

Intérêt des thérapies combinées en médecine esthétique pour le traitement du vieillissement du visage : toxine botulique, fillers et mésothérapie

Advantages of combined therapies in cosmetic medicine for the treatment of face aging: Botulinum toxin, fillers and mesotherapy

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Résumé

Les procédures non chirurgicales de médecine esthétique du visage se développent considérablement, car elles offrent de bons résultats cliniques à l'aide de techniques simples, non invasives, atraumatiques et reproductibles. La mésothérapie esthétique, ou mésothérapie anti-âge, utilise des injections intra-dermiques d'une solution nutritive et hydratante afin d'améliorer l'éclat, l'hydratation et la tonicité de la peau et de gommer les rides superficielles. L'injection sous-cutanée de fillers permet de combler les rides et dépressions ; en utilisant des produits de densité importante, il est également possible d'effectuer une véritable restructuration volumétrique du visage. Enfin, la toxine botulique agit en limitant la contraction de certains muscles de la mimique, afin de lisser les rides d'expression et sillons provoqués par la dynamique faciale. Dans cet article, nous développons le concept de thérapie combinée et décrivons notre expérience associant mésothérapie anti-âge (NCTF-135HA, Filorga, Paris, France), fillers à base d'acide hyaluronique (X-HA3 et X-HA-Volume, Filorga, Paris, France) et toxine botulique (Vistabel, Allergan, Irvine CA, USA). Une thérapie combinant mésothérapie anti-âge, injections de fillers et de toxine botulique, offre un traitement complet des 3 strates biologiques des tissus de revêtement. Cette stratégie thérapeutique non invasive permet bien souvent de satisfaire les patients par une approche globale du vieillissement de leur visage.

Mots-clés : Acide hyaluronique, filler, médecine esthétique, mésothérapie, toxine botulique, vieillissement cutané.

Summary

Non surgical cosmetic medicine procedures for the face are developing considerably, as they deliver good results using simple, non invasive, atraumatic and reproducible techniques. Aesthetic mesotherapy, also known as anti-aging mesotherapy, uses intra-dermal injections of a nutritive and moisturizing solution to improve brightness, skin hydration and tonus, and also smooth out superficial wrinkles. Subcutaneous filler injections enable to fill wrinkles and folds; by using high density products it is also able to provide genuine facial volumetric reconstruction. Finally, botulinum toxin acts by reducing certain muscle contractions to smooth out expression lines and folds induced by facial dynamics. In this article, we explore the concept of combined therapy and describe our experience associating anti-aging mesotherapy (NCTF-135HA, Filorga, Paris, France), hyaluronic acid based fillers (X-HA3 and X-HA-Volume, Filorga, Paris, France) and botulinum toxin (Vistabel, Allergan, Irvine CA, USA). A therapy combining anti-aging mesotherapy, botulinum toxin and filler injections, offers full treatment of the 3 biological levels of the covering tissues. This non-invasive therapeutic strategy brings patient satisfaction through a global approach to facial aging.

Key-words: Hyaluronic acid, fillers, aesthetic medicine, mesotherapy, botulinum toxin, cutaneous aging, combined therapies.

FACE AGING

Our face is our main interface with society and the perception of its aging is the most frequent reason for a medical consultation. The appearance of a few wrinkles and a damaged skin can seem derisory, but it is often a source of anxiety, a stamp of the years gone by. Surgical therapies are often too substantial to correct the multitude of imperfections that have accumulated. The development

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of a non surgical cosmetic medicine has enabled to offer simple, efficient solutions to numerous patients wishing to slow down facial aging. Indications of these therapeutic treatments have considerably increased over the last few years, either separately or complementary to surgery.

Facial wrinkles are principally the result of the combined action of gravity and loss of mechanical properties of soft tissues, particularly dependant on dermal elastin and collagen fibres network. Deterioration of dermal matrix is associated to the thinning of the skin's dermal layer and to a sclerosis of micro-vascularisation linked to age. The development of wrinkles is therefore naturally associated to solar ultraviolet rays that prematurely damage matrix proteins (elastin and collagen), lack of skin hydration and tobacco (that accelerates micro-vascularisation sclerosis). Redistribution, or accumulation, of adipose tissues coming with age is also responsible for the significant modification of facial volumes.

Next to these wrinkles, folds, also known as 'hyperdynamic facial lines' develop with age. Folds appear because of repeated tractions applied to the skin by the facial muscles of the underlying mimic. These lines, mostly from dynamic origin, must be differentiated from proper wrinkles due to cutaneous tissue sagging, because their different origin implies different therapeutic options.

