Volume 1 • Number 2 • July/September 2015
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
Kazakhstan Association of Aesthetic Medicine and Plastic Surgery
Korean Academy of Aesthetic Medicine
Italian Society 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

Official Journal of the International Union of Aesthetic Medicine – UIME

Editor-in-chief
Francesco Romanelli
Rome, Italy

Editors
Emanuele Bartoletti, Italy
Alfonso Carvajal Gomez, Colombia
Annarosa Catizzone, Italy
Loredana Cavalieri, Italy
Nadia Fraone, Italy
Fernando García Manforte, Spain
Sonia Lamari, Algeria
Raul Pinto, Argentina
Sandra Ramirez Naranjo, Colombia
Ferdinando Terranova, Italy
Dorota Wydro, Poland

Executive Editors
Emanuele Bartoletti, Italy
Annarosa Catizzone, Italy
Loredana Cavalieri, Italy
Nadia Fraone, Italy
Hernan Pinto, Argentina
Ferdinando Terranova, Italy

Managing Editor
Emanuele Bartoletti, Italy

Associate Editors
Patricia Frisari, Argentina – Tulegenova Gulnur, Kazakhstan – Andrzej Ignaciuk, Poland – John Kim, California (USA) – Alexander Kutubidze, Georgia – Omnia Latif, New Jersey (USA) – Leonor Lemmo, Venezuela – Mihaela Leventer, Romania – Alper Mamak, Turkey – Xavier Martin, Swiss – Gilda Marzullo, Chile – David Melamed, California (USA) – Farid-Salim Oughanem, Algeria – Olga Panova, Russia – Susan Roberts, Canada – Pilar Rodrigo Anoro, Spain – Ismael Terzano, Uruguay – Viveva Tinoco Kirby, Ecuador.

Editorial Board
Gladys Arroyave Estrada, Colombia – Ahmed Bourra, Morocco – José Cabo Soler, Spain – Alfonso Carvajal Gómez, Colombia – Andrés Eliú Castell Rodriguez, Mexico – Eduardo Civila, Uruguay – Michel Delune, California (USA) – Fernando Echeverria, Chile – Alberto Elbaum, Uruguay – Victor Garcia-Guevara, Venezuela – Jean Hebrant, Belgium – Andreij Ignaciuk, Poland – Alexander Katsitadze, Georgia – Serge Lê Huu, Swiss – Jean-Jacques Legrand, France – Mihaela Leventer, Romania – Hongcheng Liu, China – Xavier Martin, Swiss – Gilda Marzullo, Chile – Alena Mayorova, Russia – Irina Medvedeva, Ukraine – Blanca Miller Kobisher, Mexico – Mohamed Oughanem, Algeria – Olga Panova, Russia – Iván Pinto, Venezuela – Raul Pinto, Argentina – Catalin Mihai Popescu, Romania – Aicha Salhi, Algeria – Rikie Smit, South Africa – Hasan Subasi, Turkey – Vladimir Tsepkolenko, Ukraine – Viveka Tinoco Kirby, Ecuador – Ekaterina Ugrekhelidze, Georgia – Renier Van Aardt, Canada – Pedra Vega, Spain – Jerzy Woy-Wojciechowski, Poland – J. Yun, Korea – Gulnar Zhumatova, Kazakhstan.

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. **Subscription price:** € 70,00 VAT included (Four issues: March, June, September, December). Payment by cheque or VISA Card to Editrice Salus Internazionale srl.
Copyright Permission: Permission requests to photocopy or otherwise reproduce material published in this journal should be submitted by sending and e-mail to aemj@aestheticmedicinejournal.org.
Advertising: Current advertising rates and specifications may be obtained by sending and e-mail to aemj@aestheticmedicinejournal.org.
EPub [20/10/2015]

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);
- key words (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.

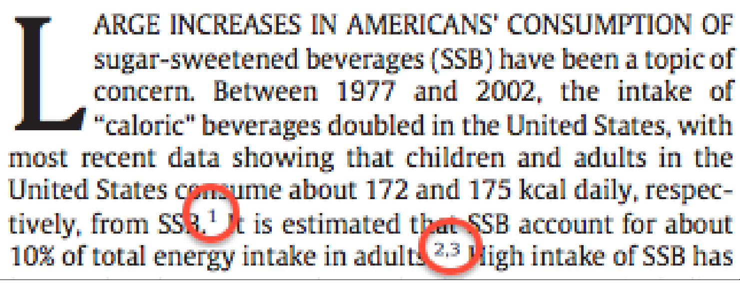
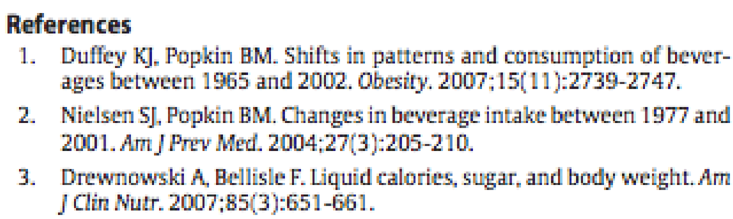
AMERICAN MEDICAL ASSOCIATION (AMA) CITATION STYLE

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.

<table>
<tr><td colspan="2">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.</td></tr>
<tr><td>In-Text Citation Example</td><td>
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</td></tr>
<tr><td>References Section Example</td><td>
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.</td></tr>
</table>

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 CO_2 laser for facial resurfacing. Today, CO_2 resurfacing is not used as much anymore, because of the long and difficult post-op. CO_2 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:	O. PANOVA (Russia)
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

CANADIAN ASSOCIATION OF AESTHETIC MEDICINE
c/o CongressWorld Conferences Inc.
220-445 Mountain Highway
North Vancouver, BC, Canada V7J 2L1
jupitis@msn.com – s.roberts@caam.ca – www.caam.ca
President: J. UPITIS

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
Dent301@163.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@une.net.co – 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
gsoam@hotmail.com – 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. – 050000 Almaty - Kazakhstan
arugulnar@hotmail.com – www.estetic.kz
President: G. ZHUMATOVA

KOREAN ACADEMY OF AESTHETIC MEDICINE
5h Floor, YD building, Chungdam – Dong, Kangnam – Ku
Seul – Korea
zzang0703@naver.com – www.ons.or.kr
President: J. YOON

MEXICAN SCIENTIFIC SOCIETY OF AESTHETIC MEDICINE
Cincinnati 8 1-307 – Col. Noche Buena – Mexico D.F. 03720 – Mexico
bmillerkobisher@yahoo.com
President: B. MILLER KOBISHER

MOROCCAN SOCIETY OF AESTHETIC MEDICINE
19, place du 16 Novembre – 2100 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
sekreteriat@ptmeiaa.pl; www.ptmeiaa.pl
President: A. IGNACIUK

ROMANIAN SOCIETY FOR AESTHETIC MEDICINE AND DERMATOLOGIC SURGERY
Sevastopol 13-17, Sector 1, Diplomat Business Center, Apt.204 – Bucharest – Romania
mirel-leventer@usa.net – www.medicina-estetica.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 1 · Number 2 · July-September 2015

Radiofrequency increases sympathetic activity and resting energy expenditure

Vincenzo Monda[1,2], Antonietta Messina[1], Filomena Palmieri[1], Giuseppe Monda[1], Fiorenzo Moscatelli[6,7], Gianluca Russo[4], Romualdo Crescenzo[5], Anna Rosa Catizzone[5], Elisabetta Fulgione[5], Laura Piombino[5], Emanuele Bartoletti[3], Dario Dorato[3], Giovanni Messina[1], Giovanni Francesco Nicoletti[2], Francesco D'Andrea[2], Marcellino Monda[1]

[1]MD, Department of Experimental Medicine, Section of Human Physiology and Unit dietetic and Sport Medicine, Second University of Napoli, Italy
[2]MD, Department of Plastic and Reconstructive Surgery, Second University of Napoli, Italy
[3]MD, Italian Society of Aesthetic Medicine
[4]MD, Italian Society of non-Ablative Radiofrequency
[5]MD, Italian Academy of Aesthetic Medicine
[6]MD, Department of Clinical and Experimental Medicine, University of Foggia, Via Napoli, 20- 71122 Foggia, Italy
[7]MD, Department of Motor, Human and Health Science, University of Rome "Foro Italico", Piazza L. de Bosis, 00135 Rome, Italy

ABSTRACT

Radiofrequency (RF) devices for aesthetic applications are becoming increasingly popular in clinics worldwide due to their demonstrated efficacy and safety combined with a relative lack of complications and downtime.

Heating of body tissues by RF energy is a mechanism for therapeutic. Such effects may be produced by local changes in tissue temperature and others may be systemic effects due to the additional thermal load on the body. An elevated core temperature increases metabolism, heart rate, respiration rate, and nerve conduction velocity. The aim of this study was to determine whether healthy subjects, non-obese, undergoing treatment with RF could see changes in Resting Energy Expenditure (REE) and Sympathetic Nervous System (SNA), Galvanic Skin Responses (GSR). Seven healthy adult males took part in the study. The study protocol consisted of the treatment of twenty minutes of radiofrequency in the abdominal region. Participants in the study were presented in the morning at 8.00 a.m. fasting for at least 12 hours, underwent measurement of REE, Heart Rate Variability (HRV) and GSR 60 minutes prior to treatment, immediately after treatment, and 120 minutes after treatment. Radiofrequency induced significant increases of REE, sympathetic activity, and GSR. This result is also useful in the interpretation of the relationship between the sympathetic nervous system and food intake in young subjects. It has demonstrated a significant influence of sympathetic activity on eating behaviour, also through an increase in thermogenesis.

Keywords
Radiofrequency devices, resting energy expenditure, sympathetic nervous system

Correspondence
Giovanni Messina, MD, PhD, Department of Experimental Medicine Second University of Naples - Via Costantinopoli, 16 I-80138 Napoli - Italy
Phone/fax: (+39) 0815665841 - (+39) 0815665844
E-mail: gianni.messina@unina2.it

Accepted for publication 10 September 2015

© 2015 Editrice Salus Internazionale srl

Introduction

As the aging population in our society continues to increase, many people are seeking technologies and treatments to help achieve a more youthful appearance. This, coupled with the general population's busy lifestyle, is leading towards a desire for procedures with minimal side effects and a limited recovery time.

Cutaneous aging is a net process resulting from intrinsic and extrinsic factors and is associated with many pathologic changes, including net reduction in dermal components, tissue degeneration, and decreased skin elasticity, all of which ultimately lead to macroscopic sagging and wrinkling. During the last decade, a number of injectable dermal fillers and laser modalities have been developed to counter the aging process.

Between the skin rejuvenation modalities, radiofrequency (RF) has emerged as a safe and effective treatment for a broad range of aesthetic and medical indications[1]. The RF devices for aesthetic applications such as body and face skin tightening, cellulite reduction, rhytids and body contouring treatments are becoming increasingly popular in clinics worldwide due to their demonstrated efficacy and safety combined with a relative lack of complications and downtime.

The mechanism of action of RF in a medical application is based on an oscillating electrical current forcing collision between charged molecules and ions, which are then transformed into heat.

The RF generated tissue heating has different biological and clinical effects, depending on the depth of tissue targeted, the frequency used, and specific cooling of the dermis and epidermis.

The depth of penetration of RF energy is inversely proportional to the frequency. Consequently, lower frequencies of RF are able to penetrate more deeply. RF technology also has the ability to non-invasively and selectively heat large volumes of subcutaneous adipose tissue. By selecting the appropriate electric field, one can obtain greater heating of fat or water. In cosmetic dermatology, RF is most commonly used to non-invasively tighten lax skin; to contour the body by influencing adipocytes; and, consequently, to improve the appearance of cellulite.

Radiofrequency emits focused electromagnetic waves, which meet resistance within the tissue, generating heat. This thermal energy affects collagen's triple helix structure, subsequently breaking the intramolecular hydrogen bonds resulting in immediate collagen contracture and subsequent neocollagenesis within the dermis without disrupting the epidermis[2].

Excessive exposure to RF energy can produce burns or other thermal damage to tissue, or, for whole body exposure, physiological stress resulting from excessive body heating. Since the 1960s, exposure guidelines for human exposure to RF energy effect in the United States and elsewhere[1,2] have been based in large part on animal studies.

In particular, the limits[1,2] for whole-body exposure are based on responses of animals subjected to whole-body exposures at levels that are sufficient to produce behavioural changes but not thermal damage to tissue.

Because of the large interspecies differences in thermoregulation, the observed responses in the animals used for these studies (chiefly, rodents and primates) may not be representative of human responses under similar exposure conditions.

Until recently there has been almost a complete lack of data from humans exposed for extended times to RF energy under conditions that are relevant to setting exposure guidelines. Several recent studies at the John B.

Pierce Laboratory in New Haven CT and the Air Force Research Laboratory (AFRL) at Brooks AFB, Texas by Adair and colleagues have measured thermoregulatory responses to extended (45 minutes) RF exposures of human volunteers under controlled environmental conditions.

These studies measured a variety of sensory and thermophysiological endpoints[3,4] in subjects exposed to RF energy at frequencies of 100, 450 and 2450 MHz.

This sophisticated method of transepidermal, non-invasive RF thermal delivery provides a variable and controversial tightening effect, which is not usually apparent, if at all, until dermal remodelling occurs a few months after the treatment.

Non-invasive tissue tightening treatments have an inherent safety limitation because energy is delivered through the skin surface and the threshold epidermal burn temperature is significantly lower than the optimal temperature for the collagen contraction.

These studies are the first, and apparently only, measurements of physiological responses of humans exposed for extended periods to RF energy of substantial parts of their bodies. The tests were conducted under carefully controlled environmental conditions and at exposure levels well above present U.S. and international limits.

While more recent thermal models for the human body are available (e.g. those proposed by Fiala D. et al. and by Xu X. et al[5,6]) the Hardy-Stolwijk model[7] was chosen for several reasons: it is a physiologically based model that was developed over a period of more than two decades and was validated by numerous human studies, and remains valid today[5,6]. Unlike some of the more recent models, source code, model parameters, and extensive commentary are readily available[7]. An elevated core temperature increases metabolism and certain other functions such as heart rate, respiration rate, and nerve conduction velocity. The largest component of daily energy expenditure, especially in people with sedentary lifestyle, is REE[8]. REE accounts for 60–75% of total daily energy expenditure and decreases with age and physical inactivity.

It is well known that Fat-Free Mass (FFM) accounts for the majority of inter-individual variability in REE. The Sympathetic Nervous System (SNS) is an important control mechanism of the body. The SNS shows physiologic fluctuations with age, which are often considered to relate to differences in the REE[9].

Activation of the SNS is measurable by various parameters, as GSR, and HRV.

HRV power spectral analysis is a well-accepted, useful, and non-invasive method, and has provided a comprehensive quantitative and qualitative evaluation of neuro-autonomic function under various research and clinical settings[10,11,12].

In general, power spectral analysis of HRV has shown at least two distinct regions of periodicity in electrocardiogram R-R intervals[13,14]. Previous investigations demonstrated that the percentage of body fat[15], energy storage[16], and glucose-induced thermogenesis[17] are correlated with differences in the power spectral components.

A series of recent studies with the HRV power spectral analysis have shown that obese young women possess significantly lower sympathetic activity against various thermogenic perturbations, such as cold exposure[18], capsaicin-containing yellow curry diet[19], and mixed food intake[20].

Unlike invasive measurements such as plasma catecholamine concentration, catecholamine turnover, and muscle sympathetic nerve activity, the HRV power spectral analysis lightens the burden imposed on subjects during an experiment and is a suitable and valuable approach to evaluating vegetative activity in large-scale of obesity research.

Although the relation between HRV and body mass index has been shown, as reported in the studies cited above, other authors have indicated that no correlation was noted between HRV and body mass index[11,21].

On the other hand, Hirsch and Mackintos have reported their perplexity about the controversial influences of autonomic nervous activity (measured by HRV) on body weight[22]. GSR is a change in electrical conductivity between two points on the respondent's skin. Fahrenberg and Wientjes[23] report GSR to be the most convenient physiological indicator for workload and GSR amplitudes may reflect the amount of affective or emotional arousal elicited by a stimulus or a situation. GSR is among the most suitable measures of arousal in studies regarding the autonomic nervous system.

The aim of this study was to determine whether healthy subjects, non-obese, undergoing treatment with radiofrequency could see changes in REE and in SNA induced, GSR.

Methods

Subjects

Twenty healthy adult males took part in the study. All participants were in good health, as defined by the absence of cardiovascular disease, and no history of endocrine disorders and were not taking any medication. Prior to data collection, the purpose of this study was explained thoroughly and informed consent was obtained from each participant, according to the Declaration of Helsinki.

Study protocol

The study protocol consisted of the treatment of twenty minutes of radiofrequency (SPARK, RF 1-4, Oxiline, San Marino) in the abdominal region.

Participants in the study were presented in the morning at 8.00 a.m., fasting for at least 12 hours, underwent measurement of REE, HRV and GSR 60 minutes prior to treatment, immediately after treatment, and 120 minutes after treatment.

Measurement of HRV responses, GSR and REE

The HRV-power spectrum was evaluated on a 5-min long ECG recording. The ECG signal was acquired on a PC at 100s/s with an electrocardiograph (Cardioline, delta-1 plus, Italy) connected to the serial port of a PC; a custom software written with LabView (National Instruments, Texas) was used for data acquisition and analysis.

All the R-waves were automatically recognised and all the R-R intervals were calculated. The R-R-intervals sequence was re-sampled to obtain a constant-time based signal (10 samples/sec).

The Fast Fourier Transform (FFT) was then applied to this signal and visualised in the form of power spectrum. The absolute values of this spectrum were, finally, summed in the low frequency (0.04-0.15 Hz; LF), and high frequency (0.15-0.40; HF) range. Low Frequency (LF) and High Frequency (HF) were the values used to estimate the sympathetic and parasympathetic activity[18].

