
BACKGROUND: There is an increased demand for soft tissue augmentation procedures. A wide range of products can provide correction through different mechanisms and it is important for clinicians to understand the biological pathways of each material. This study presents a systematic review of the pathways of commonly used fillers, with consideration of the complications associated with each. METHODS: The PubMed (National Library of Medicine) database was searched for MeSH headings for different types of fillers, including trade names, between January 1, 2000, and January 1, 2013. Article titles were screened, and only studies designed to determine the mechanism of action and histopathology of complications were included. RESULTS: When restricted to studies on biological mechanisms, 109 manuscripts were identified and the mechanisms of action of short-term and long-term degradable as well as permanent fillers were reviewed. Hyaluronic acid fillers, which are the most commonly used, form a fibrous capsule and induce limited de novo collagen. Poly-l-lactic acid and calcium hydroxyapatite are semipermanent fillers that provide long-term restoration of tissue volume by stimulating fibroblasts to lay down a matrix of collagen and elastic fibers. Polymethyl methacrylate is the only FDA-approved permanent implant that is held in place by encapsulation, providing a scaffold upon which the dermis can recover to its original thickness. DISCUSSION: Soft tissue augmentation products are variable, and no single product can be considered the most effective or ideal. An understanding of biological mechanisms may help guide physicians choose the best suited product among the various options available while minimizing the occurrence of complications.


In recent years, hyaluronan (HA) has become an increasingly attractive substance as a non-immunogenic filler and scaffolding material in cosmetic dermatology. Despite its wide use for skin augmentation and rejuvenation, relatively little is known about the molecular structures and interacting proteins of HA in normal and diseased skin. However, a comprehensive understanding of cutaneous HA homeostasis is required for future the development of HA-based applications for skin regeneration. This review provides an update on HA-based structures, expression, metabolism and its regulation, function and pharmacological targeting of HA in skin.


With an increasing understanding of the aging process and the rapidly growing interest in minimally invasive treatments, injectable facial fillers have changed the perspective for the treatment and rejuvenation of the aging face. Other than autologous fat and certain preformed implants, the collagen family products were the only Food and Drug Administration approved soft tissue fillers. But the overwhelming interest in soft tissue fillers had led to the increase in research and development of other products including bioengineered nonpermanent implants and permanent alloplastic implants. As multiple injectable soft tissue fillers and biostimulators are continuously becoming available, it is important to understand the biophysical properties inherent in each, as these constitute the clinical characteristics of the product. This article will review the materials and properties of the currently available soft tissue fillers: hyaluronic acid, calcium hydroxyapatite, poly-l-lactic acid, polymethylmethacrylate, and autologous fat (and aspirated tissue including stem cells).

**BACKGROUND:** Because Asian faces are generally flatter than Caucasian faces, Asian women are increasingly requesting facial volume enhancement. **OBJECTIVE:** To clarify the effectiveness and safety of a volumizing treatment using 20-mg/mL smooth, highly cohesive, viscous hyaluronic acid fillers in young Asian women. **MATERIALS AND METHODS:** We retrospectively reviewed 320 patients who had been treated with this filler from March 2010 to February 2012. The filler was injected in the shape of a diamond to the glabella, both malar eminences, and chin. Overall, 4 to 6 mL of filler was sufficient to enhance the volume of a face in young Asian women. Both the physicians and patients rated effectiveness on the Global Aesthetic Improvement Scale at week 4. Need for touch-up and any adverse events were also evaluated. **RESULTS:** Most patients were very satisfied with this volumizing procedure, and there were no major complications. **CONCLUSION:** The 20-mg/mL smooth, highly cohesive, viscous hyaluronic acid filler is an effective, well-tolerated treatment option in young Asian women wishing for a more-three-dimensional profile.


**SUMMARY:** Soft-tissue augmentation has become an increasingly popular option for facial rejuvenation. Hyaluronic acid fillers are part of the most rapidly expanding segment of this market, largely because of their safe drug profile and temporary nature. Despite their good safety profile, they can and do have complications ranging from superficial placement, uneven placement, granulomatous reactions, and skin necrosis. This article reviews the on- and off-label uses of hyaluronidase and presents several clinical algorithms detailing the effective and safe use of hyaluronidase to manage complications secondary to hyaluronic acid fillers.


Over the last decade, there has been increasing interest in minimally invasive cosmetic treatments, especially for facial rejuvenation. Next to botulinum toxin injection, the injection of soft tissue fillers is the second most frequent minimally invasive procedure performed in the USA. Hyaluronic acid (HA) is the most commonly used dermal filler. One of patients' main concerns about filler injections pertains to pain and discomfort. Topical anesthetics, nerve blocks, and/or the incorporation of lidocaine to the filler have been applied in order to reduce distress and pain. Despite nerve blocks being an effective form of anesthesia, they may distort the area to be treated, as well as lengthen and complicate the procedure. Studies have shown that the incorporation of lidocaine to HA fillers significantly reduces pain and discomfort. Yet, one of the dilemmas about the addition of lidocaine solution to HA fillers is the possible alteration of the physical characteristics of the product by negatively impacting the efficacy and/or duration of the filler. The concern is that the addition of lidocaine could dilute the product, creating less correction per mL, changing the product's viscosity and consequently the "lifting" ability. Also, this dilution could reduce the product's duration. There may be a difference between a physician adding an aqueous solution into a lidocaine-free version of HA and the pre-incorporated lidocaine version of HA. An aqueous solution might dilute the product, while the pre-incorporated powder lidocaine appears to avoid this problem. Juvederm(R) XC is manufactured with powder lidocaine 0.3%; it is associated with significantly less injection pain than Juvederm(R) and other lidocaine-free versions of HA.
Studies have shown that lidocaine enhances treatment comfort and optimizes the injection experience while maintaining a similar safety and effectiveness profile. Regarding the longevity, further study is necessary to determine if there is any difference in durability.


BACKGROUND: Hyaluronic Acid (HA) fillers are widely used for restoring facial volume.
OBJECTIVE: A 24-week study evaluated clinical efficacy with HA. METHODS AND MATERIALS: Included were 15 healthy subjects recruited from 4 centers, between ages of 35 to 65 years, who had a Wrinkle Severity Rating Scale (WSRS) score >/= 3, indicating moderate volume loss. Revanesse(R) Ultra (Prollenium), a HA dermal filler, was used. Primary study outcome was physicians scored facial volume correction, using the Global Aesthetic Improvement Scale (GAIS), comparing baseline (day 0) versus 24 weeks (end) and blindly assessed photographs. Subject satisfaction and comfort was evaluated using self-administered questionnaires at day 0 and at week 24. RESULTS: N = 15, 13 female and 2 males with a mean age (years) of 48.52 ( SD +/- 10.46) received treatment with HA and completed the 24-week study. At screening they had a moderate (mean 2.85, SD +/- 0.45) WSRS score. At week 24 a market facial volume restoration was shown and no adverse events were reported. All patients reported to be satisfied with the obtained results. CONCLUSION: Good - excellent volume enhancement was noted almost immediately after the HA injections, improving patient reported quality of life aspects. HA treatment was shown to be safe.