Facial aging process is very different from one individual to another and isn't homogeneous on an individual, varying widely depending on anatomical zones. Apparent aging is as much linked to the evolution of the intrinsic quality of covering tissues (skin, muscles) as to the underlying support tissues (bone, cartilage). A striking example is profile modification due to dental occlusion deterioration or lip support loss during imperfect anterior teeth repair.

To sum up this disparity in facial aging, three levels are usually described: The upper third of the face is essentially marked by expression lines; the middle third suffers mainly from skeletal and tissue involution process; the lower third is particularly subject to ptosis.

This global analysis indicates obvious treatment choices: Implication of botulinum toxin to the upper third, implication of volumizing treatments to the middle third and finally a predominant surgical implication for the lower third.

Obviously, and it is the advantage of combined therapies, junction zone of these anatomical sectors benefit advantageously from the combination of these treatments.

Ptosis and involution remain the main face aging factors; our means of action are limited on such structural aging. Cosmetic medicine will therefore aim to hide the consequences of this structural aging, by acting on superficial tissues to restore some of the volume lost and erase cutaneous folds linked to tissue sagging.

FOUNDING PRINCIPLES OF AESTHETIC MEDICINE

Any face aesthetical therapeutic treatment should be based on a detailed and personalised analysis of aging, in order to set up a genuine therapeutic strategy, as opposed to a punctual treatment. Cosmetic medicine is a tailor made medicine that cannot be standardised and that requires numerous instruments to obtain the best possible result, in a non-abrasive way.

Two main methods are commonly used in the treatment of those wrinkles and folds. Wrinkles caused by dermal aging can be treated by injection fillers that fill the underlying cutaneous space and re-plump the skin to remove folds [1]. On the opposite, aging linked to facial expressions and action of the mimic muscles can only be erased efficiently by regular injections of botulinum toxin [2], as it blocks small cutaneous muscle action and therefore smooth over the skin's surface.

These two strategies are often combined in aesthetic medicine [3], fillers are used to mask wrinkles and static imperfections, whilst botulinum toxin intervenes on the facial dynamic to neutralise excessive folds that appear during facial mimics. Like a sculptor, the cosmetic practitioner should be able, through a series of precise injections, to fill, stretch, block and finally restore the face's youthful appearance. Unfortunately, although efficient, these therapeutic treatments only aim to temporarily mask the most marked, visible signs of aging, and not to improve the intrinsic quality of the cutaneous tissue. Scars are less visible, but tissues continue to deteriorate, until finally aesthetic medicine tricks have no effect anymore.

A third approach, aesthetic mesotherapy, was developed in parallel and is now combined to the action of fillers and botulinum toxin. This technique aims to revitalise soft tissues and attempts to regenerate them through injections of various stimulating solutions.

Combined therapy based on utilisation of those three complimentary methods is therefore the natural evolution of aesthetic medicine for the face, with each of its instruments offering specific advantages, it participates in its way to anti-aging strategy.

AESTHETIC MESOTHERAPY OR ANTI-AGING MESOTHERAPY: DERMIS NOURISHMENT AND REVITALISATION

Concept of anti-aging mesotherapy

Mesotherapy is a therapeutic concept invented in 1952 by a French doctor, Michel Pistor [4]. It acts in treating different pathologies with intra-dermal injections of small doses of active products, directly in the zone to treat, in order to achieve the best efficiency. This concept is often summed up by its inventor's quote: 'a little, rarely, in the right spot'. The main applications were initially rheumato-

logic and analgesic, with injections of non-steroidal anti-inflammatory, relaxant or vasodilator solutions.

Mesotherapy was then adapted to numerous applications such as aesthetic treatments, notably intradermal injections of nourishing and moisturizing solutions for the skin and particularly the face: This is the concept of anti-aging mesotherapy.

This aesthetic mesotherapy must however be clearly differentiated from phosphatidylcholine subcutaneous injections, a method targeting the break down superficial adipose layers. This method is sometimes mistakenly assimilated to mesotherapy [5-7] and present necrosis [8] and infection risks [9] often reported in literature [10]. Anti-aging mesotherapy is usually a superficial treatment that doesn't present any significant risk.