The GSR parameters were measured simultaneously using the SenseWear Pro Armband™ (version 3.0, BodyMedia, Inc. PA, USA), which was worn on the right arm over the triceps muscle at the midpoint between the acromion and olecranon processes, as recommended by the manufacturer.

REE was measured by breath-by-breath respiratory gas exchange with the indirect calorimetric device (VMax 29, Sensor Medics, USA), using a mask. Gas analysers were calibrated before each measurement using three known standard gas concentrations. Measurements were ceased once a 5-minute steady-state period was achieved, or after 30 minutes, whichever occurred first. The indirect calorimeter was connected to an IBM-compatible personal computer for the management and storage of data.

Statistical analysis

The statistical program GraphPad Prism for Windows (v.5.01) (San Diego, CA, USA) was used for the analysis and treatment of the data. Physiological responses during the experimental session were evacuated using one-way analysis of variance (ANOVA) with repeated measurements, as well as the Student's t-test, when appropriate. When a significant F value emerged ($p<0.05$), the Bonferroni multiple comparisons test was performed to compare each group with the other ones. Data are reported as Mean (M) ± Standard Deviation (SD).

Results

Physical characteristics

The physical characteristics of the subjects participating in the study are presented in Table 1.

Responses to stress treatment

N°	20
Age **(Years)**	**24.9 ± 1,6**
Weight **(Kg)**	**72.7 ± 5.3**
Height **(m)**	**1.71 ± 7.2**
BMI **(Kg/m^2)**	**24.9 ± 1.9**

Table 1 - Physical characteristics of the subjects

Radiofrequency induced significant increases of REE, sympathetic activity, and GSR. The analysis of variance showed significant differences between the experimental conditions for REE [$F(2,57) = 2.6$, $p < 0.01$], GSR [$F(2,57) = 2.8$ $p < 0.005$], LF [$F(2,57) = 3.5$, $p < 0.001$].

Figure 1 reports the change in REE. This variable reached a peak immediately after treatment and it remained significantly elevated at 120 min after treatment, compared to basal values.

Figure 2 shows the variations of GSR. This variable reached a peak immediately after treatment and it remained significantly elevated at 90 min treatment, compared to basal value.

Figure 3 shows the change in LF. This variable reached a peak immediately after treatment and it remained significantly elevated at 120 min after treatment, compared to basal values. No ventricular arrhythmias or ST segment abnormalities were recorded.

Figure 4 shows the change in HF. HF values not show changes. The analysis of variance shows no significant effect.

Discussion

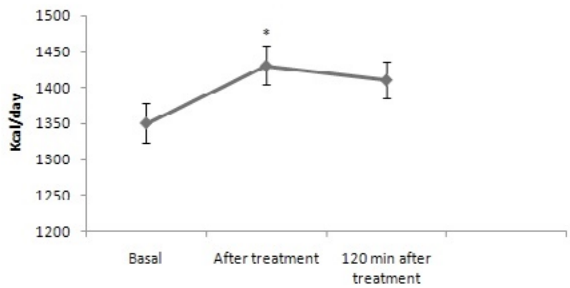


Figure 1 - Mean ± Standard Deviation of REE (Kcal/day) 60 minutes before, immediately after treatment, and 120 minutes after treatment with radiofrequency.

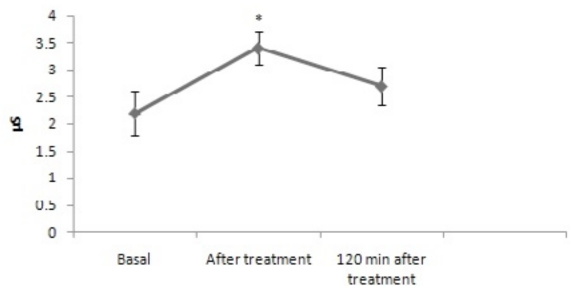


Figure 2 - Mean ± Standard Deviation of GSR 60 minutes before, immediately after treatment, and 120 minutes after treatment with radiofrequency.

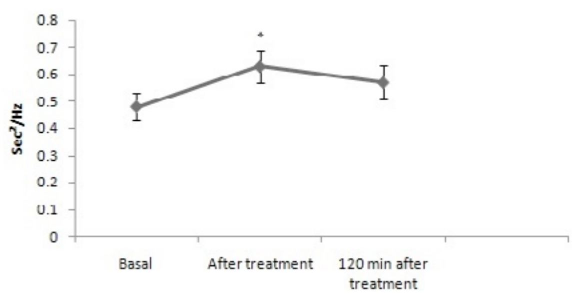


Figure 3 - Mean ± Standard Deviation of LF of HRV-power spectrum 60 minutes before, immediately after treatment, and 120 minutes after treatment with radiofrequency.

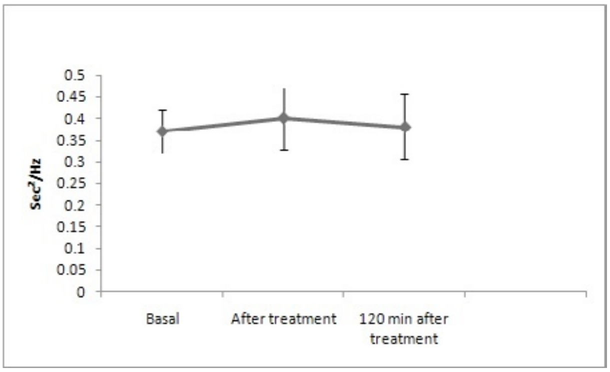


Figure 4 - Mean ± Standard Deviation of HF of HRV-power spectrum 60 minutes before, immediately after treatment, and 120 minutes after treatment with radiofrequency.

The demand for non-invasive methods of facial and body rejuvenation has experienced exponential growth over the last decade. There is a particular interest in safe and effective ways to decrease skin laxity and smooth irregular body contours and texture without downtime. These non-invasive treatments are being sought after because less time for recovery means less time lost from work and social endeavours.

The RF treatments are traditionally titrated to be non-ablative and are optimal for those wishing to avoid recovery time. Not only is there minimal recovery but there is also a high level of safety with aesthetic RF treatments.

The RF devices offer a non-ablative and non-invasive treatment option. By delivering RF energy in the form of a monopolar electric current, heat is generated because of tissue resistance to flow.

Heat damage, and the subsequent inflammatory cascade, alter collagen and produce a tightening effect[22,24].

Initially, in 2002, the Food and Drug Administration granted clearance for an RF device to treat periorbital rhytids. Later, the device was cleared for facial laxity and, in 2006, the device was cleared for treatment of non-facial skin, including the abdomen, thigh, and buttocks. Although a number of studies exist that demonstrate RF effect on facial skin, relatively fewer clinical studies have evaluated RF on non-facial skin.

To our knowledge, this is the first study to examine the effect of short-term of RF on HRV, GSR and REE. This study sheds further light on the controversial issue regarding the relationship between autonomic nervous system and body weight.

The present experiment indicates an increase of vegetative nervous activity during a treatment of RF and the increase of autonomic control regarding the sympathetic component. Such effects may be produced by local changes in tissue temperature (for example, thermally induced changes in regional blood flow) and others systemic effects may be due to the additional thermal load on the body.

An elevated core temperature increases metabolism and certain other functions such as heart rate, respiration rate, and nerve conduction velocity.

The increase of the sympathetic branch could be an important factor in the reduction of obesity. Indeed, an increase of sympathetic activity is related to a high-energy expenditure, so that an increased energetic cost could explain a decrease the body weight. The sympathetic nervous system is involved in the control of body weight[25], partly through its effect on energy expenditure[26].

The present experiment confirms also that GSR is a sensitive psycho-physiological index of stress, since the modification of GSR is related to changes in sympathetic arousal[27]. The evidence reported in this paper corroborates the validity of GRS as non-invasive tool in research on responses to stress[28].

The age-related decline in the vegetative control has been considered an important factor in the reduction of resting energy expenditure, therefore, young healthy male were analysed.

Indeed, suppression of sex hormones to post-menopausal levels reduces resting energy expenditure in young healthy women, through a reduction of autonomic nervous activity[29].

The originality of the present experiment is to emphasise the difference in the sympathetic modulation immediately after treatment with RF and that it remained significantly elevated at 120 min after treatment, compared to basal values.

This result is also useful in the interpretation of the relationship between the sympathetic nervous system and food intake in young subjects. It has demonstrated a significant influence of sympathetic activity on eating behaviour[4], also through an increase in thermogenesis[30,31]. Much experimental evidence has demonstrated that an increase in sympathetic and thermogenic activity reduces food intake. Therefore, the obesity can be due to an increase in food intake associated to a reduced activity of the sympathetic nervous system and thermogenesis.

Although food intake was not measured, the results of the present experiment are consistent with the hypothesis that a reduction in autonomic activity could play a determinant role in the increase in food intake and in the induction or maintenance of obesity.

References

1. C95.1-2005 IEEE Standard for Safety Levels with Respect to Human Exposure to Radio Frequency Electromagnetic Fields, 3 kHz to 300 GHz
2. Ahlbom A, Bergqvist U, Bernhardt JH et al. Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (up to 300 GHz). *Health Phys.* 1998; 74(4):494-522.
3. Adair ER, Mylacraine KS, Allen SJ. Thermophysiological consequences of whole body resonant RF exposure (100 MHz) in human volunteers. *Bioelectromagnetics.* 2003; 24(7):489-501.
4. Adair ER, Mylacraine KS, Cobb BL. Human exposure to 2450 MHz CW energy at levels outside the IEEE C95.1 standard does not increase core temperature. *Bioelectromagnetics* 2001; 22(6):429-439.
5. Fiala D, Lomas KJ, Stohrer M. Computer prediction of human thermoregulatory and temperature responses to a wide range of environmental conditions. *Int J Biometeorol.* 2001; 45(3):143-59.
6. Xu X, Werner J. A dynamic model of the human/clothing/environment-system. *Appl Human Sci.* 1997; 16(2):61-75.
7. Stolwijk JAJ, Hardy JD. Control of body temperature. In *Handbook of Physiology, Section 9, Reactions to environmental agents.* Edited by: Douglas HK. Bethesda, MD: American Physiological Society; 1977:45-69.
8. Heymsfield SB, Harp JB, Reitman ML, et al. Why do obese patients not lose more weight when treated with low-calorie diets? A mechanistic perspective. *Am J Clin Nutr.* 2007; 85(2):346–354.
9. Day DS, Gozansky WS, Van Pelt RE, Schwartz RS, Kohrt WM. Sex hormone suppression reduces resting energy expenditure and beta-adrenergic support of resting energy expenditure. *J Clin Endocrinol Metab.* 2005; 90(6):3312-3317.
10. Conny MA van Ravenswaaij-Arts, Louis AA Kollee, Jeroen CW Hopman, Gerard BA Stoelinga, Herman P van Geijn. Heart Rate Variability. *Ann Intern Med.* 1993; 118(6):436-447.
11. Triggiani AI, Valenzano A, Ciliberti MA. Heart rate variability is reduced in underweight and overweight healthy adult women. *Clin Physiol Funct Imaging.* 2015 Jul 25. doi: 10.1111/cpf.12281.
12. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability. Standard of measurements, physiological interpretation and clinical use. *Circulation.* 1996; 93(5):1043-1065.
13. Akselrod S, Gordon D, Ubel FA, Shannon DC, Berger AC, Cohen RJ. Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat-to-beat cardiovascular control. *Science.* 1981; 213(4504):220-222.
14. Valenzano A, Moscatelli F, Triggiani AI, et al Heart Rate Changes After Ultra-Endurance Swim From Italy to Albania: A Case Report. I*nt J Sports Physiol Perform.* (2015) doi: 10.1123/ijspp.2015-0035.
15. Petretta M, Bonaduce D, De Filippo E, et al. Assessment of cardiac autonomic control by heart period variability in patients with early-onset familial obesity. *Eur J Clin Invest.* 1995; 25(11):826-832.
16. Messina G, Valenzano A, Moscatelli F, et al. Effects of Emotional Stress on Neuroendocrine and Autonomic Functions in Skydiving. J. Psychiatry, 2015, 18:4, http://dx.doi.org/10.4172/2378-5756.1000280.
17. Messina G, De Luca V, Viggiano A, et al. Autonomic nervous system in the control of energy balance and body weight: personal contributions. *Neurol Res Int.* 2013; 2013:639280.
18. Matsumoto T, Miyawaki T, Ue H, Kanda T, Zenji C, Moritani T. Autonomic responsiveness to acute cold exposure in obese and non-obese young women. *Int J Obes Relat Metab Disord.* 1999; 23(8):793-800.
19. Matsumoto T, Miyawaki C, Ue H, Yuasa T, Miyatsuji A, Moritani T. Effects of capsaicin-containing yellow curry sauce on sympathetic nervous system activity and diet-induced thermogenesis in lean and obese young women. *J Nutr Sci Vitaminol (Tokyo).* 2000; 46(6):309-315.
20. Matsumoto T, Miyawaki C, Ue T, Kanda T, Yoshitake Y, Moritani T. Comparison of thermogenic sympathetic response to food intake between obese and non-obese young women. *Obes Res.* 2001; 9(2):78-85.
21. Antelmi I, de Paula RS, Shinzato AR, Peres CA,

Mansur AJ, Grupi CJ. Influence of age, gender, body mass index, and functional capacity on heart rate variability in a cohort of subjects without heart disease. *Am J Cardiol.* 2004; 93(3):381-385.

22. Hirsch J, Mackintosh RM. Measuring activity of the autonomic nervous system in humans. *Obes Res.* 2003; 11(1):2-4.
23. Fahrenberg J, Wientjes CJ. Recording methods in applied environments. In: Engineering psychophysiology. Issues & applications, edited by Backs RW, Boucsein W. London: Lawrence Erlbaum; 2000:111-138.
24. Fitzpatrick R, Geronemus R, Goldberg D, Kaminer M, Kilmer S, Ruiz-Esparza J. Multicentre study of non-invasive radiofrequency for periorbital tissue tightening. *Lasers Surg Med.* 2003; 33(4):232-242.
25. Bray GA. Reciprocal relation of food intake and sympathetic activity: experimental observations and clinical implications. *Int J Obes Relat Metab Disord.* 2000; 24 Suppl 2: S8-17.
26. Tentolouris N, Liatis S, Katsilambros N. Sympathetic system activity in obesity and metabolic syndrome. *Ann N Y Acad Sci.* 2006; 1083:129-152.
27. Critchley HD. Electrodermal responses: what happens in the brain. *Neuroscientist.* 2002; 8(2):132-42.
28. Messina G, Vicidomini C, Viggiano A, et al. Enhanced parasympathetic activity of sportive women is paradoxically associated to enhanced resting energy expenditure. *Auton Neurosci.* 2012; 169(2):102–106.
29. Day DS, Gozansky WS, Van Pelt RE, Schwartz RS, Kohrt WM. Sex hormone suppression reduces resting energy expenditure and beta-adrenergic support of resting energy expenditure. *J Clin Endocrinol Metab.* 2005; 90(6):3312-3317.
30. Monda M, Sullo A, De Luca V, Pellicano MP, Viggiano A. L-threonine injection into PPC modifies food intake, lateral hypothalamic activity, and sympathetic discharge. *Am J Physiol.* 1997; 273(2 Pt 2):R554-559.
31. Monda M, Viggiano A, De Luca V. Paradoxical effect of orexin A: hypophagia induced by hyperthermia. *Brain Res.* 2003; 961(2):220-228.

Aesthetic Medicine
Volume 1 · Number 2 · July-September 2015

Cellulite: Advances and Controversies on Treatments

Maurizio Giuliani[1], Panajot Papa[2], Gino Orsini[3], Maria Grazia Cifone[4]

[1]MD, Department of Life, Health & Environmental Sciences-Plastic Surgery Section - University of L'Aquila - Italy
[2]MD, Ph.D, Specialist of Plastic, Reconstructive and Aesthetic Surgery. Department of Medical Science - Albanian University - Albania
[3]MD, Ph.D, Department of Life, Health & Environmental Sciences - University of L'Aquila
[4]MD, Department of Life, Health & Environmental Sciences-Laboratory of Immunology and Immunopathology - University of L'Aquila

ABSTRACT

The therapeutical approach of cellulite aims at: 1) the reduction of the subcutaneous fat layer, 2) the increase in dermal thickness and elasticity and 3) the dissection of hypertrophic connective tissue septae, responsible for the most pronounced dermal indentions. This report analyses the vast therapeutic armamentarium for the treatment of cellulite with a focus on scientific advances and the controversies. This article provides a review of the international scientific literature and a systematic evaluation of the scientific evidence of the efficacy of the different treatments in cellulite reduction and supports various and different results.

Keywords
Cellulite, treatments, connective tissue, subcutaneous fat

Correspondence
Maurizio Giuliani, Department of Life, Health & Environmental Sciences - Plastic Surgery Section P.le S. Tommasi 1 - University of L'Aquila - Italy
E-mail: maurizio.giuliani@cc.univaq.it
Phone: +393381123435

Accepted for publication 30 July 2015

© 2015 Editrice Salus Internazionale srl

Introduction

Cellulite is a multifactorial condition and refers to a local alteration of the relief of the skin, which acquires an orange-peel, or mattress, appearance.

The orange-peel appearance results from the bulging of fat lobules out of their connective frame, into the dermis. The phenomenon is most commonly seen on hips, buttocks, and thighs but can also touch other areas, including the abdomen. Up to 90% of woman, over 20 years of age, are affected at various degrees, against only 2% of men[1].

Cellulite is seen as a normal condition by the medical community, but it is a serious cosmetic concern for most women affected by it. Although cellulite involves fat cells, it is not a manifestation of obesity, and even young women with a normal body mass index (BMI) may get it[2].