PATIENT: Male, 25 FINAL DIAGNOSIS: Diffuse alveolar hemorrhage Symptoms: Cough dry * short of breath MEDICATION: - Clinical Procedure: - Specialty: - OBJECTIVE: Unusual clinical course. BACKGROUND: Hyaluronic acid is a substance that is naturally present in the human body, especially in joints and eyes. Hyaluronic acid injectable gels have been available for the general market since 2003 as cosmetic dermal fillers and skin boosters. Diffuse alveolar hemorrhage is an acute event that threatens the life of the patient and can lead to pulmonary fibrosis. Alveolar hemorrhage associated with hyaluronic acid dermal fillers is an entity that to the best of our knowledge has never been described in the medical literature. CASE REPORT: We describe a patient who presented with dyspnea and cough after a subcutaneous injection of hyaluronic acid, with radiographic abnormalities including ground glass opacities and consolidation. The patient underwent flexible bronchoscopy and was diagnosed with diffuse alveolar hemorrhage. CONCLUSIONS: This case emphasizes that this life threatening condition may occur with the use of this medication and physicians must be aware of this disorder, as early recognition and management can reduce morbidity.


Data demonstrating the efficacy of hyaluronic acid (HA)-based mesotherapy for skin rejuvenation are scarce. The aim of the study is to assess the efficacy of non-reticulated HA-based mesotherapy on skin elasticity and complexion radiance. 55 women with cutaneous ageing signs included in the Full Analysis Set (FAS) population blindly received intradermal micro-injections (50 x 0.02 mL) of non-cross-linked HA filler with mannitol (Glytone 1, HA concentration: 14 mg/g) in one cheek and saline physiological solution in the other according to hemifacial randomisation in 3 monthly sessions. Elasticity (E1 and E2 stiffness parameters) and dermis thickness were measured by cutometry and 20 MHz echography, before (D0)
treatment and 1 (1M) and 3 months (3M) after the last injection. A trained panel blindly scored skin complexion radiance from standardised and calibrated photographs, using 100 mm analogue scales. In the FAS population, only HA filler significantly decreased E1 at 1M (-10.9 %, p = 0.026) and 3M (-10.5 %, p = 0.035) compared with D0; its effect versus the control tended to be more persistent, with a difference between treatments at 3M close to significance (p = 0.063). E2 also decreased at 1M (-8.2 %, p = 0.027) and 3M after HA-treatment only. Dermis thickness significantly increased after HA-treatment at 1M (+3.4 %, p = 0.028) and 3M (+4 %, p = 0.008), and after control-treatment at 1M only (+2.5 %, p = 0.015). The HA filler significantly improved complexion radiance at 3M compared with the control (p = 0.012) and for 51 % of subjects, their skin status. Non-reticulated HA-based mesotherapy significantly and sustainably improves skin elasticity and complexion radiance.


BACKGROUND: Intradermal injection of hyaluronic acid (HA) is currently the criterion standard to reduce the appearance of nasolabial folds (NLF). OBJECTIVE: Effects of a monophasic HA filler using cohesive polydensified matrix (CPM) technology were compared with those of nonanimal stabilized HA (NASHA). MATERIALS AND METHODS: In a double-blind, half-side comparison, 20 subjects (ages 35-65, mean 52 +/- 5.6) with symmetric NLF grade 3 to 4 were randomized to contralateral treatment with a monophasic polydensified filler (CPM) and a biphasic HA filler (NASHA). Efficacy was assessed at baseline and after 2, 24, and 48 weeks using a wrinkle severity rating scale (WSRS) for NLF, subject questionnaire, and biophysical in vivo methods. RESULTS: All subjects showed significant improvements with both fillers up to day 365. Subject questionnaires confirmed significantly less injection pain for the CPMHA, significantly greater patient satisfaction after 2 weeks with both fillers, and after 24 and 48 weeks significantly greater improvement with the CPMHA compared to baseline. WSRS and skin surface topography parameters improved significantly up to 48 weeks with both fillers. CONCLUSION: A single intradermal injection of a monophasic CPMHA and a biphasic NASHA filler showed significant improvements in WSRS and measured wrinkle depth up to 48 weeks for both fillers and significant differences in injection comfort and patient satisfaction in favor of CPMHA.


BACKGROUND: Hyaluronic acid (HA) fillers are an established intervention for correcting facial volume deficiency. Few studies have evaluated treatment outcomes for longer than 6 months. The purpose of this study was to determine the durability of an HA filler in the correction of midface volume deficiency over 24 months, as independently evaluated by physician investigators and subjects. METHODS: Subjects received treatment with Juvederm® Voluma® to the malar area, based on the investigators’ determination of baseline severity and aesthetic goals. The treatment was administered in one or two sessions over an initial 4-week period. Supplementary treatment was permissible at week 78, based on protocol-defined criteria. A clinically meaningful response was predefined as at least a one-point improvement on the MidFace Volume Deficit Scale (MFVDS) and on the Global Aesthetic Improvement Scale (GAIS). RESULTS: Of the 103 subjects enrolled, 84% had moderate or significant volume deficiency at baseline. At the first post-treatment evaluation
(week 8), 96% were documented to be MFVDS responders, with 98% and 100% graded as GAIS responders when assessed by the subjects and investigators, respectively. At week 78, 81.7% of subjects were still MFVDS responders, with 73.2% and 78.1% being GAIS responders, respectively. Seventy-two subjects completed the 24-month study, of whom 45 did not receive supplementary Voluma() at week 78. Forty-three of the 45 (95.6%) subjects were MFVDS responders, with 82.2% and 91.1% being GAIS responders, respectively. At end of the study, 66/72 subjects were either satisfied or very satisfied with Voluma(), with 70/72 indicating that they would recommend the product to others. Adverse events were transient and infrequent, with injection site bruising and swelling being the most commonly reported. CONCLUSION: Voluma() is safe and effective in the correction of mild to severe facial volume deficiency, achieving long-term clinically meaningful results. There was a high degree of satisfaction with the treatment outcome over the 24 months of the study.