Its technique consists in intracutaneous injection of a nutritive and moisturizing solution, using a thin needle, following the 'papule' technique [11]. The 0.01ml micro-injections are performed along the wrinkles with a needle and only a few millimetres apart (Image 1). Then a 'nappage' is carried out in a cross-hatching technique over the whole surface of the face, using very superficial micro-injections that create barely noticeable papules, roughly one centimetre apart (Image 2). These injections remain superficial, painless, and performed either manually with a syringe, or with an electronic gun. The latter tool enables higher injection rate (3 injections per second) and therefore enables to treat large cutaneous zones.



Image 1: Anti-aging mesotherapy solution injection method. Intradermal micro-injections are performed with a manual syringe at a few millimetres interval along the nasolabial (A) and palpebral (B) lines. Then 'nappage' of the cheeks is performed in cross-hatching technique over the whole face, with very superficial micro-injections (here shown performed with an electronic gun) (C).



Image 2: Straight after 'nappage' of the cheeks with a revitalising solution, you notice traces of numerous papules, at 1 cm intervals.

It is also possible to perform these injection sessions with a small size cannula to achieve a genuine 'bio-revitalisation'. It isn't strictly a mesotherapy because there are no multiple cutaneous punctures, but it provides the skin with the necessary nutritive elements with a much reduced number of entry points.

This is a superficial technique presenting very little side effects apart from risks of bruising if the technique is not mastered. Contra-indications are limited to taking anticoagulants and cutaneous lesions (skin treated must not be damaged or have wounds). A mesotherapy session lasts about twenty minutes. Four or five sessions, usually at 15 days intervals are necessary to obtain a visibly rejuvenated skin. An immediate 'radiant glow' effect always occurs, because from the first session, the skin recovers a bright complexion. In the long term, the skin restores its elasticity and firmness. It is a biological, progressive treatment and its results are cumulative. Sessions will therefore be scheduled every month as long as improvements are obtained. When the results have stabilised, sessions can be spaced out by 2, 3 or even 6 months depending on the patient (follow-up treatments).

Anti-aging mesotherapy uses various intracutaneous injectable solutions composed of vitamins, minerals and Hyaluronic acid (for a moisturizing action). In reality there is a certain anarchy in products currently available [6], numerous presenting uncertain sanitary security (non CE-marked, no transparent quality reference), which sometimes use potentially harmful compounds that can lead to negative results [12, 13].

Amongst the well known products available in France, NCTF®-135 (Filorga, Paris, France) [11] is a nutritive, revitalising solution for aesthetic mesotherapy. It is composed of non reticulated hyaluronic acid and 55 bioactive compounds: 14 vitamins (A, B, C, E), 4 minerals, 2 antioxidants, 24 amino acids, 6 coenzymes and 5 nucleic bases. All these compounds are renowned for their positive in vitro action on cellular proliferation and matrix protein synthesis stimulation (in particular collagen and elastin). They also provide a protective action on elastase synthesis inhibition and other matrix metalloproteases that break down and refines dermal layer. The concept is therefore very simple: wrinkles result from elastic and collagen fibre diminution, microcirculation decrease and thinning of the dermis imposed by cell senescence, oxidative stress, and tobacco and sun exposure. Cells therefore need to be stimulated and provided with the necessary compounds for extracellular matrix neo-production and thickening of the dermis. Hyaluronic acid is combined to nutritive compounds of the mesotherapy solution in order to obtain deep moisturising, as well as a tautening action on the skin.

Anti-aging mesotherapy is mostly applied to the face but also the neck, décolletage [11], back of hands, inner arms and legs, and even stomach. It always consists in moisturising the tissues, tautening them slightly and restoring their radiance.

An experience in facial mesotherapy: NCTF-135HA

There is a multitude of mesotherapy products on the market but unfortunately neither a classification, nor a consensus on the choice of product better adapted to these inventions exists [6]. Scientific literature on the subject is

also very limited. Product choice is therefore principally dependent on the practitioner's experience and the manufacturer's reputation over a few years utilisation.

We use NCTF-135HA (Filorga, Paris, France) [11], a mesotherapy solution containing 55 nutritive ingredients and 5 mg/ml of non reticulated Hyaluronic acid. NCTF-135HA is one of the most commonly used products in France and respects rigorously the principles of anti-aging mesotherapy as we envisage it: A nutritive solution, with no pharmacologic contra-indication, that follows strict sanitary security criteria (CE mark). NCTF-135HA contains more hyaluronic acid (5 mg/ml) than the NCTF-135 solution alone (0.025 mg/ml), thus providing a higher moisturising action. On the opposite we rarely use products with a higher dose of non-reticulated Hyaluronic acid (10 mg/ml), that we keep for the most dehydrated skins.