However, being overweight aggravates the presence of cellulite. Other risk factors include a predisposing genetic background, hormonal imbalance, medication that causes water retention, a sedentary lifestyle, prolonged periods of immobility, wearing tight clothes, smoking, excessive alcohol intake, unhealthy eating habits, stress, and being Caucasian. Some disorders have also been associated with cellulite, such as venous insufficiency, kidney problems, metabolic perturbations, and gastrointestinal alterations[3].

The exact aetiology of cellulite is still a matter of debate, but most scientists will agree on the involvement of reduced microcirculation, interstitial liquid infiltration (oedema), localised hypertrophy of adipocytes, oxidative stress, and persistent low-grade inflammation, combined with extracellular matrix alterations[4,5].

The extensibility, elasticity, and resilience of the skin are also abnormal[6].

The condition may start with hormone-induced activation of matrix-metalloproteinases (MMPs), which weakens capillary walls and challenges extracellular matrix integrity. As a result, fluid leaks out of vessels, and inflammatory cells are recruited within tissues where they generate inflammation and release additional MMPs. In an effort to heal, the damaged matrix of the septa becomes fibrous sclerotic. Meanwhile, hormones may also stimulate the metabolic activity of adipocytes, which increase in volume. Hypertrophic fat lobules tend to exert pressure on the surrounding capillaries, therefore adding to their fragility and hampering circulation.

The process is a reminder of what happens with aging in the upper layers of skin (dermis and epidermis) where changes are associated with MMP activation, altered biomechanical properties, reduced vessel integrity, and inflammation.

A clinical study conducted by Ortonne et al confirmed that the presence of cellulite precipitates skin aging in women over 30 years of age.

Therefore, it may be advisable to address both conditions simultaneously when treating cellulite[7,8,9].

The method most widely used to classify cellulite is that proposed by Nürnberger and Müller, which was based on 4 grades defined according to clinical presentation; **0:** no changes; **I:** visible changes at skin clamping or muscle contraction; **II:** visible changes when there is no manipulation; and **III:** visible changes associated with nodulations[10].

The methods used to evaluate the severity of cellulite include: anthropometric measurements, macro photography, bioelectrical impedance, thermogram, Doppler flowmetry, high-resolution two-dimensional ultrasound (US), nuclear magnetic resonance imaging, and skin biopsy followed by histological examination[11].

A wide range of products and treatments for cellulite reduction is available but currently existing treatments for cellulite have often shown only mild improvements in the appearance of cellulite, and most of these improvements are not maintained over time.

Studies about cellulite treatments are often limited by small patient groups, the lack of control groups, inadequate blinding of investigators, and a failure to test for statistical significance. This article provides an overview of the available treatments and their mechanisms of action.

Weight loss

Cellulite occurs in lean women and obese women and men. Weight gain, however, can accentuate the appearance of cellulite. There have been reports of weight loss and its effects on cellulite. Smalls et al revealed that weight loss can have variable effects on cellulite grade and that on average, cellulite severity decreased following weight loss[12].

This is especially true for affected individuals who have a higher body mass index (BMI) and a greater severity of cellulite grading. These individuals experienced improvement in cellulite severity with significant weight loss. Smalls at al also found an increase in skin compliance (skin looseness) in all of their study participants. Increased skin compliance did not necessarily have an impact on subjects whose cellulite improved, but it adversely affected the individuals whose cellulite became worse with weight loss.

It is not clear, however, if skin compliance plays a significant role in the aetiology of cellulite. Their study also revealed that skin dimpling did not significantly improve with weight loss, with only a slight decrease in the depth of dimples.

They attributed this finding to the fact that skin dimpling is caused by dermal collagenous septae that do not necessarily improve with weight loss.

Different regions of the body respond differently to weight loss (i.e., abdominal vs. femoral).

Mauriège et al revealed very interesting findings regarding adipose tissue; their research focused on the response to a low-calorie diet and the effects thereof on adrenoreceptor (AR) sensitivity on adipocytes of the abdominal and femoral regions in both males and females[13,14].

Their study showed that there is an overall significant reduction in fat cell weight in both sexes by 15% to 20% after an average 10-kg weight loss (P \.1 and P \.05). Basal lipolysis, maximal lipolytic response to isoproterenol (α β-AR agonist), and dobutamine and procaterol (which are β_1- and β_2-AR agonists, respectively) as well as the maximum antilipolytic effects of epinephrine (an α_2-AR agonist) were similar before and after weight loss.

However, both β_1- and β_2-AR lipolytic sensitivities and overall β-AR density were increased in both genders after weight loss; this effect was more marked in the subcutaneous abdominal adipose tissue as compared to femoral adipose tissue (P\.001 to. 05). α_2-AR antilipolytic sensitivity was reduced in adipose cells from both regions in women, but only in abdominal adipose cells in men (P\.05), even though α_2-AR density remained unchanged.

In addition, femoral adipocytes are larger in women than in men. In their study, Mauriège et al found that this difference loses its significance after weight loss, because adipose cell size reduction was found to be the same order of magnitude in both genders[13,14].

The result of their work is interesting from the viewpoint of cellulite management. Because we know that in femoral adipose cells the α_2-ARs outnumber, which are antilipolytic (as opposed to abdominal adipocytes, in which the β-ARs outnumber, with high lipolytic response to catecholamine stimulation), abdominal adipocytes are the main source of mobilising energy sources during times of calorie deprivation.

Of interest is the fact that the sensitivity of α_2-ARs decreases during times of fasting. However, their number remains unchanged. Unless weight reduction is a continuous process, femoral adipocytes will regain their size and antilipolytic activity. Further studies need to be performed to investigate the effects of a low-calorie diet over a long period of time and what effect that diet will have on femoral adipocyte α_2-AR density and sensitivity[14].

Topical Treatments

Cosmeceuticals represent a new category of products placed between cosmetics and pharmaceuticals that are intended for the enhancement of both the health and beauty of the skin[15].

These products are found in many forms, including vitamins, peptides, growth factors, and botanic extracts. In particular, cosmeceuticals containing topical vitamin formulations are increasing in popularity in skin care[16].

However, available cosmeceuticals show little effect in improving cellulite, and none has shown to lead to its complete disappearance. It is unlikely that topically applied pharmacologic agents can alter the fundamental cutaneous architecture existing in cellulite-prone areas. Therefore, various treatments currently available are only partially or temporarily effective, and topical treatments are being considered as an adjunctive cellulite treatment. Topical anti-cellulite preparations may be divided in 4 major groups according to their mechanism of action.

These treatments include agents that respectively:

- increase the microcirculation flow
- reduce lipogenesis, promote lipolysis
- restore the normal structure of dermis and subcutaneous tissue
- prevent free radical formation or scavenge free radicals.

Several pharmacologic agents available for the treatment of cellulite lack scientific evidence of long-term efficacy. Only two agents, aminophylline and retinoids, have been critically evaluated[17,18].

Furthermore Turati F. et al in their article provide a systematic evaluation of the scientific evidence of the efficacy of cosmetic products in cellulite reduction and supports a moderate efficacy in thigh circumference reduction[19].

Topical agents are often used by women to treat cellulite. Normally, they are recommended to treat mild-to-moderate cellulite and as an adjuvant treatment for severe cellulite.

Hexsel D. and Soirefmann M., in their clinical experience, including the results of a study with a small number of patients using topical treatment for cellulite, confirm that, even knowing the limited effects of topical products, there is a significant positive impact in self-esteem and in the patients' compliance when they are using topical treatment[18].

Manual/Mechanical Massage

The technique of manual lymphatic drainage (MLD), developed by the Danish biologists Emil and Estrid Vodder in 1936, is one of the main pillars of the treatment of lymphoedema, because its movements help lymphatic circulation[20].

Its purpose is draining fluids accumulated between interstitial spaces, particularly in dermis, collaborating thus for tissue fluid balance by means of pressure differentials that will promote the displacement of lymph and interstitial fluid towards the bloodstream. Superficial and gentle manoeuvres are performed throughout the path of lymphatic vessels to eliminate lymph fluids and reduce oedema[21].

Considering that MLD is a technique aimed at stimulating the lymphatic system, reducing fluid excess, and eliminating metabolic waste, and that cellulite seems to be related to metabolic changes and fluid accumulation in dermal connective tissue leading to the worsening of anatomical characteristics, MLD may be beneficial in the control of this condition.

Schonvvetter B. et al investigated the efficacy and safety of manual lymphatic drainage for cellulite management. In their work a significant reduction of elastic return of skin on buttocks, which means skin elasticity worsening, was observed and all measures obtained by ultrasound images showed no changes ($p>0.05$). Their final observations were that manual lymphatic drainage is safe but not effective as an isolated approach for cellulite management.

Further randomised, controlled or comparative studies about manual lymphatic drainage for cellulite control, as unique or combined therapeutic modality, are necessary[22].

The basis for various massage/suction techniques used for cellulite treatment rests on the premise that the condition is caused by impaired circulation. Endermologie or skin kneading is a nonpharmacological method that employs mechanical means to mobilise the subcutaneous fat in affected areas[14].

Despite the high cost of Endermologie treatment, little evidence exists to support its efficacy. Proponents of this process claim that massage/suction improves the disorganisation of subcutaneous tissue structures and improves lymphatic flow. The procedure is performed twice weekly, with each session lasting 10 to 45 minutes.

A 12-week study by Collis et al compared healthy individuals with cellulite treated with Endermologie and/or aminophylline cream (a phosphodiesterase inhibitor) and found no statistical difference in thigh measurements between patients[23].

Any subjective improvement noted by study participants was attributed secondary to weight loss and exercise rather than skin kneading. The results of this study were challenged by the fact that treatment duration was only 10 minutes and that improvement should have been analysed by more objective criteria than subjective self-assessment alone. Chang et al showed promising results using Endermologie for the treatment of thigh circumference reduction. The study group exhibited a wide range of body types, initial weights, and final results[14,24].

Out of 85 patients, 46 patients completed seven sessions of treatment and showed a mean index reduction in body circumference of 1.34 cm, while 39 patients who completed 14 sessions of treatments showed a mean index reduction in body circumference of 1.83 cm. A decrease in mean body circumference index was seen regardless of weight loss or gain in study participants.

Even though evidence exists that Endermologie can reduce the thigh circumference in a dose and time-dependent fashion, the long-term efficacy and longevity of these effects is still questionable.

Randomised controlled trials need to be conducted with objective evaluation of response as opposed to subject's satisfaction, such as the use of non-invasive imaging techniques to monitor the response of massage/suction and the persistent changes that are claimed as proposed mechanisms of action over a period of time[14].

Mesotherapy

Michel Pistor gave an intravenous injection of procaine to a man suffering from asthma in France during the 1950s, and this experience started the practice of mesotherapy. Although the asthma did not improve, the man's longstanding deafness improved temporarily. Dr Pistor concluded that injection into the subcutaneous tissues would give the best results, and claimed many health benefits from his method of injecting procaine locally.

Since the tissue into which he was injecting was of mesodermal origin, he called this technique mesotherapy[25,26].

Mesotherapy is a controversial cosmetic procedure and today falls into two categories.

Lipolytic mesotherapy using lipolytic stimulators requires more frequent treatments as the fat cells are not destroyed and can refill over time.

Ablative mesotherapy destroys fat cells with a detergent, causes inflammation and scarring from the fat necrosis, but requires fewer treatments[27].

Mesotherapy, a technique that uses the injection of various substances into the subcutaneous fat to dissolve the fat, is a popular treatment for cellulite.

However, few studies substantiate the benefit of this approach. The technique involves a series of injections delivered into the subcutaneous.

The solutions have included compounds like methylxanthines, such as caffeine, aminophylline, and theophylline, etc., which cause lipolysis via phosphodiesterase inhibition and elevation of cyclic adenosine monophosphate (c-AMP) levels, as well as hormones, enzymes, herbal extracts, vitamins, and minerals.

Herreros et al about mesotherapy claim that there is only scant scientific information about this subject published in periodicals indexed on MedLine. Most indexed publications about this subject deal with the complications of this technique and well-researched scientific studies about this technique are necessary to offer data to medical professionals that will clearly explain to patients both the benefits and the risks of these procedures[28].

The lack of a precise treatment protocol, the unpredictable outcome, and the risk of localised adverse events including oedema, ecchymosis, tender subcutaneous nodules, infection, urticarial reactions, and irregular skin contours have discouraged many clinicians from attempting this technique[14].

The one ingredient most consistently used is phosphatidylcholine (soybean lecithin extract), to which someone attribute the ability to induce lipolysis via the activation of β-ARs.

Rose et al showed that a mixed septal and lobular panniculitis with abundant fat necrosis and serous lipoatrophy is seen after phosphatidylcholine injection[14,29].

Rotunda et al and Palumbo et al have identified sodium deoxycholate, a detergent that produces nonspecific destruction of cell membranes, as a major active ingredient in this therapy[30,31].

Brown and Duncan state that the injection of PC-DC did not produce anticipated aesthetic results.

The lack of tissue specificity of PC-DC injections creates a concern regarding long-term safety especially when the drug is injected by untrained practitioners[32,33].

Carboxytherapy

Carbon dioxide (CO_2) therapy or carboxytherapy is the transcutaneous administration of CO_2 for therapeutic purposes. This treatment purports to affect fat cells and circulation. Sound physiologic principles underlie the possible mechanisms of CO_2 action, modulating its effects on the skin and subdermal layers. In a histologic study, Brandi C et al reported fracturing of the adipose tissue with release of triglycerides in the intercellular spaces and adipocytes presenting thin fracture lines in the plasma membrane[34].

These cell damages did not involve the connective spaces where the major vascular structures are located. The dermis presented a thicker appearance than before the treatment, with the collagen fibres distributed more diffusely. The same authors reported microcirculatory changes after CO_2 therapy, reflected by increased perfusion as measured by laser Doppler flowmetry and increased oxygen tension as measured by transcutaneous oxygen tension. This is to be expected from the Bohr Effect on the oxygen dissociation curve.

Ferreira et al, in a blind, interventional, cross sectional study, investigated CO_2 injection in the dermis of Wistar rats. Treated rats showed intense collagen turnover in their skin samples compared with control animals, which had saline injections[35].

These findings support the subjective clinical findings of improved skin texture after CO_2 therapy.

Brandi C et al showed increased skin elasticity up to 55.5%, as measured by the Cutometer SEM 474 Courage-Khazaka (CK Electronics, Koln, Germany), when carboxytherapy is combined with liposuction for the treatment of cellulite on lateral thighs[36,37].

Cryolipolysis

Cryolipolysis is an interesting technique for the treatment of cellulite and localised adiposities.

The principle behind this technology exploits the premise that adipocytes are more susceptible to cooling than other skin cells. Precise application of cold temperatures triggers the death of adipocytes that are subsequently engulfed and digested by macrophages[38,39].

No changes in subcutaneous fat are noticeable immediately after treatment. An inflammatory process stimulated by apoptosis of adipocytes, as reflected by an influx of inflammatory cells, can be seen within 3 days after treatment and peaks at approximately 14 days thereafter as the adipocytes become surrounded by histiocytes, neutrophils, lymphocytes, and other mononuclear cells.

At 14–30 days after treatment, macrophages and other phagocytes surround, envelope, and digest the lipid cells as part of the body's natural response to injury. Four weeks after treatment, the inflammation lessens and the adipocyte volume is decreased. Two to three months after treatment, the interlobular septa are distinctly thickened and the inflammatory process further decreases. By this time, the fat volume in the treated area is apparently decreased and the septae account for the majority of the tissue volume[40,41].

In clinical studies, cryolipolysis was shown to reduce subcutaneous fat at the treatment site by up to 25% after one treatment. Improvements were seen in 86% of treated subjects[42].

Krueger et al do not deny the effectiveness of the technique but observe that more randomised, controlled, double-blind studies with a sufficient number of subjects and objective measurements with high reproducibility are needed to evaluate the short-term and long-term efficacy and side effects of cryolipolysis. Further research should be directed towards identifying more ideal settings and maintenance programmes[43].

Ultrasound (US-HIFU)

Ultrasound (US) has long been an intriguing medical modality because of its non-invasive nature, low cost, and relatively low rate of complications[44].

Sound is transmitted by mechanical vibrations; ultrasound technology utilises vibrations that are outside of the range of human hearing.

The frequency threshold between audible sound waves and ultrasound waves is fixed at 20 kHz.

Hertz (Hz), international unit of measurement of the frequency, represents the number of cycles per second of compression and expansion. US parameters are wavelength, frequency, propagation speed, intensity and attenuation.

Ultrasounds effects on biological tissues are mechanical, thermal and cavitational. US waves through fat tissue create microcavities with a series of expansion and compression cycles on cell membranes, leading to cell disruption and fat liquefaction. Palumbo P et al studied the action of “low frequency, high intensity US” on “ex vivo” human adipose tissue by evaluating the biological effects induced[45].

The authors investigated the effects of both external and surgical ultrasound-irradiation by evaluating, the sample weight loss and fat release, the histological architecture alteration the apoptosis induction as well the influence of saline buffer tissue-infiltration on the effects of ultrasound irradiation. The experimental results demonstrated that both transcutaneous and surgical ultrasound exposure caused a significant weight loss and fat release and the effectiveness of US was much higher when the tissue samples were previously infiltrated with saline buffer.

Evaluation of histological characteristics of US-irradiated samples showed a clear alteration of adipose tissue architecture as well a prominent destruction of collagen fibres that were dependent on US intensity and most relevant in saline buffer-infiltrated samples.

The structural changes of collagen bundles present between the lobules of fat cells were confirmed through scanning electron microscopy (SEM) which clearly demonstrated how ultrasound exposure induced a drastic reduction in the compactness of the adipose connective tissue and an irregular arrangement of the fibres with a consequent alteration in the spatial architecture.

The analysis of the composition of lipids in the fat releases from adipose tissue after US treatment with surgical device showed, in agreement with the level of adipocyte damage, a significant increase mainly of triglycerides and cholesterol.