IMPORTANCE: Dermal injection of cosmetic fillers can lead to irreversible blindness when injected in the forehead, and this possible adverse effect is not typically mentioned to patients. OBSERVATIONS: Vision loss from central retinal artery occlusion occurring, after cosmetic facial enhancement, was irreversible in 3 patients. However, 1 patient had a small amount of recovery with aggressive therapy. CONCLUSIONS AND RELEVANCE: Cosmetic facial fillers are not approved for use in the forehead, but off-label use for enhancement in this region is common. To our knowledge, there have been no prior reports of blindness caused by filler injected into the forehead. We present findings of central retinal artery occlusion due to fillers in 3 patients shortly after their cosmetic procedures. The filler presumably enters the central retinal artery via the rich external-internal carotid anastomoses and becomes embedded in the retinal tissues, potentially leading to irreversible and severe vision loss. Physicians performing cosmetic enhancement procedures involving facial fillers need to be aware of this potential complication and should include significant vision loss as a possible rare complication.


Vascular occlusion causing blindness is a rare yet greatly feared complication of the use of facial aesthetic fillers. The authors performed a review of the aesthetic literature to ascertain the reported cases of blindness and the literature reporting variations in the vascular anatomy of the human face. The authors suggest a small but potentially helpful addition to the accepted management of the acute case. Cases of blindness, mostly irreversible, from aesthetic filler injections have been reported from Asia, Europe, and North America. Autologous fat appears to be the most frequent filler causing blindness. Some cases of partial visual recovery have been reported with hyaluronic acid and calcium hydroxylapatite fillers. The sudden profusion of new medical and nonmedical aesthetic filler injectors raises a new cause for alarm about patient safety. The published reports in the medical literature are made by experienced aesthetic surgeons and thus the actual incidence may be even higher. Also, newer injectors may not be aware of the variations in the pattern of facial vascular arborization. The authors present a summary of the relevant literature to date and a suggested helpful addition to the protocols for urgent management.

BACKGROUND: A unique case is presented in whom an allergic reaction to Restylane filler, associated with migrating granulomas, persisted despite medical interventions. A histopathological study was requested for evidence at court. METHODS: Hematoxylin-eosin, alcian blue and colloidal iron staining were applied to skin sample biopsies obtained 5 months and 3 years after the hyaluronic acid (HA) injection. RESULTS: The histological staining highlighted the presence of the filler inside the foreign body granuloma and in the derma of a biopsy obtained after 5 months; a small amount of filler was discovered within a granulomatous reaction 3 years after the injection. CONCLUSIONS: Smaller fragments of HA display inflammatory, angiogenic and immune-stimulatory activities. Intradermal skin testing before the start of HA filler therapy, and before each subsequent injection, may prevent legal implications for the plastic surgeon. Informed consent to skin tests should be obtained.


Abstract In a minority of patients undergoing liposuction, superficial irregularities (or skin depression) in the operated area may occur. Macrolane is a gel composed of hyaluronic acid (HA), used for volume restoration of soft tissues. In this study, the authors investigated the effectiveness, maintenance, and safety of Macrolane as a "non-surgical" treatment to correct skin depression after liposuction. Twelve female patients were included. Macrolane was injected at a subdermal superficial plane using an intramuscular or spinal needle. In all patients, Macrolane was successful in correcting skin depression. No relevant side effects were observed. At 8 months post-injection, a persistence of correction of 60-70% was still present in 90% of the patients. In conclusion, Macrolane filler injections are a predictable, safe, and long-lasting non-surgical procedure to fill contour defects that arise after liposuction, and represent a good option for patients who refuse to undergo an additional surgery to fill the arisen skin depressions.


We report a case series of seven patients with bacterial cellulitis of the face complicating a filler injection for cosmetic reason, treated in a university hospital from 2005 to 2012. There were seven women aged 34 to 57 years. Two patients had a deep collection requiring surgical excision combined with antibiotics. Five patients were treated with antibiotics only. In two cases the bacteria was found streptococcus A and in one case Staphylococcus aureus. One patient required hospitalization in an intensive care unit. Only patients who needed surgical treatment showed moderate aesthetic sequelae.


BACKGROUND: Within the last few years, hyaluronic acid (HA) fillers and radiofrequency (RF) devices have shown significant promise for skin rejuvenation. But the effects of HA only lasted for a relatively short duration. Therefore, we tried a new combination therapy of intradermal RF and HA filler. OBJECTIVE: To evaluate the clinical efficacy of combination therapy of intradermal RF and HA filler for nasolabial fold (NLF) wrinkle reduction. MATERIALS AND METHODS: Ten Korean female volunteers with mild to severe NLFs were
enrolled. In the control group, five subjects were treated with HA filler alone. In the experimental group, the other five subjects were treated with intradermal RF prior to HA filler. Efficacy was evaluated based on the change on the Wrinkle Severity Rating Scale (WSRS) and the Global Aesthetic Improvement Scale (GAIS) from baseline. RESULTS: At 12 and 24 weeks after treatment, the experimental group showed significantly greater improvement in mean WSRS score compared to the control group. And two (40%) of the five patients in the experimental group achieved 'very much improved' and two (40%) showed 'much improved' at 12 weeks after treatment. CONCLUSIONS: Intradermal RF treatment prior to HA filler injection may provide synergistic and long-lasting effects for the reduction of NLF wrinkles.


BACKGROUND: Hyaluronic acid (HA) is the most frequently injected filler for soft tissue augmentation in the United States. OBJECTIVE: To systematically review published evidence for aesthetic use of small- and large-gel-particle HA. METHODS AND MATERIALS: Clinical data on anatomic area, level of evidence, patient population, trial design, endpoints, efficacy, and safety were extracted from PubMed. RESULTS: Fifty-three primary clinical reports were analyzed. The highest-quality efficacy evidence was for the nasolabial folds (NLFs), with 10 randomized, blind, split-face, comparative trials. Several randomized, blind trials supported treatment of the glabella, lips, and hands. Lower-level evidence (from studies with nonrandomized, open-label, or retrospective designs) was recorded for the nasojugal folds (tear troughs), upper eyelids, nose, infraorbital hollows, oral commissures, marionette lines, perioral rhytides, temples, and cheeks. Common adverse events (AEs) across anatomic areas were pain, bruising, swelling, and redness. Serious AEs were uncommon (8 events in 8 patients of 4,605 total patients) and were considered to be unrelated (7 events) or probably unrelated (1 event) to treatment. CONCLUSION: The efficacy and safety of small- and large-gel-particle HA are well established for NLFs; evidence for the glabella, lips, and hands is more limited. Preliminary reports in other anatomic regions suggest efficacy without major complications.