In cases treated solely with NCTF-135HA (Image 3), after 5 sessions at 15 days intervals, the cutaneous quality of faces treated has been scored by practitioners and patients by using reproducible images and a simplified grading index. In the month following the last injection, on 40 patients, we observed an average improvement of more than 140% on cutaneous brightness, more than 130% in hydration and over 100% in cutaneous tonus. Finally the average diminution of fine lines and wrinkles was superior to 70% improvement. Moisturizing and cutaneous brightness improvements were immediate but cutaneous tonus and wrinkle correction were more progressive, thus confirming the advantage of a protocol in 5 sessions.



Image 3: Facial treatment by aesthetic mesotherapy (using NCTF-135HA solution). After 5 sessions of the treatment, the skin has recovered significant radiance, tonus and hydration, and superficial wrinkles have been erased.

By systematizing, 3 phases were clearly identified during treatment. The first 15 days (after the first session) are part of the initialisation phase: The main immediately visible results are brightness and hydration and the beginning of wrinkle disappearance. After a month and a half (corresponding to 3 sessions at 15 days intervals) we enter the reparation phase with much more noticeable results in terms of cutaneous tonus and wrinkle diminution. The last phase is one of maintenance and result consolidation with follow-up sessions.

Please note that some adverse side effects have occurred in all intradermal injection treatments: Half of the number of patients showed a slight cutaneous erythema on injection zones, 20% of them showed a very slight oedema or slight bruises. All those effects disappeared after a 48 h period.

No other adverse side effect has been noted. There is no risk of overcorrection. At the time of result evaluation, 1 month after the end of the treatment sessions, all patients were satisfied with the results. The psychological extent of these simple, efficient rejuvenating treatments cannot be ignored [14]; as a first therapeutic gradient phase in aesthetic medicine, mesotherapy helps to establish confidence between patients and their practitioners.

Mesotherapy on its own therefore provides a progressive and visible improvement in the quality of the skin following 4 criteria: Brightness increase, hydration, skin tonus and reduction of superficial wrinkles.

SCULPT THE FACE AND CONTROL MUSCULAR BALANCES: FILLERS AND BOTULINUM TOXIN

Actual aesthetic medicine strategies often combine fillers, to correct static defaults, and botulinum toxin, to correct lines linked to the face dynamic. This approach is particularly efficient on the nose, in medical rhinoplasty [3].

Treatment with filling products (fillers)

The main purpose of dermal fillers is to fill asymmetric and static facial folds, in order to restore the face's harmony and necessary volumes. A number of filling products are available on the market and selected according to the clinical situation. The choice of product will often, however, depend on the practitioner's preferences, as there are no standardised rules in terms of product selection.

Resorbable, temporary fillers are the most numerous available on the market. They are mostly highly reticulated hyaluronic acid gels (X-HA3, Juvederm®, Restylane®, Teosyal®...), polylactic acid gels (New Fill®, Sculptra®) or calcium hydroxyapatite gels (Radiesse®).

On the opposite, non-resorbable filling products are mostly polyacrylamide gels (Aquamid®, Bio Alcamid®, Artecoll®, Outline®). In theory these fillers offer long term aesthetic result stability, but they should be banned because of the unpredictable complications they can generate.

Filler injections can be done without anaesthesia [3], but the treatment is more comfortable with an anaesthetic cream applied 30 minutes prior or with a xylocaine injection, especially for lip treatment. The treatment is often performed in a slow, linear way, during the whole needle withdrawal, following the linear technique and the fan technique. Quantities injected are deposited at regular intervals to avoid nodularities. A slight cutaneous massage following the injection will allow better product diffu-

sion and harmonious implant. The results are visible immediately.

Of all fillers available, hyaluronic acid is the main reference [1, 15-17]. This molecule is a natural ubiquitous polysaccharide, present in all tissues, in particular connectives, and in all animal species. Mildly immunogenic, it doesn't pose an allergy risk (if it is purified properly), which makes it a product adapted to common use. This glycosaminoglycan has the ability to bind the equivalent of 1000 times its volume in water, which makes it the obvious choice to increase tissue volume, thus thickening the skin's dermal layers. In man, the quantity of hyaluronic acid in the skin decreases with age, and the phenomenon plays a key role in elasticity loss and skin dehydration, leading to wrinkle formation. In its original state, hyaluronic acid is degraded by enzymes (hyaluronidases) and free radicals produced by oxidative stress; local antioxidants action therefore protects this molecule.