US exposure had been shown to induce apoptosis as shown by the appearance DNA fragmentation.

Accordingly, US treatment led to a down-modulation of the procaspase-9 expression and to an increased level of the caspase-3 active form[45,46].

High-intensity focused ultrasound has been used effectively for non-invasive body sculpting to either tighten skin by contracting collagen fibres or remove adipose tissue stores via ablation[47].

Previous studies have demonstrated that optimal results are obtained when the patients have a BMI less than 30 kg/m^2 and have at least 1 cm of adipose tissue beyond the treatment area[48,49].

Average treatment times are reported at 45 to 60 minutes with minimal to no recovery time. Patient satisfaction rates have been reported as high as 70% at 3 months follow-up.

Fatemi et al have shown that within 18 weeks of HIFU-mediated adipose tissue ablation, 95% of the cellular debris had been reabsorbed, without post treatment changes in patients’ lipid profiles or comprehensive metabolic panels[49,50,51].

Radiofrequency (RF)

Radiofrequency (RF) energy is produced by an electromagnetic field. Radiofrequency energy is conducted electrically to tissue, and heat is produced when the tissue’s inherent resistance (impedance) converts the electrical current to thermal energy.

This reaction is dictated by the following formula: energy (J) = I2 X R X T (where I = current, R = tissue impedance, and T = time of application)[52].

High-impedance tissues, such as subcutaneous fat, generate greater heat and account for the deeper thermal effects of RF devices. The first device in this area was a monopolar radiofrequency (RF) device that was FDA approved for the non-invasive tightening of periorbital rhytides using this proven mechanism of skin tightening[53].

Disadvantages of that first generation device included inconsistency of clinical results and significant discomfort during treatment.

Newer bipolar and monopolar RF devices are constantly being developed to improve results and minimise discomfort. Both monopolar and bipolar RF devices have been used for cutaneous applications.

Monopolar systems deliver current through a single contact point with an accompanying grounding pad that serves as a low resistance path for current flow to complete the electrical circuit. Monopolar electrodes concentrate most of their energy near the point of contact, and energy rapidly diminishes as the current flows toward the grounding electrode.

Bipolar devices pass electrical current only between two positioned electrodes applied to the skin.

No grounding pad is necessary with these systems because no current flows throughout the rest of the body. Lately, even tripolar RF systems have been devised.

Tripolar treatments exclusively utilise the effects of combining unipolar RF and bipolar RF energies in one applicator to simultaneously heat deep and superficial tissue layers, while protecting the surface skin. The tripolar RF technology uses sophisticated algorithms to control the treatment electrodes, which change the current and polarity to achieve variable energy focus in different fat layers resulting in visible clinical results[54].

Lolis and Goldberg in their review on radiofrequency concluded that its results are modest and found mostly in non-randomised and non-controlled studies that assessed efficacy by subjective methods, which makes it difficult to draw conclusions about its benefit[55].

On the contrary, a clinical study by Franco et al shows that RF devices can be used to selectively heat subcutaneous adipose tissue and induce lethal thermal damage to adipose tissue while sparing the overlying and underlying tissues.

Thermal exposures to 43–45 Celsius degrees over several minutes may result in a delayed adipocyte death response. This may have a role in decreasing overall waist circumference and fat removal as well.

Uniform heating of subcutaneous tissue at sustained therapeutic temperatures has been shown to trigger apoptosis of cells.

A decrease in fat volume is supposed to be seen 3–8 weeks after treatment[56].

A randomised human tissue studies published by De La Casa Almeida M et al have shown a high voltage electroporation apoptotic effect on up to 30% of the adipocytes in the field of treatment, leading to a permanent RF induced fat reduction[57].

Acoustic Wave Therapy (AWT)

Shockwaves transmit mechanical energy from the place of generation to distant areas. They display a single, mainly positive pressure pulse of large amplitude that is followed by comparatively small tensile wave components[58].

When using shockwaves for therapy, effects that make the pressure pulse even steeper as a result of nonlinearity in the propagation medium, as well as phenomena such as refraction and diffraction at acoustic interfaces, must be taken into consideration. The fact that shockwaves selectively effect acoustical interfaces (connecting two media, each with a different density; e.g. oil/water) and pass through homogenous elastic tissue without damage to the majority of the area is medically important. Unfocused extracorporeal shockwaves radially spread with an energy flow density per pulse smaller than 0.1 mJ/mm^2; their power decreases by one third for every centimetre of penetration into the tissue.

The biological mechanism of action after a shockwave is still unknown to a large extent.

Biological reactions of liberation of different agents (measured by immunohistochemistry) such as vascular endothelial growth factor (VEGF), endothelial nitric oxide synthase (ENOS), and proliferating cell nuclear antigen (PCNA) have been reported.

On the subcellular level, the damages are: increase of permeability of the cell membrane, lesions of the cytoskeleton, and changes to mitochondria, endoplasmic reticulum, and nuclear membrane of the cell that may lead to apoptosis. Shockwaves are also effective as a means of increasing local blood circulation and metabolism, as well as having a high antibacterial effect[59,60,61].

To date, the potential molecular and cellular mechanisms of action of shock waves on skin/fat tissue described in the literature can be summarised in: stimulation of blood and lymph circulation, increased membrane permeability, stimulation of the exchange of blood lipids, stimulation of metabolism, reduced oxidative stress, increased antioxidants (including ascorbic acid), induction of neocollagenogenesis and neoelastinogenesis, increased angiogenesis, expression of vascular endothelial growth factor, endothelial nitric oxide synthase, and proliferating cell nuclear antigen, apoptosis of fat cells triggered by inflammation[62].

On the topic Schlaudraff KU et al claim that radial shock wave therapy is a safe and effective treatment option for cellulite but the individual clinical outcome cannot be predicted by the patient's individual cellulite grade at baseline, BMI, weight, height, or age[63].

Nassar AH et al conducted a randomised, controlled clinical study to investigate the safety and efficacy of acoustic wave therapy in body contouring and the results obtained were not statistically significant[64].

Low-Level Laser Therapy (LLLT)

The first reports of Low-Level Laser Therapy (LLLT) were published by Endre Mester from the Semmelweiss University in Hungary. He originally noticed hair regrowth in mice exposed to a ruby laser (694 nm) and later used HeNe laser (632.8 nm) to stimulate wound healing in animal models and subsequently in clinical studies[65,66,67].

The mechanism of action of LLLT on fat remains somewhat controversial. Neira et al in their first article attributed the effects of LLLT on adipocytes to formation of transitory micropores, which were visualised on Scanning Electron Microscope[68,71,72].

These pores were proposed to allow the release of intracellular lipids from adipocytes. One possible explanation might be that, increased ROS levels following LLLT initiate a process known as lipid peroxidation where ROS reacts with lipids found within the cellular membranes, and temporarily damages them by creating pores. However, in an attempt to replicate Neira data, Brown et al failed to visualise any transitory micropores[71].

Another possible mechanism of action for release of lipids was proposed to be through activation of the complement cascade, which could cause induction of adipocyte apoptosis and subsequent discharge of lipids. To investigate the complement activation theory, Caruso-Davis et al exposed differentiated human adipocytes to plasma.

With and without irradiation there was noted to be no difference in complement-induced lysis of adipocytes. Although no enzymatic assays were done to determine levels of complement within the plasma, the group concluded that laser does not activate complement[67,74].

Lastly, in contrast to Neira findings, it was observed that the external cell membrane preserved its normal appearance in electron microscopy, presenting neither ruptures nor pores, and no other signs of lipolysis were observed, except for the disposition of fused fatty vacuoles. An additional paper called into question the ability of red light (635 nm) to penetrate effectively below the skin surface and into the subdermal tissues[68,74].

In a supportive commentary Peter Fodor stated; "One could postulate that the presence of the black dots on SEM images on the surface of fat cells reported by Neira et al. could represent an artefact" [69,74].

It is also possible that LLLT stimulates the mitochondria in adipocytes that in turn leads to an increase ATP synthesis with subsequent upregulation of cAMP; the increased cAMP could activate protein kinase which could stimulate cytoplasmic lipase, this enzyme converts triglycerides into fatty acids and glycerol, which can both pass through pores formed in the cell membrane causing a shrinkage in adipocytes[70,73,74].

However, Caruso-Davis et al findings from in vitro studies on human fat cells obtained from subcutaneous fat, irradiated with 635–680 nm LLLT for 10 minutes demonstrated no increase of glycerol and fatty acids suggesting that fat loss from the adipocytes in response to laser treatment was not due to a stimulation of lipolysis, nevertheless they did detect increased plasmatic triglyceride levels which further supported the formation of pores in adipocytes[69,74].

Conclusions

Cellulite is a multifactorial condition that is present in 80-90 % of post-pubertal women. Despite its high prevalence, it remains a major cosmetic concern for women.

Several therapeutic options for cellulite are available today but none has been shown to lead to clinical resolution. While many treatments claim to be able to improve the appearance of cellulite, the long-term effectiveness of these treatments and whether the logic behind these treatments can lead to a long-term improvement, has not been extensively reviewed. Many studies emphasise that only a combination of treatments may control cellulite but there is a need of studies to evaluate the actual contribution of each modality when combined with other modalities[14].

Luebberding S et al recently published a systematic review about the cellulite treatments. In total, 67 articles were analysed for the following information: therapy, presence of a control group, randomisation, blinding, sample size, description of statistical methods, results, and level of evidence.

Most of the evaluated studies, including laser and light-based modalities, radiofrequency, and others had important methodological flaws; some did not use cellulite severity as an endpoint or did not provide sufficient statistical analyses.

Of the 67 studies analysed in this review, only 19 were placebo-controlled studies with randomisation. Some evidence for potential benefit was only seen for acoustic wave therapy (AWT) and the 1440 nm Nd:YAG minimally invasive laser.

The conclusions of the review claim that no clear evidence of good efficacy could be identified in any of the evaluated cellulite treatments[75].

References

1. Emanuele E, Bertona M, Geroldi D. A multilocus candidate approach identifies ACE and HIF1A as susceptibility genes for cellulite. *J Eur Acad Dermatol Venereol.* 2010; 24(8):930-935.
2. Kruglikov I. The pathophysiology of cellulite: can the puzzle eventually be solved? *J Cosmet Dermatol Sci Appl.* 2012; 2(1):1-7.
3. Rossi AB, Vergnanini AL. Cellulite: a review. *J Eur Acad Dermatol Venereol.* 2000; 14(4):251-262.
4. Terranova F, Berardesca E, Maibach H. Cellulite: nature and aetiopathogenesis. *Int J Cosmet Sci.* 2006; 28(3):157–167.
5. de la Casa Almeida M, Suarez Serrano C, Rebollo Roldán J, Jiménez Rejano JJ. Cellulite's aetiology: a review. *J Eur Acad Dermatol Venereol.* 2013; 27(3):273-278.
6. Draelos ZD. The disease of cellulite. *J Cosmet Dermatol.* 2005; 4(4):221-222.
7. Ortonne JP, Zartarian M, Verschoore M, Queille-Roussel C, Duteil L. Cellulite and skin aging: is there any interaction? *J Eur Acad Dermatol Venereol.* 2008; 22(7):827-834.
8. Khan MH, Victor F, Rao B, Sadick NS. Treatment of cellulite: Part I. Pathophysiology. *J Am Acad Dermatol.* 2010; 62(3):361-370.
9. Dupont E, Journet M, Oula ML, et al. An integral topical gel for cellulite reduction: results from a double-blind, randomised, placebo-controlled evaluation of efficacy. *Clin Cosmet Investig*

Dermatol. 2014; 7:73-88.
10. Nürnberger F, Müller G. So-called cellulite: an invented disease. *J Dermatol Surg Oncol.* 1978; 4(3):221-9.
11. Hexsel DM, Dal'forno T, Hexsel CL. A validated photonumeric cellulite severity scale. *J Eur Acad Dermatol Venereol.* 2009; 23(5):523-8.
12. Smalls LK, Hicks M, Passeretti D, et al. Effect of weight loss on cellulite: gynoid lipodystrophy. *Plast Reconstr Surg.* 2006; 118(2):510-6.
13. Mauriège P, Imbeault P, Langin D, et al. Regional and gender variations in adipose tissue lipolysis in response to weight loss. *J Lipid Res.* 1999; 40(9):1559-71.
14. Khan MH, Victor F, Rao B, Sadick NS. Treatment of cellulite: Part II. Advances and controversies. *J Am Acad Dermatol.* 2010; 62(3):373-384.
15. Martin KL, Ailor SK. An ounce of prevention. *Mo Med.* 2011; 108(1):64-68.
16. Manela-Azulay M, Bagatin E. Cosmeceuticals vitamins. *Clin Dermatol.* 2009; 27(5):469-474.
17. Hexsel D, Zechemeister do Prado D, Goldman MP: Topical management of cellulite, in Goldman M, Hexsel D (eds): Cellulite: Pathophysiology and Treatment. London, England, Informa Health Care, 2010, pp 62-68.
18. Hexsel D, Soirefmann M. Cosmeceuticals for Cellulite. *Semin Cutan Med Surg.* 2011; 30(3):167-170.
19. Turati F, Pelucchi C, Marzatico F, et al. Efficacy of cosmetic products in cellulite reduction: systematic review and meta-analysis. *J Eur Acad Dermatol Venereol.* 2014; 28(1):1-15.
20. Leduc A, Leduc O. Drenagem linfática teoria e prática. Traduzido por Marcos Ikeda. São Paulo: Manole; 2000.
21. Godoy JMP, Godoy MFG. Drenagem linfática manual: novo conceito. *J Vasc Bras.* 2004; 3:77-80.
22. Schonvvetter B, Laudicéia Marques Soares J, Bagatin E. Longitudinal evaluation of manual lymphatic drainage for the treatment of gynoid lipodystrophy. *An Bras Dermatol.* 2014; 89(5):712-18.
23. Collis N, Elliot LA, Sharpe C, Sharpe DT. Cellulite treatment: a myth or reality: a prospective randomised, controlled trial of two therapies, endermologie and aminophylline cream. *Plast Reconstr Surg.* 1999; 104(4):1110-4.
24. Chang P, Wieseman J, Jacoby T, Salisbury AV, Eresk RA. Non-invasive mechanical body contouring: (Endermologie) a one-year clinical outcome study update. *Aesthetic Plast Surg.* 1998; 22(2):145-53.
25. Pistor M. Mesotherapy. Paris: Librairie Maloine S.A.;1964.
26. Caruso MK, Roberts AT, Bissoon L, Stan Self K, Guillot TS, Greenway FL. An evaluation of mesotherapy solutions for inducing lipolysis and treating cellulite. *JPRAS.* 2008; 61(11):1322-4. (edited)
27. Sarkar R, Garg VK, Mysore V. Position paper on mesotherapy. *Indian J Dermatol Venereol Leprol.* 2011; 77(2):232-7.
28. Herreros FO, Moraes AM, Velho PE. Mesotherapy: a bibliographical review. *An Bras Dermatol.* 2011; 86(1):96-101.
29. Rose PT, Morgan M. Histologic changes associated with mesotherapy for fat dissolution. *J Cosmet Laser Ther.* 2005; 7:17-9.
30. Rotunda AM, Suzuki H, Moy RL, Kolodney MS. Detergent effects of sodium deoxycholate are a major feature of an injectable phosphatidylcholine formulation used for localised fat dissolution. *Dermatol Surg.* 2004; 30(7):1001-8.
31. Palumbo P, Melchiorre E, La Torre C, et al. Effects of phosphatidylcholine and sodium deoxycholate on human primary adipocytes and fresh human adipose tissue. *Int J Immunopathol Pharmacol.* 2010; 23(2):481-489.
32. Brown SA. Commentary on: Metabolic and structural effects of phosphatidylcholine and deoxycholate injections on subcutaneous fat: a randomised, controlled trial. *Aesthet Surg J.* 2013; 33(3):409-10.
33. Duncan D. Commentary on: Metabolic and Structural effects of phosphatidylcholine and deoxycholate injections on subcutaneous fat: a randomised, controlled Trial. *Aesthet Surg J.* 2013; 33(3):411-413.
34. Brandi C, D'Aniello C, Grimaldi L, et al. Carbon dioxide therapy in the treatment of localised adiposities: clinical study and histopathological correlations. *Aesthetic Plast Surg.* 2001; 25(3):170-174.
35. Ferreira JCT, Haddad A, Tavares SA. Increase in collagen turnover induced by intradermal injection of carbon dioxide in rats. *J Drugs Dermatol.* 2008; 7(3):25–30.
36. Brandi C, D'Aniello C, Grimaldi L, Caiazzo E, Stanghellini E. Carbon dioxide therapy: effects on skin irregularity and its use as a complement to liposuction. *Aesthetic Plast Surg.* 2004; 28(4):222-225.
37. Lee GS. Carbon dioxide therapy in the treatment of cellulite: An audit of clinical practice. *Aesthetic Plast Surg.* 2010; 34(2):239-243.
38. Manstein D, Laubach H, Watanabe K, Farinelli W, Zurakowski D, Anderson RR. Selective cryolysis: a novel method of non-invasive fat removal. *Lasers Surg Med.* 2008; 40(9):595-604.
39. Zelickson B, Egbert BM, Preciado J, et al. Cryolipolysis for non-invasive fat cell destruction: initial results from a pig model. *Dermatol Surg.* 2009; 35(10):1462-1470.
40. Nelson AA, Wasserman D, Avram MM.