Injection of dermal fillers for soft tissue augmentation is a minimally invasive cosmetic procedure with growing popularity. However, patients often express concern about pain with such procedures. A topical anesthetic cream formulated with lidocaine/tetracaine 7%/7% was approved by the United States Food and Drug Administration in 2006 and recently reintroduced to the market for use during superficial dermatological procedures. A Phase 3 study was conducted to assess the efficacy and safety of lidocaine/tetracaine 7%/7% cream versus placebo cream when used to induce local dermal anesthesia during injections with hyaluronic acid. Mean visual analog scale scores significantly favored lidocaine/tetracaine 7%/7% cream. A significant percent of subjects also indicated that lidocaine/tetracaine 7%/7% cream provided adequate pain relief and that they would use lidocaine/tetracaine 7%/7% cream again. Investigators also rated lidocaine/tetracaine 7%/7% cream significantly better than placebo cream for providing adequate pain relief and on the assessment of pain scale. Lidocaine/tetracaine 7%/7% cream was safe and well tolerated with most subjects reporting no erythema, edema, or blanching. No related adverse events were reported with
lidocaine/tetracaine 7%/7% cream; one related adverse event of erythema was reported with placebo cream. The results of this study indicate that lidocaine/tetracaine 7%/7% cream is efficacious and safe at providing pain relief for soft tissue augmentation with hyaluronic acid.


Penile girth enhancement is a controversial subject but demands for enhancement are increasing steadily. Although various fillers have been widely used for soft tissue augmentation, there is no reliable material for this particular situation. Here we report a case of an acute hypersensitivity reaction in a man after his first self-injection of a filler material, which, he claimed, was hyaluronic acid gel for penile girth enhancement and glans penis augmentation.


OBJECTIVE: Evaluation of the efficacy and tolerability of highly crosslinked hyaluronic acid injections in treating the enophthalmous orbit. METHODS: Retrospective study of 11 enophthalmic patients who received an intraorbital injection of Juvederm(R) Voluma between June 2007 and October 2008. The mean follow-up was 19 months (range 12-25 months). RESULTS: Twelve orbits of 11 patients were treated, including nine with post-enucleation socket syndrome (PESS). Volume loss was corrected in 66.67% of cases (eight orbits) with only one intraorbital injection. Two patients requested an additional injection, achieving a final success rate of 83.33%. A rate of 16.67% (two orbits) developed some bruising, mild swelling and hypersensivity at the injection site within 24 hours of administration of the filler, representing minor, temporary side-effects of which the patients had been forewarned. Persistent edema was noted in 16.67% of cases, likely due to an overcorrection of ptosis, and ptosis was exacerbated in 16.67% of cases (two orbits). One ptosis was corrected after several months, with no particular difficulties related to the hyaluronic acid. No additional complications were identified. CONCLUSION: Juvederm(R) Voluma appears to be an effective filler for reduction of enophthalmos with a single intraorbital injection. In our experience, this product seems to have a longer duration of action than reported by the manufacturer and appears to perform like a semi-permanent or even permanent filler.


IMPORTANCE: Even when administered by experienced hands, injectable soft-tissue fillers can cause various unintended reactions, ranging from minor and self-limited responses to severe complications requiring prompt treatment and close follow-up. OBJECTIVES: To review the complications associated with injectable soft-tissue filler treatments administered in the Williams Rejuva Center during a 5-year period and to discuss their management. DESIGN AND SETTING: Retrospective medical record review in a private practice setting. PARTICIPANTS: Patients receiving injectable soft-tissue fillers and having a treatment-related complication. INTERVENTIONS: Injectable soft-tissue filler treatments. MAIN OUTCOME MEASURES: A retrospective medical record review was conducted of patients undergoing treatment with injectable soft-tissue fillers between January 1, 2007, and December 31, 2011, and identified as having a treatment-related complication. RESULTS: A total of 2089 injectable soft-tissue filler treatments were performed during the study period, including 1047 with hyaluronic acid, 811 with poly-L-lactic acid, and 231 with calcium hydroxylapatite.
Fourteen complications were identified. The most common complication was nodule or granuloma formation. Treatment with calcium hydroxylapatite had the highest complication rate. CONCLUSIONS AND RELEVANCE: Complications are rare following treatment with injectable soft-tissue fillers. Nevertheless, it is important to be aware of the spectrum of potential adverse sequelae and to be comfortable with their proper management. LEVEL OF EVIDENCE: 4.


OBJECTIVE: This paper shows the importance of the methodization in teaching facial dermal filling on the training of physicians who intend to work or are already working in the area of facial aesthetics. METHODS: The methodology is based on the procedures performed in Iz Clinic of Plastic Surgery from 2007 to 2010, where the results of the use of dermal filling products were observed. RESULTS: We chose the hyaluronic acid for the methodization of education. Even being a safe procedure, the dermal filling needs to be done by trained professionals because some complications may occur. The theoretical discussion of facial anatomy, physiology and classification of aging, rheological characteristics of products and application techniques underpin the practical part, in which the live demo or supervision of the procedure is performed. The idealization of classes, both theoretical and practical, proposed in this work proved to be of great value in teaching physicians. CONCLUSIONS: The success of this method can be seen from the results achieved by students and by observing the drop in reports of adverse effects. After learning the techniques of facial dermal filling with products based on hyaluronic acid, a doctor may perform this therapy with other fillers, with harmonious results.