Hyaluronic acid used as subcutaneous filler is reticulated so as to limit its enzymatic depolymerisation and extend its life in the injected zone.

Reticulating agents are numerous, but the most commonly used and the safest is BDDE (1-4 butanediol diglycidyl ether).

Elimination of this reticulating agent's free form also determines the quality of the hyaluronic acid's purity.

There are many different hyaluronic acids on the market presenting different cross-linking degrees, depending on clinical applications required.

On the opposite, hyaluronic acid used in mesotherapy injectable solutions is not reticulated. It is injected in a superficial intradermal way, because it possesses most of all a moisturising and stimulating function and its purpose isn't to fill folds.

Choice of filler: experience of X-HA3 and X-HA-Volume

Again, given the plethora of products available, the choice in hyaluronic acid depends on practitioners' experience and manufacturers' reputation. We will choose in priority a product offering maximal tolerance (dependant on its purification during production), and suitable volumizing effect. We chose X-HA3 (Filorga, Paris, France), that corresponds to those requirements and most importantly contains a very homogeneous and polyvalent texture. Depending on their density and diffusing properties (linked to their degree and type of cross-linking), fillers are more or less best adapted to the 3 main types of injections: Medium wrinkles, deep set wrinkles and lips. The homogeneous texture, density and medium viscosity of X-HA3 enables to treat the 3 types with the same product; this one has therefore become our hyaluronic acid first choice. The secret of this polyvalent texture is the product composition: A cross-linked hyaluronic acid combined with a fraction of free hyaluronic

acid. By massaging the injected zone, the gel gradually becomes homogeneous without creating lumps, and fixes itself durably thanks to its elasticity. This gel is particularly easy to use on delicate zones such as the lips, that are mobile and very vascular (4 and 5).



Image 4: Treatment of lower and middle facial zones using the combined method. Mesotherapy (with NCTF-135HA) improved overall cutaneous aspect, whilst filler injections (with NCTF-135HA) have filled the most deep set jugal and nasolabial wrinkles and have restored the cheeks volumes.



Image 5: Treatment of the upper lip and nasolabial wrinkles using the combined technique. Straight after injections of revitalising solution and fillers, cutaneous tissues regain their brightness, and the filling effect is immediate, but a slight erythema has also appeared.



Image 6: Filling of a deep set hollow at the base of the nose, through subcutaneous injection of a substantial volume of dermal filler (reticulated hyaluronic acid X-HA Volume).

Alongside this polyvalent tool, we also use X-HA-Volume (Filorga, Paris, France), a version twice as viscous as this hyaluronic acid (because more reticulated). This product restores an important volume by subcutaneous injection; it treats volume losses linked to aging and sculpts the face naturally and without surgery. The zones treated in particular are the cheeks, cheekbones, chin, face contour, temporal zone and the base of the nose (6). Face contour can be remodelled, volumes can be restored and deepest wrinkles can be treated. Injections are always deep, epidermal, subcutaneous or supraperiosteal.

According to our experience, patients treated by this type of filler can show slight oedema or slight erythema in 40% of cases, and superficial bruises in less than 10% of cases. These side effects only last a very short time, less than a week in average. Evaluated patient satisfaction is always good because such treatments are simple and results are instantly noticeable. These deep injections require very good knowledge of the anatomy and injection techniques in order for these operations to be performed safely.

Treatment using botulinum toxin

Controlling facial wrinkles using botulinum toxin is an old therapeutic technique [2]. Combined with the use of fillers, these toxin injections enable very wide application zones in facial remodelling [3].

Botulinum toxin [2] is a myorelaxant substance that interrupts neuromuscular junction thus preventing nervous influx transmission to the muscles. This toxin has been used since 1975 to control certain facial twitches and strabismus in children. This molecule has been used in France for pathological indications since 1990. In that same time period, use of this toxin in cosmetic medicine appeared, through observation of pathological indication side effects such as cutaneous wrinkle diminution. It has officially been used for inter brow wrinkle treatment in the USA since 2002, and in France since 2003 (Vistabel, Allergan, Irvine, CA, USA). Numerous other utilisations now exist in aesthetic medicine to treat forehead wrinkles, crow's feet wrinkles and most recently, nasal wrinkles. Its action on facial muscular balances, notably in terms of the eye contour, allows to erase wrinkles and reposition certain key elements such as the eyebrow for example. It is also possible, in expert indications, to use the toxin on the face's middle third and lower third (depressor anguli oris muscle, platysma muscle...) [18].