Cryolipolysis for reduction of excess adipose tissue. *Semin Cutan Med Surg.* 2009; 28(4):244-249.
41. Avram MM, Harry RS. Cryolipolysis for subcutaneous fat layer reduction. *Lasers Surg Med.* 2009; 41(10):703-708.
42. Alian HR, Avram MM. Cryolipolysis: a historical perspective and current clinical practice. *Semin Cutan Med Surg.* 2013; 32(1):31-34.
43. Krueger N, Mai SV, Luebberding S, Sadick NS. Cryolipolysis for non-invasive body contouring: clinical efficacy and patient satisfaction. *Clin Cosmet Investig Dermatol.* 2014; 7:201-205.
44. Kennedy JE. High-intensity focused ultrasound in the treatment of solid tumours. *Nat Rev Cancer.* 2005; 5(4):321-7.
45. Palumbo P, Cinque B, Miconi G, et al. Biological effects of low frequency high intensity ultrasound application on ex vivo human adipose tissue. *Int J Immunopathol Pharmacol.* 2011; 24(2):411-422.
46. Zoccali G, Orsini G, Scandura S, Cifone MG, Giuliani M. Multi-frequency ultrasound-assisted liposuction: 5 years of experience. *Aesthetic Plastic Surgery.* 2012; 36(5):1052-61.
47. Jewell ML, Solish NJ, Desilets CS. Non-invasive body sculpting technologies with an emphasis on high-intensity focused ultrasound. *Aesthetic Plast Surg.* 2011; 35(5):901-12.
48. Stephan PJ, Kenkel JM. Updates and advances in liposuction. *Aesthet Surg J.* 2010; 30(1):83-97.
49. The American Academy of Cosmetic Surgery. 2006 Guidelines for Liposuction Surgery. Available at: http://www.cosmeticsurgery.org/media/2006 liposuction guidelines.pdf. Accessed March 26, 2010.
50. Fatemi A. High-intensity focused ultrasound effectively reduces adipose tissue. *Semin Cutan Med Surg.* 2009; 28(4):257-62.
51. Tadisina KK, Patel MN, Chopra K. High-intensity focused ultrasound in aesthetic plastic surgery. *Eplasty.* 2013; 13:ic56.
52. Fitzpatrick R, Geronemus R, Goldberg D, Kaminer M, Kilmer S, Ruiz-Esparza J. Multicentre study of non-invasive radiofrequency for periorbital tissue tightening. *Lasers Surg Med.* 2003; 33(4):232-42.
53. Sadick NS, Mulholland RS. A prospective clinical study to evaluate the efficacy and safety of cellulite treatment using the combination of optical and RF energies for subcutaneous tissue heating. *J Cosmet Laser Ther.* 2004; 6(4):187-90.
54. Sachdev M, Hameed S, Mysore V. Non-ablative lasers and non-laser systems in dermatology: current status. *Indian J Dermatol Venereol Leprol.* 2011; 77(3):380-388.
55. Lolis MS, Goldberg DJ. Radiofrequency in cosmetic dermatology: a review. *Dermatol Surg.* 2012; 38(11):1765-76.
56. Franco W, Kothare A, Goldberg DJ. Controlled volumetric heating of subcutaneous adipose tissue using a novel radiofrequency technology. *Lasers Surg Med.* 2009; 41(10):745-750.
57. De La Casa Almeida M, Suarez Serrano C, Medrano Sánchez EM, Diaz Mohedo E, Chamorro Moriana G, Rebollo Salas M. The efficacy of capacitive radio-frequency diathermy in reducing buttock and posterior thigh cellulite measured through the cellulite severity scale. *J Cosmet Laser Ther.* 2014; 16(5):214-24.
58. Wess O. Physics and technology of shock wave and pressure wave therapy. 9th International Congress of the International Society for Musculoskeletal Shockwave Therapy (ISMST) News Letter ISMST. 2006; 2:2–12.
59. Koshiyama K, Kodama T, Yano T, Fujikawa S. Structural change in lipid bilayers and water penetration induced by shock waves: molecular dynamics simulations. *Biophys J.* 2006; 91(6):2198–205.
60. Kato K, Fujimura M, Nakagawa A, et al. Pressure-dependent effect of shock waves on rat brain: induction of neuronal apoptosis mediated by a caspase-dependent pathway. *J Neurosurg.* 2007; 106(4):667–76.
61. Naranjo García P. Shockwave Therapy to treat cellulite. Prime-journal.com. 2012:56-60.
62. Adatto MA, Adatto-Neilson R, Novak P, Krotz A, Haller G. Body shaping with acoustic wave therapy AWT(®)/EPAT(®): randomised, controlled study on 14 subjects. *J Cosmet Laser Ther.* 2011; 13(6): 291–296.
63. Schlaudraff KU, Kiessling MC, Császár NB, Schmitz C. Predictability of the individual clinical outcome of extracorporeal shock wave therapy for cellulite. *Clin Cosmet Investig Dermatol.* 2014; 23;7:171-83.
64. Nassar AH, Dorizas AS, Shafai A, Sadick NS. A randomised, controlled clinical study to investigate the safety and efficacy of acoustic wave therapy in body contouring. *Dermatol Surg.* 2015; 41(3):366-370.
65. Mester E, Szende B, Gartner P. The effect of laser beams on the growth of hair in mice. *Radiobiol Radiother (Berl).* 1968; 9(5):621–626.
66. Mester E, Spiry T, Szende B, Tota JG. Effect of laser rays on wound healing. *Am J Surg.* 1971; 122(4):532–535.
67. Mester E, Korényi-Both A, Spiry T, Scher A, Tisza S. Stimulation of wound healing by means of laser rays. Clinical and electron microscopical study. *Acta Chir Acad Sci Hung.* 1973; 14(4):347–356.
68. Neira R, Arroyave J, Ramirez H, et al. Fat liquefaction: effect of low-level laser energy on adipose tissue. *Plast Reconstr Surg.* 2002;

110(3):912–922; discussion 923–925.
69. Caruso-Davis MK, Guillot TS, Podichetty VK, et al. Efficacy of low-level laser therapy for body contouring and spot fat reduction. *Obes Surg.* 2011; 21(6):722–729.
70. Kolari PJ, Airaksinen O. Poor penetration of infra-red and helium neon low power laser light into the dermal tissue. *Acupunct Electrother Res.* 1993; 18(1):17–21.
71. Brown SA, Rohrich RJ, Kenkel J, Young VL, Hoopman J, Coimbra M. Effect of low-level laser therapy on abdominal adipocytes before lipoplasty procedures. *Plast Reconstr Surg.* 2004; 113(6):1796–1804; discussion 1805–1806.
72. Nestor MS, Zarraga MB, Park H. Effect of 635nm low-level laser therapy on upper arm circumference reduction: A double-blind, randomised, Sham-controlled Trial. *J Clin Aesthet Dermatol.* 2012; 5(2):42–48.
73. Honnor RC, Dhillon GS, Londos C. cAMP-dependent protein kinase and lipolysis in rat adipocytes. II. Definition of steady-state relationship with lipolytic and antilipolytic modulators. *J Biol Chem.* 1985; 260(28):15130–15138.
74. Avci P, Nyame TT, Gupta GK, Sadasivam M, Hamblin MR. Low-level laser therapy for fat layer reduction: a comprehensive review. *Lasers Surg Med.* 2013; 45(6):349–357.
75. Luebberding S, Krueger N, Sadick NS. Cellulite: An Evidence-Based Review. *Am J Clin Dermatol.* 2015; 16(4):243-56.

Aesthetic Medicine
Volume 1 · Number 2 · July-September 2015

R3 facial rejuvenation through minimal incisions vertical endoscopic lifting (MIVEL) and superficial enhanced fluid fat injection (SEFFI): endoscopic repositioning, tissue regeneration, volume restoration

Alessandro Gennai[1], Francesco Pietro Bernardini[2]

[1]MD, Plastic Surgeon - Studio Gennai, Via delle Lame 98 - 40122 Bologna, Italy
[2]MD, Oculoplastic Surgeon

ABSTRACT

The Authors aimed at analysing the prominent factors in the facial ageing process in order to define the best procedure for noticeable, natural and long-lasting results.

The Authors have defined the population that most requests facial rejuvenation (women in the 45-55 years age range) as well as the areas of the face most targeted by the ageing process (the periocular, malar, zygomatic and perioral zones) and its factors (volume loss, cutaneous ageing, tissues descent).

Upon the previous considerations, the Authors have standardised a method which aims at correcting the main causes of ageing through volumes restoration and tissues regeneration thanks to the S.E.F.F.I. technique (Superficial Enhanced Fluid Fat Injection) and tissue repositioning which is obtained by the M.I.V.E.L. technique (Minimal Incisions Vertical Endoscopic Lifting). This method was acronymised into “R3” (Restoration, Regeneration, Repositioning).

Keywords
Endoscopic plastic surgery, endoscopic facelift, endoscopic brow lift, fat graft, lipofilling

Correspondence
Alessandro Gennai. Studio Gennai, Via delle Lame 98 - 40122 Bologna, Italy.
Phone: +390516494945 - +393485267800
E-mail: www.gennaichirurgia.it; agennai@gennaichirurgia.it; agennai@mac.com

Accepted for publication 30 July 2015

© 2015 Editrice Salus Internazionale srl

Introduction

The Authors posed themselves three fundamental questions in order to acknowledge the statistically preferable surgical method for the correction of the facial ageing process.

1. What sex are our patients?
2. What is our patients' average age?
3. Which face areas are most involved in the cutan ous ageing process?
4. What mainly happens in these areas?

Our cases: Since 2001, we have had 421 surgical facial rejuvenation cases that show us that the average age of patients who undergo facial rejuvenation surgery is 46 years old and that 87% of them are women. To evaluate which are the most involved areas in the ageing process of the face and what occurs to them in the meanwhile, we have compared 50 women (among our patients in the 45-55 age range) to photos of their own faces 20 years earlier.

We have therefore evaluated three parameters:

a. Loss of volume
b. Cutaneous ageing
c. Tissue descent

The central area of the face resulted as the most involved in the ageing process.

We have furthered our analysis by dividing the central area of the face into 4 subareas: (SC= Superior Complex, LC = Lateral Complex, IC = Inferior Complex and OC = Oral Complex) (Fig. 1) and we evaluated each of them on our previous parameters basis (Table 1).

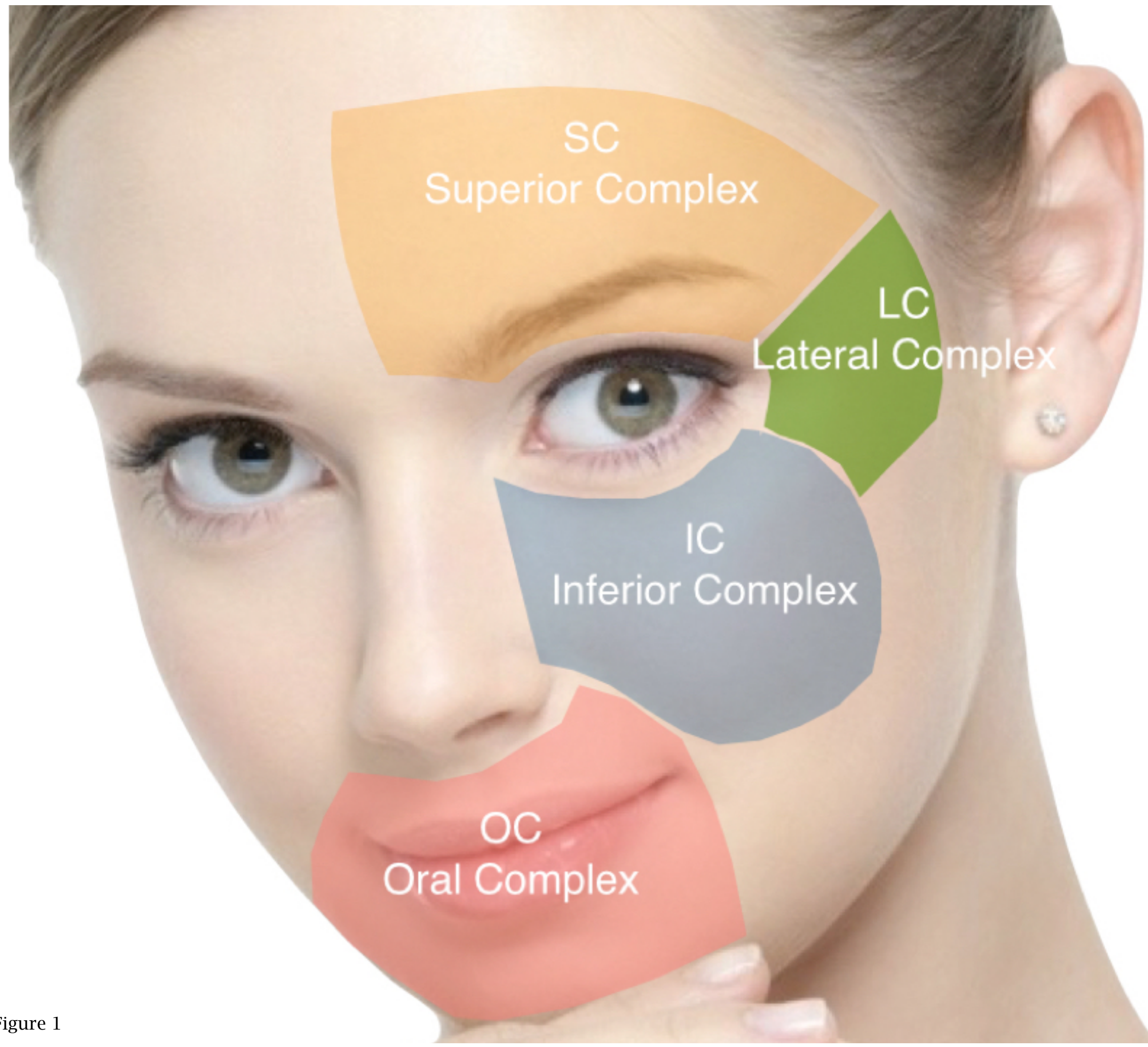


Figure 1

Table 1	skin aging	deflation	descent
Superior Complex	++	++	+++
Lateral Complex	++	+++	0
Inferior Complex	++	+++	++
Oral Complex	+++	+++	0
score	9+	11+	5+

Our study highlighted the loss of volume as the main cause of the ageing process, followed by cutaneous ageing and tissue descent, respectively holding the second and third place.

The Authors have therefore selected the S.E.F.F.I. technique[1,2,3] as the most indicated for volume restoration and tissue regeneration, with the MIVEL technique[4,5,6] as the most suitable for tissue endoscopic repositioning. The techniques have been originally designed by one of the Authors (AG) and subsequently standardised by the two Authors (AG and F.P.B)[1,2,3,4,5].

Materials and methods

A retrospective analysis of 447 consecutive facial rejuvenation procedures, from January 2001 to June 2015, was performed.

The study was conducted in accordance with tenets of the Declaration of Helsinki and the treatment techniques were performed according to internal standardised protocols.

All procedures were performed in 2 private centres, and therefore international review board approval was not required.

M.I.V.E.L. and S.E.F.F.I. are performed in the same surgical procedure; M.I.V.E.L. is performed first in all patients.

S.E.F.F.I. Superficial Enhanced Fluid Fat Injection

Traditional fat grafting techniques rely on Coleman's harvesting technique[9] with 4 by 2 mm side-port cannulas, followed by fat injection in the deep plane. A well-known disadvantage of this technique is that even deep fat implantation is risky in the eyelids because it can potentially cause visible lumps under the thin eyelid skin. Moreover, the adipose tissue harvested with large side ports cannulas (often>2 mm) was formed by big lobules which made certain areas, e.g. the periocular zone, virtually untreatable due to a contour irregularity risk.

In some areas, deep graft was actually unfeasible, as it would involve wide dissections if associated to surgical practices.

These observations led us to explore three issues:

- improving the adipose tissue survival
- making the tissue more fluid and more

homogenous for a superficial graft
- enhancing the adipose tissue regenerative action

Injecting adipose tissue diffusely (avoiding "bolus") and superficially (where the vascular dermal plexus is richer) increases the superficial contact of adipose cells hence the survival chances.

In order to do so, it is necessary to dispose of fluid tissue with small adipose lobules that does not create cutaneous superficial irregularities.

It became apparent that the cutaneous quality improvement was due to the SVF action (Stromal Vascular Fraction) of the harvested adipose tissue.

Actually, many pluripotent cellular lines can be found in the SVF and, among them, a rich presence of pre-adipocytes, also known as ADSCs (Adipose Derived Stem Cells). ADSCs consist of 2 cellular lines: the MSCs (Mesenchymal Stem Cells) and the HSCs (Hematopoietic Stem Cells).

It is thanks to the action of these two pluripotent SVF cellular lines that the adipose tissue great potential in the regenerative field was eventually discovered. A potential that goes way beyond simple volume restoration.

ADSCs are the precious fraction, the "gold", that can be found in the "river" of the adipose tissue.

In order to gather this "gold" we need a fine sieve, an accurate and delicate preparation as well as a precise and superficial graft: this is what SEFFI is.

SEFFI fundamental steps are:

a. harvesting with small side-ports (0.5 and 0.8 mm) cannulas
b. delicate wash and centrifugation
c. enrichment with PRP[6]
d. superficial grafts
e. injecting prevalently by needle

Adipose tissue has great potentials but it must be handled carefully and delicately, following accurate protocols based on scientific studies. Only in this way will we be able to take advantage of its great regenerative power and maximise the adipocyte's survival rate.

In the picture, the areas treated with different types of SEFFI (0.8 and 0.5) are highlighted as well as the injected average quantities (Fig. 2).

M.I.V.E.L. Minimal Incisions Vertical Endoscopic Lifting

Such technique requires an endoscopic approach through 2 mm long incisions in the scalp. After an infiltration of anaesthetic solution (1:100,000 and 1:400,000) an orbital frame complete dissection is performed; such dissection, in the superior portion of the orbital frame is on the sub-periosteal plane, while in the lateral and inferior portion it is super-periosteal and under the orbicular muscle (Fig. 3).