This study aimed to describe the technique used by the authors in treating tear-trough deformity and to illustrate the effectiveness of high-frequency diagnostic ultrasound in the assessment of dermal filler longevity. In this consecutive interventional nonrandomized case series, 22 patients (18 women and 4 men) were evaluated. They ranged in age from 29 to 65 years (mean, 46.59 years +/- 10.0 years). The patients were given multiple hyaluronic acid injections in the tear-trough area between 2009 and 2011. The injected areas then were evaluated with sonographic scans during the follow-up period. All the patients were examined preoperatively, 7 days after injection, then after 1, 6, and 12 months, and finally once a year. Pre- and postoperative photographs using standard positioning and lighting were taken as well as high-frequency ultrasound scans using a 15-MHz scanner with an axial resolution of 15 mm. The injection technique consisted of three to five injections perpendicular to the skin. These were administered just under the orbital rim, creating three column-shaped hyaluronic acid deposits deep in the orbicularis oculi muscle, from 0.2 mm to 0.5 mm below the orbital rim. Approximately 0.1 ml-0.3 ml was injected at a time. This technique creates a deep scaffolding that can fill the orbital hollow. The amount of filler used in each area ranged from 0.1 ml to 0.3 ml (mean, 0.267 ml +/- 0.128 ml), whereas the mean filler quantity in each eyelid was 0.45 ml +/- 0.14 ml. During the follow-up visit 1 week after...
the treatment, 21 patients (90 %) required a second series of injections either in the exact same areas or right next to the injected area to obtain a smoother appearance of the skin surface. During the sonographer examination, it was always possible to identify and measure the filler at the site of the injection. LEVEL OF EVIDENCE IV: This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Accidental intra-arterial filler injection may cause significant tissue injury and necrosis. Hyaluronic acid (HA) fillers, currently the most popular, are the focus of this article, which highlights complications and their symptoms, risk factors, and possible treatment strategies. Although ischemic events do happen and are therefore important to discuss, they seem to be exceptionally rare and represent a small percentage of complications in individual clinical practices. However, the true incidence of this complication is unknown because of underreporting by clinicians. Typical clinical findings include skin blanching, livedo reticularis, slow capillary refill, and dusky blue-red discoloration, followed a few days later by blister formation and finally tissue slough. Mainstays of treatment (apart from avoidance by meticulous technique) are prompt recognition, immediate treatment with hyaluronidase, topical nitropaste under occlusion, oral acetylsalicylic acid (aspirin), warm compresses, and vigorous massage. Secondary lines of treatment may involve intra-arterial hyaluronidase, hyperbaric oxygen therapy, and ancillary vasodilating agents such as prostaglandin E1. Emergency preparedness (a “filler crash cart”) is emphasized, since early intervention is likely to significantly reduce morbidity. A clinical summary chart is provided, organized by complication presentation.

BACKGROUND: Hyaluronidase (HYAL) has been recommended in the emergency treatment of ischemia caused by accidental intra-arterial injection of hyaluronic acid (HA) dermal fillers. To date, there have been no published studies showing that HYAL can pass through intact arterial wall to hydrolyze HA emboli. OBJECTIVE: The goal of this study was to study whether or not HYAL could cross intact human facial arterial wall to hydrolyze HA filler. MATERIALS AND METHODS: Short tied-off segments of fresh human cadaver-sourced facial artery specimens, overfilled with a monophasic dermal filler (dermal filler "sausages"), were immersed in either HYAL or normal saline as controls. At 4 and 24 hours, the vessels were removed from the preparations, and one end of each vessel was cut open. RESULTS: Only the HYAL-immersed specimens showed degradation of filler gel. CONCLUSION: In conclusion, cross-linked HA is susceptible to hydrolysis by HYAL when contained within the intact facial artery in a cadaver model, indicating that direct intra-arterial injection of HYAL is likely not necessary to help restore the circulation of ischemic tissues. This bench study provides support for the current recommended treatment of accidental intra-arterial injection with HYAL injection diffusely into ischemic tissues.

BACKGROUND: Hyaluronic acid dermal fillers are frequently used for lip augmentation, and a new filler has been developed with characteristics especially suited for the lips. METHODS:
Four European sites treated 60 subjects with Juvederm® Volbella injectable gel in the perioral area, and subjects returned to the clinic at 1, 3, 6, 9, and 12 months for follow-up. The primary effectiveness endpoint established a priori was a Month 3 responder rate on the 4-point Lip Fullness Scale (LFS) of ≥40% and statistically > 0%, where responders improved ≥ 1 point from baseline on the investigator’s assessment of LFS. At follow-up, subjects assessed lip fullness goal achievement, the look and feel of their lips, and their satisfaction with the effects of treatment. RESULTS: The Month 3 LFS responder rate was 93.2% (P < 0.0001), so the primary endpoint was met, and clinical effectiveness was demonstrated. The responder rate over time showed that 78.0% of subjects still had improved lip fullness at Month 9 and 48.3% at Month 12. After treatment 98.3% of subjects reported that their lip fullness goal had been achieved, and this was maintained at 86.4% at Month 9 and 56.9% at Month 12. At Month 1, 81.0% of subjects reported that their lips felt smooth, and 91.4% reported that their lips looked natural (scores of 7-10 on an 11-point scale, where 0 was an unfavorable outcome and 10 was a favorable outcome). Similarly, 96.6% of subjects reported being satisfied (scores between 7 and 10 on an 11-point scale where 0 = very dissatisfied, 10 = very satisfied) at Month 1, and by Month 12 more than 80% of subjects were still satisfied. There were no severe adverse events related to treatment. CONCLUSION: Juvederm® Volbella injectable gel is well tolerated and has been demonstrated to provide a smooth and natural improvement in lip fullness that lasts for up to 1 year.


BACKGROUND: Most of the hyaluronic acid (HA)-based dermal fillers currently on the market are chemically modified with cross-linkers to improve the mechanical properties and duration in vivo. OBJECTIVE: To investigate differences in the properties of dermal fillers that can be related to the respective cross-linking and manufacturing methods used. METHODS AND MATERIALS: Thirteen commercially available HA fillers were analyzed. Two different measures of gel strength were used: the elastic modulus (G') determined by rheology and a measure of the swelling capacity of the gel (c(min)). The degree of modification was determined using nuclear magnetic resonance spectroscopy, and the cross-linking ratio was determined using size exclusion chromatography coupled with mass spectrometry. RESULTS: There was a wide variation in gel strength, and the degree of modification varied between 1% and 8% for the HA fillers investigated. CONCLUSIONS: Both measures of gel strength, G' and c(min), can be used because the results from the two methods are well correlated. No differentiation in filler properties could be seen as a result of manufacturing process used, except that the nonanimal stabilized HA stabilization process resulted in products with high gel strength and a low degree of modification.


