedicinaestetica.it
congresso@lamedicinaestetica.it
www.lamedicinaestetica.it

9-21 May – Pretoria (South Africa)
The 10th Aesthetic Medicine Congress of South Africa
Aesthetic & Anti-aging Medicine Society of South Africa
Venue: CSIR Convention Centre
President of the Congress: Riekie Smit
info@aesthmed.co.za
www.aesthmed.co.za

16-17 September – Paris (France)
37th National Congress of Aesthetic Medicine and Dermatologic Surgery
French Society of Aesthetic Medicine
French Association of Morpho-Aesthetic and Anti-Aging Medicine
National Institute of education in aging prevention
Venue: Palais de Congres
www.sfme.info
congress@sfme.info

2017

22-24 September - Almaty (Kazakhstan)
9th National Congress of Aesthetic Medicine and Plastic Surgery
Kazakhstan Association of Aesthetic Medicine and Plastic Surgery
President: G. Zhumatova
info@estetic.kz
www.estetic.kz

27-29 October - Istanbul (Turkey)
21th World Congress of Aesthetic Medicine
Turkish Society of Aesthetic Medicine
President: Hasan Subasi
Rumeli Caddesi Durak Apt N° 2, D.7
Nisantasi, Istanbul - Turkey
www.estetiktipdernegi.org.tr
subasihasanm@superonline.com

Volume 2 • Number 1 • January/March 2016
www.aestheticmedicinejournal.org

Contents