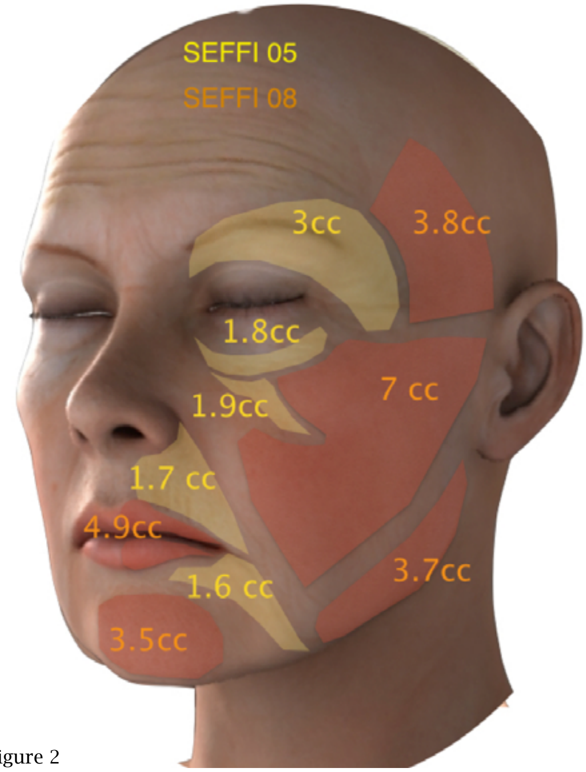


Figure 2

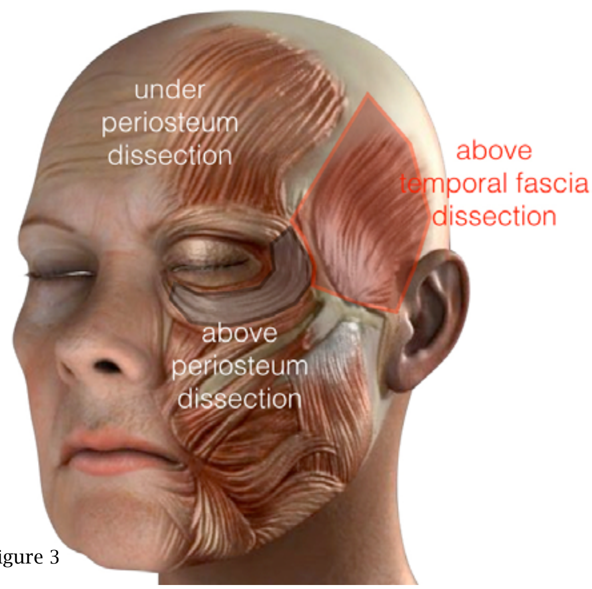


Figure 3

This dissection requires the complete loosening of tissues, which must be obtained respecting the nervous and vascular structures.

The endoscopic procedure not only makes the approach less invasive compared to the long incisions of the open approach, but it also makes tissue loosening much safer in that, thanks to the endoscopic vision, the surgeon has a direct and magnified view of the vascular and nervous anatomic structures.

At the end of the endoscopic dissection, the tissues are fixed in their original positions along vertical vectors through some suspension stitches (Gennai's stitches) (Fig. 4).

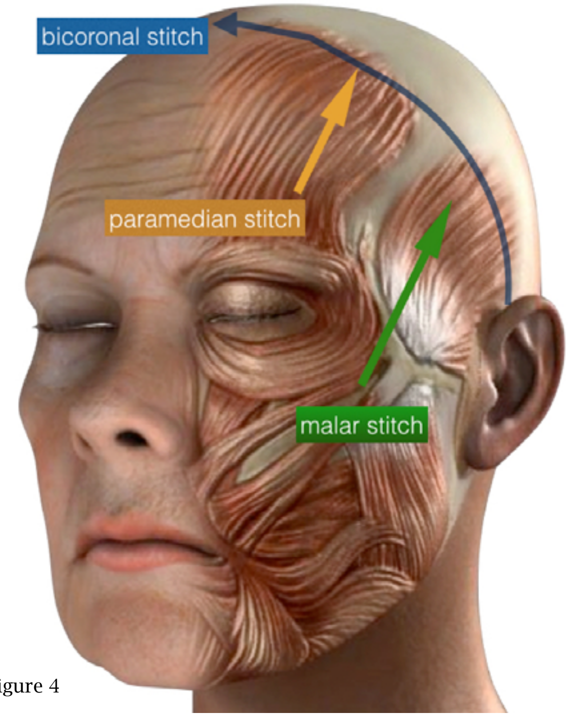


Figure 4

The endoscopic procedure is less invasive compared to the long incisions required for the open approach, and is safer given that the endoscopic vision allows the surgeon to have a direct and magnified view of the vascular and nervous anatomic structures.

Clinical assessment of facial rejuvenation included a retrospective evaluation of pre-treatment and post-treatment photographs by the authors at 3, 6 and 12 months post-operatively, in terms of tissue repositioning, skin regeneration (increase the aspect of the skin, reduction of wrinkles and fine lines) and volume restoration. Scoring was scaled according to 1 = no effect, 2 = satisfactory, 3 = good 4 = optimal.

Results

Clinical assessment was performed for all 447 consecutive patients.

No major complications were recorded. Tissue repositioning was evaluated as "good" and "optimal" in all patients. Skin regeneration was classified as "satisfactory" in 10%, and "good" or "optimal" in 90% of patients. Volume restoration was evaluated as "not satisfactory" in 20% of patients and "good" or "optimal" in the remaining 80% of patients.

The aforementioned procedures have been performed under assisted local anaesthetic in 73% of the cases in DH, while 27% of the cases were under general anaesthetic followed by one night's observation (Figs. 5a-b, 6a-b, 7a-b, 8a-b).

Figure 5a

Figure 5b

Figure 6a


Figure 6b

Figure 7a


Figure 7b

Figure 8a

Figure 8b

Discussion

The three most important factors of facial ageing are volume loss, skin ageing and tissue depletion.

Following previous investigations, the authors identified:

- The average age of facial rejuvenation patients is 46 years old.
- The factor acting in facial rejuvenation according to patient survey results is principally volume loss, followed by skin ageing, and finally descent of tissue depletion.
- The area of the face most involved in facial ageing is the central zone.

Moving from our evaluation, we can reach the conclusion that if we want to effectively correct facial ageing we must in the first place correct volume loss, skin ageing, and then, tissue descent. If necessary, this should be combined with ancillary techniques such as superior and inferior blepharoplasty.

In our vision of facial rejuvenation, we believe it is necessary to:

1. Reposition tissues along vertical vectors
2. Restore lost volumes
3. Regenerate the skin

This is why we have decided to call "R3" our approach to facial rejuvenation.

To effectively correct facial ageing for a natural and long lasting surgical facial rejuvenation, the M.I.V.E.L. and S.E.F.F.I. techniques are promising. S.E.F.F.I. corrects volume loss and skin ageing whilst M.I.V.E.L. fixes tissue in its original position along vertical vectors, with the Gennai suspension stitches[3].

The harvested adipose tissue has great potential, but should be handled carefully and delicately to take advantage of its great regenerative power and maximise its survival rate. In the recent year many studies focused on micro fat graft; Tonnard et al[10] has described nanofat; they proved the nanofat was rich in stromal vascular fraction (SVF) but there were no viable adipocytes; Stuzin's[8] comment underlines the fact that the substance that the author term nanofat, is not fat at all. Trivisonno et al[7] proved that harvesting fat with small side port cannulas carried a two-fold increase in ADSC content compared to traditional harvesting cannulas.

The S.E.F.F.I. technique is designed to harvest more fluid and more homogenous fluid fat trough very small side-port cannulas (0.8–0.5 mm). This tissue harvested thought the small side-port cannulas did not need mechanical or chemical manipulation in order to obtain a smooth fluid tissue; we only gently washed and centrifuged tissue then enhanced with PRP before to inject the Enhanced Fluid Fat in superficial layer where the vascular dermal plexus is richer. The adipose tissue regenerative action is enhanced along with their chances of survival, whilst reducing the risk of cutaneous superficial irregularities.

Our principal concern of this technique (which is the same for any fat grafting and filler technique) is the potential risk of vascular accidents. Improper injection in particular area of the face exposes the patient of the risk of disastrous results[11,12].

To decrease these potential risks we didn't treat nose and glabella areas, we injected in the very superficial layer (dermis or subdermis), performed aspiration prior to injection, local vasoconstrictor, applied very low pressure, stopped injection when the resistance increased, performed linear retrograde injection and injected using small syringes (1 -3 ml)[13].

To effectively correct facial ageing for a natural and long-lasting surgical facial rejuvenation, the M.I.V.E.L. and S.E.F.F.I. techniques are promising. The S.E.F.F.I. technique corrects the volume loss and regenerates the skin, and M.I.V.E.L. corrects the descent of tissue without pulling and cutting the skin though an endoscopic approach which is less invasive than the open approach, and safer, allowing direct and magnified view of the vascular and nervous anatomic structures.

References

1. Gennai A. Endochirurgia estetica del volto. SEE Editrice Firenze; 2011:32-58.
2. Gennai A, Saponaro A, Iozzo I. El rol del lifting endoscópico fronto-témporo-orbitario enel nuevo concepto de rejuvenecimiento facial: Mini-Invasivo, tensión moderada, restauración de volúmenes. The importance of brow-temporal-orbital endoscopic facelift in the new concept of facial rejuvenation: low invasiveness, moderate tension, volume restauration. *Cirurgia Plástica Ibero-Latinoamericana.* 2009; 35(1):27-34.
3. Bernardini FP, Gennai A, Izzo L, Devoto MH. Minimal incisions vertical endoscopic lifting and fat grafting as a systematic approach to the rejuvenation of the periocular aesthetic unit. *Ophthal Plast Reconstr Surg.* 2013; 29(4):308-315.
4. Bernardini FP, Gennai A, Izzo L, et al. Superficial Enhanced Fluid Fat Injection (SEFFI) to Correct Volume Defects and Skin Ageing of the Face and Periocular Region. *Aesthet Surg J.* 2015; 35(5):504-15.
5. Gennai A. Dal lipofilling al S.E.F.F.I. In: Colombo G, Ruvolo V, Atlante iconografico di chirurgia e medicina estetica. I fondamenti step by step. Cavinato Editore International; 2014:23-135.
6. Blanton MW, Hadad I, Johnstone BH et al. Adipose stromal cells and platelet-rich plasma therapies synergistically increase revascularization during wound healing. *Plast Reconstr Surg.* 2009; 123(2 Suppl):56S-64S
7. 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.
8. Stuzin JM.Discussion: Nanofat grafting: basic research and clinical applications. *Plast Reconstr Surg.* 2013; 132(4):1027-28.
9. Coleman SR. Facial re-contouring with lipostructure. *Clin Plast Surg.* 1997; 24(2):347-367.
10. Tonnard PL, Verpaele AM, Peeters G, Hamdi M, Cornelissen M, Declercq H. Nanofat grafting: basic research and clinical applications. *Plast Reconstr Surg.* 2013; 132(4):1017-26.
11. Yang HM, Lee JG, Hu KS, Kim HJ. New anatomical insights on the course and branching patterns of the facial artery: clinical implications of injectable treatments to the nasolabial fold and nasojugal groove. *Plast Reconstr Surg.* 2014; 133(5):1077-1082.
12. Carruthers JD. Discussion: New anatomical insights on the course and branching patterns of the facial artery: clinical implications of injectable treatments to the nasolabial fold and nasojugal groove. *Plast Reconstr Surg.* 2014; 133(5):1083-1084.
13. Lazzeri D, Agostini T, Figus M, Nardi M, Pantalone M, Lazzeri S. Blindness following cosmetic injections of the face. *Plast Reconstr Surg.* 2012; 129(4):994-1012.

Aesthetic Medicine
Volume 1 · Number 2 · July-September 2015

Morphological study as the gold diagnostic standard: myth or reality?

Tamila Kanareitseva[1], Elena Karpova[2], Sergey Markin[3], Olga Danischuk[4], Vladimir Reshetin[5]

[1]MD, I.M. Sechenov First Moscow State Medical University
[2]MD, Danischuk's clinic, medical centre of plastic surgery and cosmetology
[3]MD, City Clinical Hospital, Moscow Health Department
[4]MD, Institute of Advanced Professional Training, Russian Federal Medico-Biological Agency
[5]MD, City Clinical Hospital, Moscow Health Department

ABSTRACT

Two cases of complications that developed in the late period after polyacrylamide gel (PAAG) injection into the breasts are reported. Surgically removed tissues were stained with haematoxylin and eosin for morphological examination. Both reported cases show that biopsies obtained from the central zone of filler (PAAG) injection have a morphological pattern that is characteristic for this filler. Complications in these two observations were associated with migration of the gel into peripheral regions of the breast, outside the area of injection. Morphological pattern at these sites was typical for CaHa-containing fillers. An analysis of comparisons of clinical and morphological features of the two cases is presented. Practical recommendations for the verification of the filler that can help exclude errors in the assessment of morphological changes in tissues are proposed. Morphological examinations of nine specimens are reported in this article, by means of which the fate of injected filler (PAAG) is tracked from the central zone to the peripheral sites, where the morphological pattern becomes atypical. The role of microphages in filler resorption is shown, together with the phenomenon of vessel embolisation with multinucleated gigantic foreign cell bodies. The main conclusion is based on the importance of labelling the specimen with designation of the central and the peripheral zone with the aim of avoiding diagnostic errors.

Keywords
Polyacrylamide gel, complications

Correspondence
Tamila Kanareitseva, MD, I.M. Sechenov First Moscow State Medical University, Moscow, Russia, +7(917)553-73-34, patanat_fppov@mail.ru

Accepted for publication 30 July 2015

© 2015 Editrice Salus Internazionale srl

Introduction

The turn of the XXI century has marked the unprecedented development of the injection plasty technique. According to the American Association of Plastic Surgeons, 8.3 million such procedures were conducted worldwide in 2003, with the number reaching 12 million in 2004. This fact was accompanied by the increase of absolute number of complications in the short (days-months) as well as in the long (beyond 1 year) term.

The reasons for these complications are due to the technical mistakes during the gel injections in the first place and, on the other hand, to the physical and chemical properties of the injectable agent and tissue reaction caused by it. More than 10 groups of preparations are being used in cosmetic clinics at present, all of which are different in physical properties and chemical composition.

All of them can evoke clinical complications based on the certain morphological alterations in tissue in the area of filler injection. Complications can manifest clinically as tumour-like formations, infiltration, nodules, gel displacement, etc. Vascular reactions may be accompanied by the appearance of ecchymosis (petechiae), bruises, hematomas, and events of vessel occlusion or embolisation leading to the formation of necrosis.

Inflammatory changes can induce generation of long-standing oedema, papular-pustular nodules, resembling bacterial infection, although being, in fact, sterile. Infectious complications are very rarely observed. However, in cases of disregard for sterility during the conduction of manipulation abscesses and fissures may form at the site of filler injection.

All this diversity of complications in most cases entails development of productive inflammatory changes in tissues, which result in granuloma formation.

The experience in morphological study of operative and biopsy material from patients with contour injection plasty, accumulated by clinics worldwide, provides the researchers with an opportunity to define with certainty the nature of the injected material, which gives them the right to consider the morphological study to be the gold standard of diagnostics[1,2,3].

In our previous works, we described morphological patterns of tissue changes in the remote period after injection of fillers of different composition. On the basis of these morphological studies, we concluded that it was possible to conduct the verification of the filler, which had caused this or that particular complication.

However, the examination of operative material from two patients made us revise the viewpoint that considered the postulate, that morphology is the gold diagnostic standard, absolutely right.

Case studies

<u>*Case study 1*</u>

Patient E., 49 years old, in 1999 underwent contour breast plasty with the injection of PAAG for correction. In 2009, a small gel displacement into the subcutaneous layer of the right lateral side of the chest without signs of inflammation was noted.

A procedure of displaced gel fragments' removal was conducted with elimination of the newly formed subcutaneous pocket by means of fixation of the skin and subcutaneous fat to underlying tissues.

In 2011, a new gel accumulation was seen again in the same zone with a tendency towards enlargement.

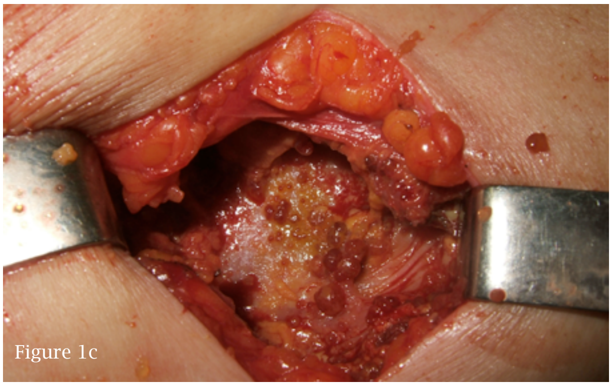
A decision was made to remove the gel and revise the retromammary space.

During the surgery, focal conglomerates of gel were found in adipose cellular tissue and intramuscularly with fibrotic changes of the surrounding tissue.

Macroscopically, gel had different structure, from unchanged (in subcutaneous fat) (Fig. 1a) to destructed in the form of 'semolina grains' (Fig. 1b). Furthermore, gel agglomerates in the form of circular bodies were located along the muscles and blood vessels, firmly attaching to them. These agglomerates had a vinous-blue colour, a size of 0.2 x 0.2 cm and resembled "clusters of grapes". Remote tissues were also subjected to morphological study.


Figure 1a


Figure 1b



Figures 1a-b-c - Unaltered PAAG in subcutaneous fat (1-a), destructed PAAG (1-b) and compact gel accumulations in the shape of a "cluster of grapes" located along the blood vessels and muscle fibres (1-c) in patient E.