Although dermal fillers are generally accepted as safe and well-tolerable cosmetic tools, adverse reaction still forms a prognostic problem. The aim of this study was to demonstrate the clinicopathologic patterns of dermal filler complications in our center. A 5-year single-center study that included patients complained from filler complications and referred to the dermatopathology unit in Al-Azhar University for histologic assessment. The study included 38 female patients with an average age of 47 years. The mean onset of complications was 14.6 +/- 5.27 months after injection. The injected material included hyaluronic acid (18.4%), silicone (52.6%), bovine collagen (15.8%) and polyacrylamide hydrogel (13.2%). Most lesions were located on the face (55.3%), less commonly on the hands (18.4%), buttocks (21%), and
rarely on the vulva (5.3%). The clinical spectrum included indurated plaque (23.7%), nodular lesion (31.6%), inflammatory mass (15.8%), atrophic lesion (10.5%), skin discoloration (13.1%) and ulceration (5.3%). Histologically, granulomatous reaction was the major finding, either a foreign body granuloma (34.2%) or infectious granuloma (13.2%). Other histologic reactions included dermal pseudocysts with chronic inflammation (26.3%), dermal fibrosis (15.8%), and eosinophilic panniculitis (10.5%). Our results confirmed that dermal fillers could be manifested with variable clinical presentations and show different histologic reactions. Because of long-standing duration until complications occur, history taking is crucial and should be emphasized in every suspected patient. It is hoped that this article will increase awareness for recognition of these variable complications and help select the appropriate therapy.

31. Fakhari, A. and C. Berkland (2013). "Applications and emerging trends of hyaluronic acid in tissue engineering, as a dermal filler and in osteoarthritis treatment." Acta Biomater 9(7): 7081-7092. Hyaluronic acid (HA) is a naturally occurring biodegradable polymer with a variety of applications in medicine, including scaffolding for tissue engineering, dermatological fillers and viscosupplementation for osteoarthritis treatment. HA is available in most connective tissues in body fluids such as synovial fluid and the vitreous humor of the eye. HA is responsible for several structural properties of tissues as a component of extracellular matrix and is involved in cellular signaling. Degradation of HA is a stepwise process that can occur via enzymatic or non-enzymatic reactions. A reduction in HA mass or molecular weight via degradation or slowing of synthesis affects physical and chemical properties such as tissue volume, viscosity and elasticity. This review addresses the distribution, turnover and tissue-specific properties of HA. This information is used as the context for considering recent products and strategies for modifying the viscoelastic properties of HA in tissue engineering, as a dermal filler and in osteoarthritis treatment.

32. Farhi, D., et al. (2013). "The Emervel French survey: a prospective real-practice descriptive study of 1,822 patients treated for facial rejuvenation with a new hyaluronic acid filler." J Drugs Dermatol 12(5): e88-93. BACKGROUND: Emervel consists of a range of 5 hyaluronic acid (HA) fillers (Touch, Classic, Lips, Deep, and Volume), with a fixed HA concentration (20 mg/mL), and various degrees of cross-linking and calibration. OBJECTIVES: To describe the current use of Emervel fillers in France. METHODS: Prospective multicenter, cross-sectional, real-practice, descriptive survey, including 1,822 patients injected with Emervel fillers for face rejuvenation by 58 French physicians between September 2010 and July 2011. The injection modalities were left to the respective physician's discretion. RESULTS: The physicians were dermatologists (52.3%), surgeons (43.8%), or general practitioners (14.1%). Nasolabial folds (NLF) with a mean severity 2.4 were mainly injected with Emervel Deep (51.0%) and Emervel Classic (36.0%) (mean volume: 1.0 mL), and primarily with the linear retrograde (LR) technique (89.3%). Marionette lines (ML), with a mean severity 2.6 were mainly injected with Emervel Deep (52.5%) and Emervel Classic (34.6%) (mean volume: 0.8 mL), and mainly with the LR technique (79.5%). More than 90% of patients had scores of 0 or 1 for erythema, bruising, edema, and pain. No serious adverse events were reported up to 15 months after the injection. CONCLUSION: These data could contribute to upcoming international consensus on optimal injection modalities of the Emervel range of HA fillers.
Objectives: Facial age, health, and attractiveness assessments play a major role in human social interaction and affect the way we perceive and think about others. Modern cosmetic dermatology provides a bewildering array of facial treatment procedures with botulinum toxin type A and dermal filler application being the most requested. The authors sought to determine the effect of facial rejuvenation procedures, such as application of incobotulinumtoxin A and dermal filler injections, on people's perception of age, health, and attractiveness. Methods: Ten women underwent three consecutive facial rejuvenation procedures with incobotulinumtoxin A, calcium hydroxylapatite, and a hyaluronic acid. Digital facial images were taken before treatment and after each subsequent treatment and presented to a total of 150 third-party assessors who judged the images for age, health, and attractiveness. Results: Each procedure was associated with a significant reduction in perceived age and an increase in perceived health and attractiveness compared with pre-treatment images. The effects were cumulative such that faces perceived as the youngest, healthiest, and most attractive had received all three treatments, followed in descending order by incobotulinumtoxin A and calcium hydroxylapatite treatment, and incobotulinumtoxin A alone. Conclusion: The authors demonstrate that naive judges are readily able to perceive the effect of nonsurgical facial rejuvenation procedures with incobotulinumtoxin A, calcium hydroxylapatite, and hyaluronic acid in terms of age, health, and attractiveness judgments. These effects were greatest when incobotulinumtoxin A and dermal filler treatments were combined.

BACKGROUND: Hyaluronic acid (HA) gels have been used as filler material in the aesthetic field. Although the native HA molecule is without specificity of species and organs, synthetic cross-linked gels have differences in chemical composition and three-dimensional structure. Different technologies are employed in cross-linking, and the products have varying rheological properties. OBJECTIVE: To determine whether the gels with differing chemical composition have differing histologic behavior when injected into human skin to determine if the histology changes after 14 days of implantation. MATERIALS AND METHODS: Human volunteers consented to having controlled placement of HA intradermally into forearm or buttock skin. The trials were conducted in a single clinic in association with the Hopitaux Universitaires de Geneve, Geneva, Switzerland. The biopsies were taken immediately after implantation of the product and at day 14. Standard paraffin sections were prepared and stained with hematoxylin and eosin and Alcian blue and examined by an independent pathologist. RESULTS: Results show that each type of HA has a predictable histologic behavior in the skin. Biphasic gel has demonstrated deposition in big pools, often deep in the reticular dermis. The pools compress the collagen fibers. The papillary dermis and superficial reticular dermis are free of HA. Monophasic monodensified gels show large pools of hyaluronans throughout all the thickness of the reticular dermis. This material breaks up the collagen fibers of most of the dermal plane. The papillary dermis is free of exogenous hyaluronans. Monophasic polydensified cohesive gel penetrates into the dermis in a diffuse, evenly distributed manner, except in the papillary dermis, which remains free of exogenous material. CONCLUSION: The different types of cross-linked HA have different behaviors in the dermis immediately after their injection. The patterns are consistent between patients and
are predictable. These histologic patterns do not change when biopsies are examined at 2 weeks.