Without referencing back to all of the toxin indications, its combination with fillers is more and more frequent, particularly in medical rhinoplasty [3, 19]. Aesthetic medicine logical treatments can only be performed after a precise, dynamic study of the face (speech, smile, breathing...) where the muscles responsible for deformations are determined and the role of muscular movements in wrinkle and imperfection appearance is assessed.

COMBINED THERAPEUTIC TREATMENTS IMPACT

Various therapeutic tools currently at our disposition have enabled us to develop non surgical cosmetic medicine procedures [20]. The 3 tools described previously combine and complete each other naturally (Image 7 to 9): Fillers are used to fill large static defaults, botulinum toxin prevents the appearance of dynamic folds and mesotherapy looks at improving the intrinsic quality of cutaneous envelope.



Image 7: Treatment of dark circles by combined method. X-HA3 filler injections have erased cutaneous folds and anti-aging mesotherapy (NCTF-135HA) has improved the skin's appearance.



Image 8: Treatment of nasolabial folds by combined method: X-HA3 filler injections have filled residual static folds, and aesthetic mesotherapy (NCTF-135HA) has improved cutaneous tissue radiance.

This notion of combined therapy offers obvious biochemical logic. Mesotherapy solutions contain numerous nutritive compounds, as well as non reticulated hyaluronic acid in order to temporarily 'fill' the tissues with water. These solutions therefore naturally combine with reticulated hyaluronic acid used to fill wrinkles and imperfections. Moreover the mesotherapy solution's antioxidant compounds have a protective action on hyaluronic acid injected simultaneously.

These combined therapies also offer a therapeutic gradient logic, with step by step, short and long term results. Indeed, nutritive mesotherapy in itself presents interesting results, and the incorporation of small hyaluronic acid concentrations in the various anti-aging revitalising cocktails allow to add a slight redensifying effect for biological stimulation's benefit.

This atraumatic, completely reversible approach is the first step in comforting patients in their cosmetic requests and strengthen their trust. Mesotherapy solution injections are then completed by cross-linked hyaluronic acid fillers presenting longer term results. Revitalising and filling products complete each other in order to constitute an integrated global treatment. This cosmetic medicine therapeutic gradient is natural, efficient and, according to our experience, extremely well tolerated by the patient.

A technical tissue logic also exists for these combined therapeutic treatments: mesotherapy acts on intradermal level, botulinum toxin acts on muscular level and fillers on subcutaneous level. By using this toxin, fillers and anti-aging mesotherapy in synergy, we can restructure facial volumes by acting on 3 tissue levels, in order to obtain homogeneous light reflections on the face and a harmony between the different face zones (Image 9).



Image 9: Complete face treatment by combined method. The cheeks' volumes have been remodelled through dermal filler injections (X-HA Volume), and the skin has regained substantial brightness and tonus thanks to the combined mesotherapy treatment (NCTF-135HA). Finally, botulinum toxin injections (pre-existing and follow-up treatment) allow to maintain frontal, periorbital and nasal wrinkle smoothing.

Even with the advantage of this combined approach obvious, it will probably require a number of years of methodical experience feedback before this doctrine can be validated scientifically. Actual techniques depend above all on clinical validations and practitioners experience of using them for a few years. In a way, anti-aging mesotherapy itself suffers even more from confusion and the plethora of injectable solutions available on the market [12, 21], of which numerous are developed and manufactured without meeting a clear quality reference (such as CE marked). Even more so than validating general concepts of these combined therapeutic treatments that obviously function, it is a serious ranking and validation of available products that is actually required.

CONCLUSION

The aim of facial rejuvenation is to satisfy the patient's demand by obtaining the best results possible thanks to simple, non-invasive, atraumatic and reproducible techniques. Non surgical aesthetic medicine procedures are developing considerably, because they offer relative innocuousness and a reversibility that other surgical treatments don't offer. Anti-aging mesotherapy with a nourishing and moisturizing solution can be applied to all situations, because the aim is foremost to improve intrinsic characteristics of covering tissues. It is a painless, risk free, ambulatory treatment that is natural and progressive and its side effects are limited to slight redness and oedemas. A therapy combining anti-aging mesotherapy, hyaluronic acid filler injections and botulinum toxin injections offer a complete treatment of the three biological layers of cover-

ring tissues. This therapeutic strategy frequently provides a satisfactory and sufficient solution to patients suffering psychologically from face aging.

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