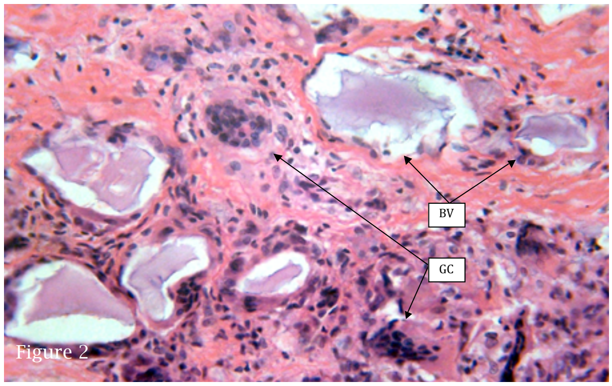


Figure 2 - Typical morphological pattern of complication that developed after PAAG injection in patient G. Haematoxylin and eosin staining x100 BV-basophilic vacuoles; GC-giant cells of foreign bodies.

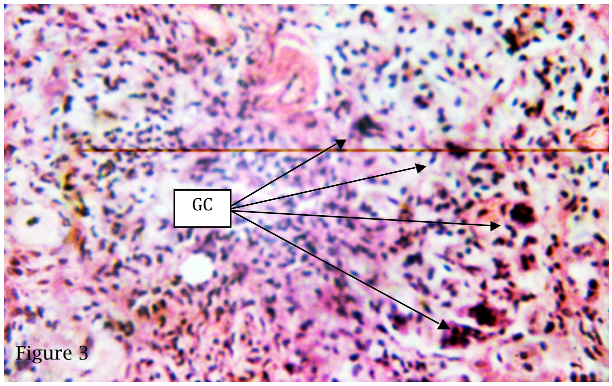


Figure 3 - Atypical morphological pattern of complication that developed after PAAG injection in patient G. Multinucleated small-sized foreign body cells. Haematoxylin and eosin staining x100 BV-basophilic vacuoles; GC-giant cells of foreign bodies.

Case study 2

Patient G., 39 years old, in 1999 underwent contour injection breast plasty with the injection of PAAG. In 2010, after trauma to the lower inner quadrant of the left breast, a focal skin discoloration was seen.

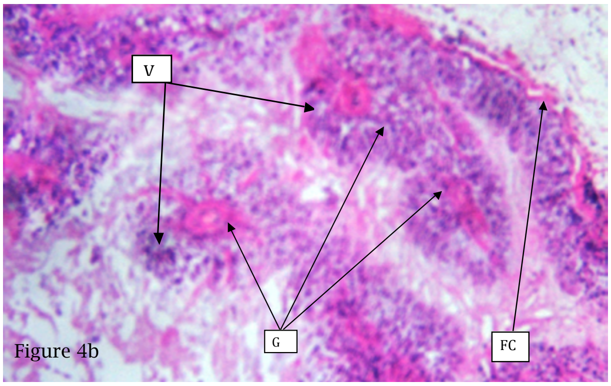
In eight months a suppurative inflammation with a sinus duct formation developed. With the aim of maintaining equivalent breath size in two months after the relief of inflammation, PAAG was removed from both mammary glands. On revision of the right breast dense gel masses were found, which resembled a "cluster of grapes". Remote tissues were subjected to morphological study.

On the examination of tissues, derived from multiple studies in the late period (in 10-12 years after PAAG injection) from the zone of original gel injection both patients had a characteristic morphological pattern of complication. In tissues a multitude of basophile vacuoles of different sizes and shapes were found, located between fibrous stromal fibres, surrounded by solitary multinucleated foreign body giant cells (Fig. 2). In some sections injected gel in the form of a basophile amorphous mass was surrounded by thickened capsule of connective tissue. Similar description of a morphological pattern of complication after PAAG injections is mentioned in the works of other authors[4,5,6]. Together with the typical for this filler changes, we discovered morphological patterns in tissues, that are more characteristic for calcium hydroxyapatite (CaHa)-containing fillers, such as Radiesse (Fig. 3). Atypical morphological pattern of complication after PAAG injection is characterised by the presence of macrophages and multiple multinucleated small-sized foreign body cells, surrounding the altered gel residues.

A similar morphological pattern is reported by other authors, yet as a complication of injection of preparations containing CaHa-microspheres[7,8]. Moreover, the authors stress, that multinucleated foreign body cells accumulated around the microspheres, which looked like nuclear-free bodies with an intensive blue staining (microcalcifications).

The comparison of clinical and morphological findings from both cases allowed us to conclude that after long-term presence of injected PAAG, its destiny at different sites is not the same. So, gel, obtained from the area of the injection of the preparation (central zone), remains intact for a long time (Fig. 2).

The gel, present in minor quantities in zones of displacement, as in patient E., or in direct contact with adjoining surrounding tissues, as in patient G., had a dense consistency and resembled macroscopically a "cluster of grapes" (Fig. 4a). On the microscopic examination of multiple biopsy materials, we noted that gel resorption begins first of all in these peripheral areas. On the detailed analysis of biopsy samples taken from circular bodies, forming the 'cluster of grapes', the latter looked like encapsulated masses of altered gel that contained granulomas inside it with blood vessels in their centres (Fig. 4b).



Figures 4a-b - Macroscopic view of the removed specimen in the shape of a "cluster of grapes" (4a) and its morphological structure (4b). Haematoxylin and eosin staining x40.
FC-fibrous capsule; G-granulomas of the foreign bodies; V- vessels in the centre of granulomas.

In other sections of the peripheral zone, as a result of thickening, gel turned into rounded eosinophilic particles of small size (microglobules). Around such particles, there were multiple multinucleated small-sized foreign body cells, which 'attack' and thereafter engulf gel microglobules (Figs. 5a-b).

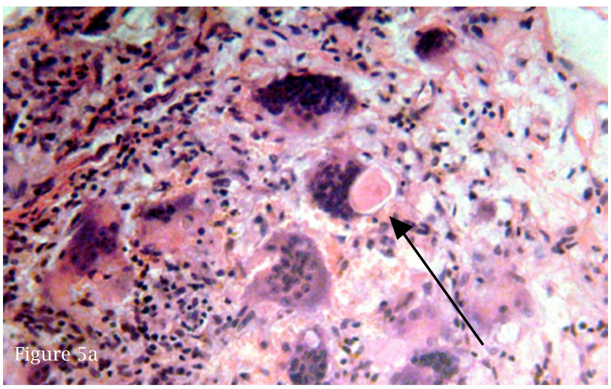
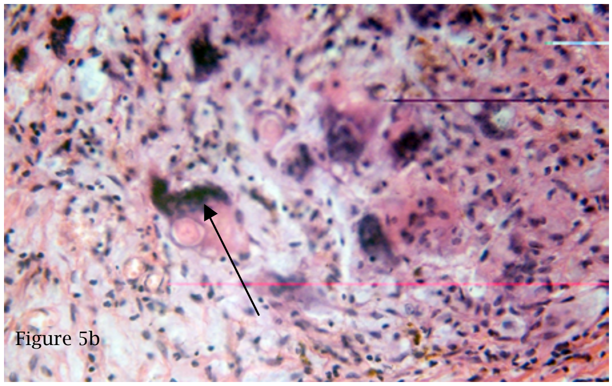
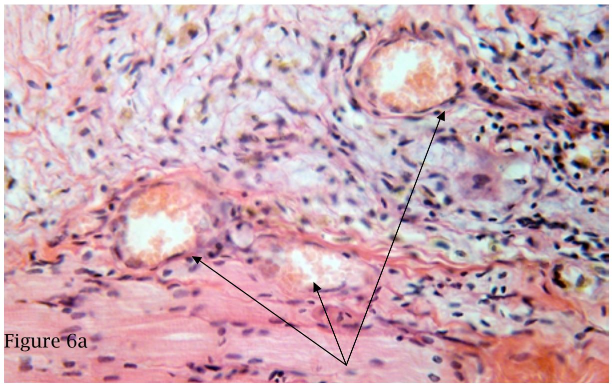
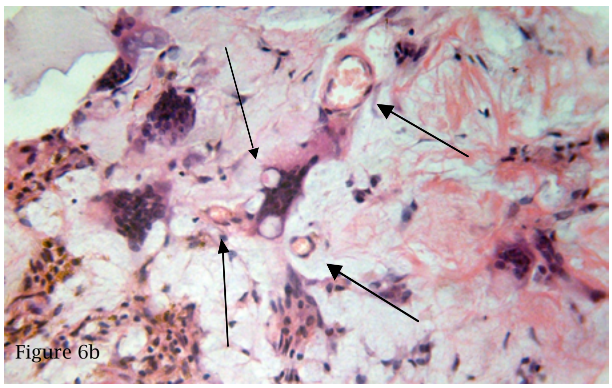


Figure 5a - A multinucleated cell "attacks" a microglobule (arrow)
Figure 5b - A microglobule in cytoplasm of a foreign body cell (arrow)



Later on occurs the subsidence of productive inflammatory process, morphological manifestation of which is, together with resorption of thickened gel residues, fibrosis accompanied by neoangiogenesis with generation of blood vessels of different calibre (from capillary type vessels to arterioles) (Figs. 6a-b).

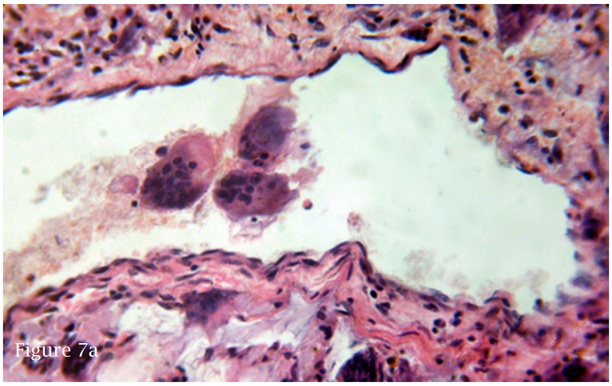


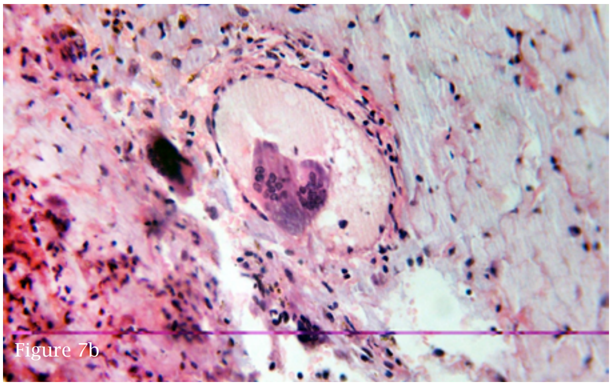


Figures 6a-b - Newly formed blood vessels of different calibre (arrow). Haematoxylin and eosin staining x200

The final outcome of productive inflammation reduction process is the detection of phenomenon of vessel embolisation with gigantic multi-nucleated foreign body cells.

Emboli can be presented by separate cells as well as by their groupings (Figs. 7a-b).





Figures 7a-b - Multinucleated foreign body cells in blood vessels. Haematoxylin and eosin staining x400

Results and discussion

Morphological study of tissue samples necessitated us defining two zones of presence of injected PAAG: central, where the greater quantity of gel is located (the original injection site), with complication pattern that is typical for PAAG; and peripheral, with lesser quantity of the filler in the area of direct contact with tissues (vessels and muscle) or in the area of its displacement with atypical morphological pattern of complication for PAAG.

Turning back to the possibility of recognition of morphological study as a gold diagnostic standard, we reckon that, in the majority of cases this postulate can be considered true. However, in presented examples, having come across certain diagnostic difficulties, we came to the conclusion that to establish a correct diagnosis, one must also consider clinical information, in particular: medical history, duration of the process, macroscopic changes, and the zone, from which the material was taken. Consequently, in the case of our patient E., when by the time of development of complications in the form of gel displacement (peripheral zone) the name of the filler injected ten years ago could not be exactly established, only the hint of its long-term presence allowed to verify it as PAAG, despite of resemblance of the morphological changes to CaHa-containing preparations, after injections of which complications usually arise in an earlier period (from a few months to one year).

Atypical productive inflammatory reaction in both cases is caused by *endogenously formed eosinophilic* microglobules, appeared as a result of PAAG transformation during its prolonged residence in peripheral zones.

Whereas in the case of CaHa-containing filler injections, the origin of a resembling productive inflammatory reaction is due to the original presence of calcium microspheres in the preparation in the form of microglobules of *basophilic* staining.

This fact explains the similarity of morphological patterns that can lead to erroneous diagnosis.

Conclusions

To avoid the morphological error in filler identification one should take into account clinical data: medical history, time of preparation's residence in tissue, macroscopic changes with compulsory labelling of the zone, from which the material was taken. One ought to be extremely careful in the interpretation of obtained results and obligatory conduct thorough morphological comparisons, especially with the emergence of newer fillers on the world market.

The main conclusion is based on the importance of labelling the specimen with designation of the central and the peripheral zone with the aim of avoiding diagnostic errors.

References

1. Lemperle G, Morhenn V, Charrier U. Human histology and persistence of various injectable filler substances for soft tissue augmentation. *Aesthetic Plast Surg.* 2003; 27(5):354-366.
2. Zimmermann US, Clerici TJ. The Histological aspects of fillers complications. *Semin Cutan Med Surg.* 2004; 23(4):241-250.
3. Requena L, Requena C, Christensen Z, Zimmermann US, Kutzner H, Cerroni L. Adverse reactions to injectable soft tissue fillers. *J Am Acad Dermatol.* 2011; 64(1):1-34.
4. Gómez-de la Fuente E, Alvarez-Fernández JG,

Pinedo F, et al. Cutaneous adverse reaction to Bio-Alcamid implant. *Actas Dermosifiliogr.* 2007; 98(4):271-5.

5. Karagozoglu KH, van der Waal I. Polyacrylamicle soft tissue filler nodule mimicking a mucoepidermoid carcinoma. *Int J Oral Maxillofac Surg.* 2008; 37(6):578-580.
6. Karim RB, Hage JJ, van Rozelaar L, Lange CA, Raaijmakers J. Complications of polyalkylimide 4% injections (Bio-Alcamid) a report of 18 cases. *J Plast Reconstr Aesthet Surg.* 2006; 59(12):1409-14.
7. Ahn MS. Calcium hydroxylapatite: Radiesse. *Facial Plast Surg Clin North Am.* 2007; 15(1):85-90.
8. Jansen D, Graivier MH. Evaluation of a calcium hydroxylapatite-based implant (Radiesse) for facial soft-tissue augmentation. *Plast Reconstr Surg.* 2006; 118(3 Suppl):22S-30S.

Aesthetic Medicine
Volume 1 · Number 2 · July-September 2015

Combined Use of Cosmetic Ingredients and CO_2 at High Pressure and Very Low Temperature for the Treatment of Skin Ageing

Hernán Pinto, MD, PhD

Instituto de Investigaciones para las Especialidades Estéticas y del Envejecimiento (i2e3), Barcelona.

ABSTRACT

The industry's ability to create new devices has exceeded all expectations. However, technological progress has been directly proportional to a blurring of the lines between science and business. The technology we have tested for this paper, called Coolifting™, is based on the non-invasive administration of active ingredients by means of CO_2 pulses at very high pressure and very low temperature. The purpose of this paper is the assessment of this device.

Keywords
Beauty, hydration, lifting, cooling, anti-ageing

Correspondence
Hernán Pinto, MD, PhD, MSc - Av. Francesc Macia 46, At 1ª – Barcelona, Spain
Phone: +34 636835848
E-mail: hpinto@i2e3.com

Accepted for publication 10 September 2015

© 2015 Editrice Salus Internazionale srl

Introduction

The industry's ability to create new devices has exceeded all expectations. By including different treatment principles and technologies in compact spaces, with power autonomy and great portability, treatments that could only be imagined ten years ago are now a reality. However, technological progress has been directly proportional to a blurring of the lines between science and business: useless devices have been designed; techniques that provide lesser results but higher economic gain have been developed; and sometimes, aesthetic medicine has succumbed to marketing. This is why all devices are tested at i2e3 (Instituto de Investigaciones para las Especialidades Estéticas y del Envejecimiento).

The number of studies and papers published on the use of carboxytherapy in aesthetic medicine is growing exponentially[1].

Nowadays, not only is there significant evidence of its usefulness[2], but also various information regarding its application as a complement of many other treatments, such as liposuction[3], and its role in modulating physiological processes, such as the Bohr Effect[4].

Its vasodilating effect and the concomitant increase in blood perfusion have been strongly documented for over 25 years[5], and are excellent for stimulating tissue oxygenation, among other things[6].

On the other hand, the deleterious effects of extreme cold on human tissues are well-known[7-9].

However, the use of extremely low temperatures as a treatment principle is much more recent.

Cold is used in myriad ways in medicine: as an anti-inflammatory, as an analgesic[10], as an adipocytolytic[11], and as a vasoconstrictor, among others. Cold is applied in isolation or combined with other physical principles[12]. Its analgesic and vasoconstrictor effects mean that it will be present in any booth, medical office, and operating room around the world.

The technology we have tested for this paper, called Coolifting™, is based on the non-invasive administration of active ingredients by means of CO_2 pulses at very high pressure and very low temperature. The purpose of this paper is the assessment of the Coolifting™ device.

Materials and methods

Subjects

16 healthy women were included in this study. Inclusion criteria: a) 35 to 50 years old; b) no severe, skin, face or systemic pathologies; c) not undergoing any chronic treatment or receiving any daily medication; d) no aesthetic medical treatments or procedures during one month prior to the session.

Sample

Every subject had measurements recorded immediately prior to the therapeutic session (control measurement, S0) and 24-36 hours after the therapeutic session (S1).