BACKGROUND: Silicone is one of the oldest and longest lasting of the dermal fillers. Microdroplet silicone injections have proven to be safe and effective. This paper describes how to obtain microdroplet silicone (1,000 centistokes) in a consistent manner, including a discussion of its efficacy and safety. METHODS AND MATERIALS: A simple, permanent method of tissue augmentation is described. U.S. Food and Drug Administration-approved liquid silicone (Silikon(R)) is emulsified with cross-linked hyaluronic acid through a Luer-Lok to Luer-Lok connector between two 3-cc syringes. This stable emulsion is injected through a 27G needle or through a 25G or 27G microcannula into the middermis, subcutaneous tissue, or periosteum. RESULTS: The results of 95 cases are described. The emulsion is most beneficial for distensible acne valleys, nasolabial folds, glabellar frown lines, augmentation of the vermilion border of the lips, and projection of the nose, cheekbones, and chin. Exterior nasal deviations and soft tissue defects are also improved. Complications are minimal and include temporary bruising, erythema, and mild edema. Any temporary small nodules are easily leveled with massage. Occasionally, it takes a repeat session at 1 month to completely elevate depressions. The resulting elevations remain stable during the 2-year follow-up period. No silicone granulomas have developed. CONCLUSIONS: This methodology has replaced many indications for temporary, semipermanent, or permanent fillers.


BACKGROUND: Microcannulas with blunt tips for filler injections have recently been developed for use with dermal fillers. Their utility, ease of use, cosmetic outcomes, perceived pain, and satisfaction ratings amongst patients in terms of comfort and aesthetic outcomes when compared to sharp hypodermic needles has not previously been investigated. OBJECTIVE: To compare injections of filler with microcannulas versus hypodermic needles in terms of ease of use, amount of filler required to achieve desired aesthetic outcome, perceived pain by patient, adverse events such as bleeding and bruising and to demonstrate the advantages of single-port injection technique with the blunt-tip microcannula. MATERIALS AND METHODS: Ninety-five patients aged 30 to 76 years with a desire to augment facial, decollete, and hand features were enrolled in the study. Subjects were recruited in a consecutive manner from patients interested in receiving dermal filler augmentation. Each site was cleaned with alcohol before injection. Anesthesia was obtained with a topical anesthesia peel off mask of lidocaine/tetracaine. Cross-linked hyaluronic acid (20 mg to 28 mg per mL) was injected into the mid-dermis. The microcannula or a hypodermic needle was inserted the entire length of the fold, depression or lip and the filler was injected in a linear retrograde fashion. The volume injected was variable, depending on the depth and the extent of the defect. The injecting physician assessed the ease of injection. Subjects used the Visual Analog Scale (0-10) for pain assessment. Clinical efficacy was assessed by the patients and the investigators immediately after injection, and at one and six months after injection using the Global Aesthetic Improvement Scale (GAIS) and digital photography. RESULTS: Overall, the Global Aesthetic Improvements Scale (GAIS) results were excellent (55%), moderate (35%), and somewhat improved (10%) one month after the procedure, decreasing to 23%, 44%, and 33%, respectively, at the six month evaluation.
There was no significant differences in the GAIS score between the microcannula and the hypodermic needle. However, the Visual Analog Scale for pain assessment during the injections was quite different. The pain was described as 3 (mild) for injections with the microcannula, increasing to 6 (moderate) for injections with the hypodermic needle. Bruising and ecchymosis was more marked following use of the hypodermic needle. CONCLUSION: Using the blunt-tip microcannula as an alternative to the hypodermic needles has simplified filler injections and produced less bruising, ecchymosis, and pain with faster recovery.


BACKGROUND: Dermal fillers have continually been under development to increase safety, efficacy, and longevity. Biostimulatory dermal fillers, such as calcium hydroxylapatite fillers, have already been shown to be superior in efficacy compared to nonanimal stabilized hyaluronic acid (NASHA)-based fillers. AIMS: In this randomized split-face study, we compared a novel biostimulatory polycaprolactone (PCL)-based dermal filler with a NASHA-based dermal filler, for safety, efficacy, and duration of cosmetic correction for the treatment of nasolabial folds (NLFs). PATIENTS/METHODS: Forty subjects received a PCL-based dermal filler in one of their NLFs, and a NASHA-based dermal filler on the contralateral side. Efficacy was evaluated based on the Wrinkle Severity Rating Scale and Global Aesthetic Improvement Scale. RESULTS: After 6, 9, and 12 months post-treatment, NLFs treated with the PCL-based dermal filler showed statistically significant improvements on the Wrinkle Severity Rating Scale and greater improvements on the GAIS compared to NLFs treated with the NASHA-based dermal filler. Both products were found to be equally safe and well tolerated. CONCLUSION: Our results suggest that PCL-based dermal fillers offer longer-lasting performance over NASHA-based dermal fillers in NLFs treatment.

38. Galeano, M., et al. (2011). "Systemic administration of high-molecular weight hyaluronan stimulates wound healing in genetically diabetic mice." Biochim Biophys Acta 1812(7): 752-759. Hyaluronic acid (HA), an essential component of the extracellular matrix, is an efficient space filler that maintains hydration, serves as a substrate for assembly of proteoglycans and is involved in wound healing. Although numerous pieces of evidence demonstrate beneficial effects in promoting wound healing in diabetes, a systemic approach has never been tested. We used an incisional wound healing model in genetically diabetic mice to test the effects of systemic injection of HA. Diabetic (n=56) and normoglycemic (n=56) mice were subjected to incision and randomized (8 groups of 7 animals each) to receive HA at different doses, 7.5, 15 and 30mg/kg/i.p., or vehicle (0.9% NaCl solution) for 12 days. At the end of the experiment animals were sacrificed and skin wounds were excised for histological, biochemical and molecular analysis. Histology revealed that the most effective dose to improve wound repair and angiogenesis in diabetic mice was 30mg/kg. Furthermore HA injection (30mg/kg) improved the altered healing pattern in diabetic animals, increased skin remodeling proteins TGF-beta and transglutaminase-II and restored the altered expression of cyclin B1/Cdc2 complex. Evaluation of skin from diabetic animals injected with HA revealed also an increase in HA content, suggesting that systemic injection may be able to restore the reduced intracellular HA pool of diabetic mice. Finally HA markedly improved skin mechanical properties. These promising results, if confirmed in a clinical setting, may improve the care and management of diabetic patients.