Device

Coolifting™, BeautyGun S.L., Barcelona, Spain. It is a 1.2 kg gun-like device that is loaded with a session-kit provided by the manufacturer, consisting of: a) a CO_2 33 g cartridge, and b) a 4 ml vial with the active principles (sorghum bicolour extract, wheat protein, hyaluronic acid) and other ingredients as per the technical specifications.

Measurements

There are valid methods to measure optical, mechanical and tactile properties of the skin[1].

Data was obtained under partially controlled ambient conditions (temperature and humidity) using different test probes, cameras and diagnosis devices:

- Cutometer® MPA 580, Courage Khazaka, GmbH, Köln, Germany.
- Corneometer® CM825, Courage Khazaka, GmbH, Köln, Germany.
- Frictiometer® FR700, Courage Khazaka, GmbH, Köln, Germany.
- Glossymeter® GL200, Courage Khazaka, GmbH, Köln, Germany.
- Reveal Imager®, Canfield Scientific, Inc., New Jersey, USA.

Questionnaires

Single-question, closed-answer and self-assessed questionnaires were answered by patients 24 hours after treatment. Question posed: Have you noticed any improvement in your skin? Possible answers: No (1 point); Don't know/Not sure (2 points); Yes (3 points); Yes, great changes (4 points); Yes, spectacular changes (5 points).

Therapeutic session

All sessions were performed by the same professional. Sessions lasted 4 minutes (parameter set by the manufacturer, cannot be changed).

A drying towel was applied to the skin prior to the session. No antiseptic agent was used. Application was performed in right and left cheek areas.

Analysis

Descriptive statistics were used to analyse the sample. Means and standard deviations were used as central tendency and dispersion indexes, respectively. A "Shapiro-Wilk Test" was used to assess normal distribution. Whenever it was verified, a "Student T Test" was used to compare means and determine statistical significance.

When normal distribution was rejected, non-parametrical "Wilcoxon T Test" was used to determine statistical significance and median was used instead of the mean. Two-tailed tests for paired samples were used. SPSS 17.0 for Windows® (Statistical Product and Service Solutions Ibérica, S.L.U., Madrid, Spain) was the software used for statistical analysis.

Results

The sample analysed consisted of 16 women (n=16) with a mean age of 41.875 (SD 2.825) years old. S0 stands for the control pre-treatment measurement and S1 for the final 24 hours post-treatment measurement.

Questionnaires

Table 1 shows the answers to the question *Have you noticed any improvement in your skin?*

Answer	*n.*
No	0
Don't know/Not sure	0
Yes	10
Yes, great	5
Yes, spectacular	1

Table 1. Questionnaire answers. "n" represents the number of patients that provided that answer.

Corneometry

S0 mean hydration: 60.934% (SD 8.474). S1 mean hydration: 66.337% (SD 7.649); p=0.068.

Frictiometry

S0 mean smoothness: 525,125 (SD 201.772). S1 mean smoothness: 391.012 (SD 167.628); p=0.049. Frictiometry scale 1 to 1000 points (according to manufacturer device set-up).

Glossymetry

Variable 1: total gloss. S0 mean gloss: 4.582 (SD 1.171). S1 mean gloss: 5.567 (SD 1.476); p=0.048.

Variable 2: isolated gloss, after DSC (diffuse scattering correction). S0 mean gloss: 2.536 (SD 1.084). S1 mean gloss: 3.419 (SD 1.508); p=0.008.

Cutometry

Data was obtained from 19 variables (Table 2).

	n	Pre-treatment (SD)	Post treatment (SD)	*p*
R0	16	0.349 (0.091)	0.333 (0.106)	>0.05
R1	16	0.132 (0.056)	0.107 (0.049)	>0.05
R2	16	0.65 (0,077)	0.711 (0.085)	<0.05
R3	16	0.424 (0.112)	0.400 (0.130)	>0.05
R4	16	0.223 (0.083)	0.204 (0.078)	>0.05
R5	16	0.377 (0.107)	0.396 (0.100)	>0.05
R6	16	0.514 (0.136)	0.474 (0,010)	>0.05
R7	16	0.249 (0.055)	0.266 (0.047)	>0.05
R8	16	0.220 (0.060)	0.202 (0.039)	>0.05
R9	16	0.078 (0.030)	0.071 (0.033)	>0.05
F0	16	11.460 (3.584)	10.493 (2.735)	>0.05
F1	16	0.097 (0.186)	0.830 (0.096)	>0.05
F2	16	1.343 (0.452)	1.355 (0.435)	>0.05
F3	16	7.803 (1.789)	7.662 (1.849)	>0.05
F4	16	15.521 (4.173)	14.155 (3.449)	>0.05
Q0	10	63.644 (14.068)	61.911 (11.229)	>0.05
Q1	10	0.574 (0.071)	0.566 (0.054)	>0.05
Q2	10	0.411 (0.073)	0.410 (0.051)	>0.05
Q3	10	0.163 (0.041)	0.157 (0.015)	>0.05

Table 2. Cutometry variables: comparison before and after treatment. "n" number of patients. SD: standard deviation. p: statistical significance. "R" variables: linear measurements, "F" and "Q" variables: area measurement.

Reveal Camera

This device performs standard and polarised pictures and shows a mexametric pigment distribution: melanin and haemoglobin. It was not possible to observe clinical differences though some pictures seemed to show a slight difference in melanin distribution (Fig. 1).

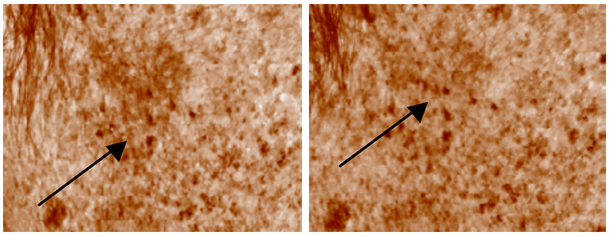


Figure 1. Melanin distribution. Top: pre-treatment. Bottom: post-treatment. Black arrow shows a slight change in colour.

Discussion

Aesthetic treatments are applied seeking both instant and long-term effects. The former ("flash" effects) are deemed qualitative and are usually due to tissue changes mostly associated with changes in a physical variable, such as water retention or light reflection. These changes may occur almost instantly and, as discussed in this paper, have statistical and clinical repercussions. Not only have gloss (p=0.048; p=0.008) and smoothness (p=0.049) increased in a statistically significant degree, but also all patients have noticed a change subjectively. 100% of patients have reported a real and noticeable improvement: 31.25% rated it as a "great" improvement, and one patient rated it as a "spectacular" improvement. Although this information is subjective, it is of great importance in aesthetic medicine. Further research will be necessary in order to explore this subjective component adequately.

The situation is different when it comes to assessing those tissue properties that depend on the number of cells performing a certain function or the greater or smaller degree of synthesis of certain molecules. These are quantitative properties, whose paradigmatic example is elasticity. Other examples may be the other mechanical properties of skin, such as distensibility or the depletion of the adaptation response to mechanical stress. These properties will be affected by multiple different variables. However, for this example in particular, they will depend mostly on the quantity, quality, and layout of skin fibre proteins.

Observing the clinical impact resulting from changes in processes where protein synthesis is stimulated is neither easy nor quick. When the purpose is to make physiological changes that will have an effect on tissue such that they can be noted macroscopically, patience is required.

Such is the case of cutometry. Although the R2 variable has resulted in positive and statistically significant changes (p=0.041), the fact that significance was isolated means that we should think that this finding is important but has no great impact on global cutometry analysis. Undoubtedly, much more attractive than the statistical significance of R2 is the overall trend of all 19 cutometry variables as a whole. R0 represents the passive behaviour of the skin when force is applied to it. It is the first maximal amplitude, the highest point of the first curve, and finds correlation with skin firmness. R2 represents the portion of the elasticity curve between the maximal amplitude and the skin re-deformation capability.

This is the elasticity of the skin and the closer the value gets to 1, the more elastic the tissue is. R5 also correlates with elasticity, but analyses the elastic component solely, not anchoring it to the viscous component. Another elastic variable that was analysed was R6. It represents the elastic part of the visco-elasticity curve.

The smaller the value, the higher the elasticity. R7 represents the relation between the elastic portion of the elasticity curve and the complete curve: the closer the value is to 1 (100%), the more elastic the curve is. "F" and "Q" parameters are "areas" and are highly dependent on the maximum amplitude of the curve.

All cutometry variables have evolved positively, indicating greater elasticity and firmness, and lower depletion in response to mechanical stress. This will surely be a promising approach for this treatment in the future. However, the design of this study is not sensitive to the small and quick changes in the mechanical properties of skin. The second sampling is so immediate (24 hours post-treatment) that the phenomenon does not have enough time to reach significant levels.

The pulsed mechanical stimulus, the action of CO_2, and even the release of NO may partly explain this phenomenon. Future research with serial application protocols and medium-term follow-up is recommended. These designs may assess whether the positive trend in the skin's mechanical properties observed in this study will materialise into statistically significant changes.

Hydration has improved from a clinical standpoint, although the improvement has not been statistically significant. This observation may have been partly biased, as initial mean hydration was 60.934%. These values are relatively good and much more difficult to improve than lower values, such as those from which we have started in other studies.

An explanation for this apparently better initial hydration may be found in sample selection: The 16 volunteers were women between 35 and 50 years old with no pathologies. However, this fact has made it possible to confirm the interesting improvement of this treatment on skin smoothness.

In previous studies, we have had to deal with an uncomfortable fact: the spectacular improvement in hydration conditions biased the interpretation of frictiometry[13].

A corneal layer with higher water content opposes more greatly to friction than a dryer one. In other studies, we witnessed that patients with poor initial hydration levels greatly improved their condition, misleading frictiometry results and interpretation. Further investigations with layered initial comparable hydration-level groups will be required to confirm these observations.

The overall conclusions of this study regarding the test of the Coolifting™ device are:

i. It can achieve significant skin beauty enhancement in the very short term by improving tissue gloss ($p<0.05$).
ii. It can achieve significant skin beauty enhancement in the very short term by improving tissue smoothness (C).
iii. It can probably achieve significant skin beauty enhancement in the very short term by improving tissue hydration (correct tendency, $p=0.068$).
iv. It can probably achieve significant skin beauty enhancement in the long term by improving skin mechanical properties such as elasticity and firmness (correct tendency, only R2 $p<0.05$).
v. It can possibly have a role in skin beauty enhancement in the long term by improving pigment distribution (isolated observations).

Since it is logical to assume to some extent a dose-dependent effect, further studies with higher exposure protocols and long-term follow-up may provide new evidence. In addition, designs that include male subjects will be necessary to extrapolate these results to the general population.

References

1. Millán E. Carboxytherapy in Pinto H, *Principios de Medicina Estética*, Ed. Ruiz del Amo, 2013: 221-236.
2. Koutna N. Carboxytherapy: a new non-invasive method in aesthetic medicine. *Cas Lek Cesk.* 2006; 145(11):841-3.
3. Brandi C, D'Aniello C, Grimaldi L, Caiazzo E, Stanghellini E. Carbon dioxide therapy: effects on skin irregularity and its use as a complement to liposuction. *Aesthetic Plast Surg.* 2004; 28(4):222-5.
4. Sakai Y, Miwa M, Oe K, et al. A novel system for transcutaneous application of carbon dioxide causing an "artificial Bohr effect" in the human body. *PLoS One.* 2011; 6(9):e24137.
5. Hartmann B, Drews B, Bassenge E. CO2-induced acral blood flow and the oxygen partial pressure in arterial occlusive disease. *Dtsch Med Wochenschr.* 1991; 116(43):1617-21.
6. Ito T, Moore JI, Koss MC. Topical application of CO2 increases skin blood flow. *J Invest Dermatol.* 1989; 93(2):259-62.
7. Haxthausen H. Adiponecrosis e frigore. *Br J Dermatol.* 1941; 53:83-89.
8. Rotman H, et al. Cold Panniculitis in Children: Adiponecrosis e frigore of Haxthausen. *Arch Dermatol.* 1966; 94:720-1.
9. Beacham B, Cooper H, Buchanan S, Weary P. Equestrian Cold Panniculitis in Women. *Arch Dermatol.* 1980; 116(9):1025-7.
10. Patel R, Halem M, Zaiac M. J. The combined use of forced cold air and topical anaesthetic cream for analgesia during the treatment of palmar hyperhidrosis with botulinum toxin injections. *J Drugs Dermatol.* 2009; 8(10):948-51.
11. Pinto H, García-Cruz E, Melamed G. Study to evaluate the Action of Lipocryolisis. *Cryo Letters.* 2012; 33(3)177-81.
12. Pinto H, Melamed G. Contrast lipocryolysis pre and post session tempering improves clinical results. *Adipocyte.* 2014; 3(3)212-4.
13. Pinto H, Garrido-Gorgojo L. Study to Evaluate the Aesthetic Clinical Impact of an Autologous Anti-ageing Serum. *J Drugs Dermatol.* 2013; 12(3)322-6.

2015

19-21 February - Malaga (Spain)
30th Spanish 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

14 March – Bucharest (Romania)
Course: Treatment of Vascular Lesions Romanian Society for Aesthetic Medicine and Dermatologic Surgery
Venue: Hotel Novotel
Calea Victoriei 37B - Sector 1
010061 BUCHAREST, ROMANIA
Organizer: Dr. Mihaela Leventer
mihaelaleventer@drleventercentre.com
www.drleventercentre.com

3-4-5 April – Marrakech (Morocco)
International Congress of Dermastic Moroccan Association of Surgical Dermatology – Cosmetic Aesthetic Medicine – Anti-Aging Medicine
Venue: Le Meridien Nfis
President: Ahmed Bourra
www.dermastic.asso.ma
dermastic.asso@hotmail.com

24-25 April – Brussels (Belgium)
25th Congress of the Belgian Society of Aesthetic Medicine
Venue: Radisson Blu Royal Hotel
Rue Fossé aux Loups, 47 – Brussel
Organisation
Jean Hebrant – Hugues Cartier
www.sbme-bveg.be
info@aesthetic-medicine.be

15-16-17 May – Rome (Italy)
36th National Congress of the Italian Society of Aesthetic Medicine
10th National Congress of the Italian Academy of Aesthetic Medicine
Venue: Congress Centre Rome Cavalieri
President of the Congress: Emanuele Bartoletti
sime@lamedicinaestetica.it
congresso@lamedicinaestetica.it
www.lamedicinaestetica.it

28-29 May – Odessa (Ukraine)
International conference
“Important issues of current plastic surgery, aesthetic medicine and dermatology”
Ukrainian Society of Aesthetic Medicine
President: Vladimir Tsepkolenko
office@virtus.ua

29-30 May – Pretoria (South Africa)
The 9th 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

27-28 June – Tblisi (Georgia)
III International Congress of Aesthetic Medicine
Georgian Society of Aesthetic Medicine
Venue: “Expo Georgia” Event Hall # 3
Co-organiser:
Scientific-Professional Society of Dermatovenereologists of Georgia
Department of Dermatovenereology of TSMU
Tel. +995 (32) 2 250565 - +995 5 5 77545108
info@gsoam.ge
www.gsoam.ge

16-17 July – Montevideo (Uruguay)
Congress of the Uruguayan Aesthetics Medical Society
President: Alberto Elbaum
www.sume.com.uy

3- 14 August - Buenos Aires (Argentina)
Degree course in Aesthetic and Anti-Aging Medicine
Practical module
Argentinian Society of Aesthetic Medicine
SOARME
Director: Prof. Dr. Raúl Pinto
info@soarme.com
www.soarme.com

22-23 September – Odessa (Ukraine)
Seminar and master class
“Regenerative technologies in aesthetic medicine”
Ukrainian Society of Aesthetic Medicine
President: Vladimir Tsepkolenko
office@virtus.ua

25-26 September – Paris (France)
36th 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

1-3 October – Quito (Ecuador)
VII Ecuadorian Congress of Aesthetic Medicine
Ecuadorian Society of Aesthetic Medicine
Venue: Swissotel Quito
President of the Congress: Viveka Tinoco Kirby
seem2008cg@gmail.com
www.seem.com.ec

2-4 October - Warsaw
XV International Congress of Aesthetic and Anti-aging Medicine
X International Conference – Lasers and other sources of energy in aesthetic medicine
Polish Society of Aesthetic and Anti-Aging Medicine of Polish Medical Society
Venue: Warsaw-Hilton Poland
President: Andrzej Ignaciuk
sekretariat@ptmeiaa.p
www.ptmeiaa.pl

7 November – Lausanne (Switzerland)
XIV Congress of the Swiss Society of Aesthetic Medicine
Venue: Beau-Rivage Palace
President: Xavier Martin
www.ssme.ch
xmartin@worldcom.ch

6-7 November – Toronto (Ontario – Canada)
CAAM 12th Annual Conference
Canadian Association of Aesthetic Medicine
Venue: The Westin Prince Hotel
CAAM Office Executive Director: Susan Roberts
s.roberts@caam.ca
www.caam.ca

12-15 November – Miami (Florida – Usa)
20th World Congress of Aesthetic Medicine
“Discoveries in Aesthetic Medicine”
American Academy of Aesthetic Medicine
Union International de Medicine Esthetique
Venue: JW Marriott Miami
President: Michel Delune
www.aaamed.org/20wcam
wcam@aaamed.org

14 November – Madrid (Spain)
VI Monographic days of SEME
Spanish Society of Aesthetic Medicine
www.seme.org

26-27 November – Alger (Algeria)
14th National Congress of Aesthetic Medicine and Surgery
Algerian Society of Aesthetic Medicine
Venue: Hotel Hilton
President: Mohamed Oughanem
oughanem_m@hotmail.com
www.same-dz.com

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

25-26-27 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
Presidente: 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 of the Congress: Emanuele Bartoletti
sime@lamedicinaestetica.it
congresso@lamedicinaestetica.it
www.lamedicinaestetica.it

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

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 1 • Number 2 • July/September 2015
www.aestheticmedicinejournal.org

Contents