   BACKGROUND: There are numerous dermal fillers available to injectors in the US and Europe for the correction of age-related volume loss in the midface and perioral regions. Product availability differs between these two aesthetic markets due to US Food and Drug Administration (FDA) regulatory requirements. The purpose of this study is to discuss differences in filler selection by two practitioners in the US and Europe based upon both stylistic approach and filler availability in each market. OBJECTIVE: To analyse and discuss the approach to midface as well as lip and perioral volume restoration by two independent dermatologists working in the US and Italy. METHODS: Seven patients were selected for discussion and divided into two groups: 1) those requiring midface volumization and 2) those undergoing perioral or lip volume replacement. Patients in the midface group were injected with Juvederm Voluma(R) XC, Juvederm(R) Volift(R) with lidocaine, Restylane(R) L(R), Perlane-L(R) or Radiesse(R). Patients in the perioral and/or lip group were injected with Juvederm(R) Volbella, with lidocaine, or Belotero Balance. Patients were photographed before and immediately after injection to evaluate aesthetic outcomes. In each case, filler selection was based upon patient characteristics, anatomical considerations and inherent filler properties.

   RESULTS: All patients were extremely satisfied with their treatments. There were no significant immediate or delayed complications following treatment with any of the dermal fillers used. CONCLUSIONS: Volume restoration in the midface and perioral or lip region can be effectively achieved using a variety of dermal fillers. The dermal filler portfolio available in Europe is exponentially larger than that in the US. Product selection in either market is ultimately the result of the physician's experience injecting each dermal filler, as well as his or her personal preferences.


   SUMMARY: Injectable fillers are increasingly used for midface augmentation, which can be performed for facial rejuvenation and treatment of HIV facial lipoatrophy. A variety of temporary and permanent filler agents has been developed, including calcium hydroxylapatite, collagen, liquid silicone, polytetrafluoroethylene, hyaluronic acid, poly-l-lactic acid, and polyacrylamide gel. Facial fillers are sometimes encountered on radiologic imaging incidentally and should not be mistaken for pathology. Alternatively, patients with facial fillers may undergo imaging specifically to evaluate associated complications, such as infection, overfilling, migration, foreign-body reaction, and scarring. Therefore, it is important to be familiar with the imaging appearances of the various filler materials and their complications.


   Background: High-resolution ultrasound (HRUS) is a useful tool in defining anatomic and dynamic soft tissue relationships in the periocular area. It also allows visualization of hyaluronic acid (HA) gel within the soft tissue. Objectives: The authors investigate the difference in the distribution pattern between 2 HA fillers in the periocular tissue using HRUS. Methods: The charts of 10 patients who underwent periocular injection using HA gel filler and were subsequently examined with HRUS were reviewed. Half of the patients (n = 5)
were treated with Restylane-L (Medicis Aesthetics, Inc, Scottsdale, Arizona) and the remaining 5 with Belotero Balance (Merz Aesthetics, Inc, San Mateo, California). Ultrasonographic evaluation (Logiq p6; GE Healthcare, Waukesha, Washington) was performed before and immediately after HA filler injection.

Results: The HA appears as a hypoechoic image within the soft tissue plane on HRUS. Restylane-L filler formed a localized hypoechoic image within the tissue, with some spread into bubbles or pearl-like configuration. Belotero Balance spread more widely into the tissue plane and diffused into an elongated or spindle-shaped hypoechoic image.

Conclusions: Our preliminary data suggest that HA gel fillers with differing production technologies show distinct spread and distribution patterns in the periorbicular tissues on HRUS examination.


BACKGROUND: Hyaluronic acid (HA) fillers are FDA approved for improving the appearance of the nasolabial folds. Previous reports on the use of HA for this treatment have focused on injections directly into the location of the desired correction. To our knowledge, a study has not been done evaluating the efficacy of injecting a low volume of HA into the adjacent area of volume loss to correct both volume loss and adjacent lines. OBJECTIVE: The objective of this study was to compare the effectiveness and safety of three HA injection protocols including deep dermal cheek injection, mid- to deep dermal local nasolabial fold injection, and both injections for the correction of nasolabial folds. METHODS: This was a split-face, randomized study evaluating the use of three injection techniques - (i) deep bolus injection into the mid- to lateral cheek, (ii) local mid- to deep dermal injection into the nasolabial fold, and (iii) both deep injection into the mid- to lateral cheek and local mid- to deep dermal injection into the nasolabial fold - for the treatment of moderate to severe nasolabial folds. Wrinkle severity and Global Aesthetic Improvement Scales were measured before and 4-6 weeks after treatment as assessed by a blinded investigator. RESULTS: Patient and physician observations showed improvement both globally and in wrinkle severity score with each technique used with no statistical difference between techniques. Patients showed a slight preference for injection to both the mid- to lateral cheek and nasolabial fold, which was associated with the greatest amount of filler product administered. No serious adverse events were reported. CONCLUSION: Injection of a dermal filler, at low volumes, into either the nasolabial fold or mid- to lateral cheek results in similar improvement to the correction of the nasolabial folds.


PURPOSE:: To examine with histology the anatomical location of hyaluronic acid gel injected to the eyebrow of cadaver specimens. METHODS:: The authors dissected 5 fresh hemifacial cadaver specimens following preperiosteal injection of hyaluronic acid gel to the eyebrow. Following tissue fixation, full-thickness soft-tissue sections were obtained followed by histologic examination. RESULTS:: Histologic examination revealed the location of hyaluronic acid gel at the intended preperiosteal plane in all 5 specimens. Very dense retro-orbicularis oculi fat septa appeared to limit the anterior displacement of filler in each specimen.

CONCLUSIONS:: This study provides a greater understanding of the anatomical barriers and
boundaries that help to determine, in part, the anatomical position of hyaluronic acid gel when injected to the preperiosteal eyebrow. The high degree of histologically confirmed consistency of product location of eyebrow injections noted in this study stands in contrast to the variability of position of gel injected in the infraorbital hollows.


**BACKGROUND:** Acne scarring is a prevalent and challenging cosmetic issue, which is often addressed by multiple modalities. A low-viscosity non-animal stabilized hyaluronic acid (NASHA) dermal filler, injected in microdoses into the mid-to-superficial dermis, may provide a useful new approach to improving the appearance of depressed acne scars.

**MATERIALS and METHODS:** Twelve consecutive patients with moderate to severe acne scarring, who had completed a series of fractional laser resurfacing, underwent microinjections of 20 mg/mL hyaluronic acid (HA) gel into discrete depressed acne scars on the face.

**RESULTS:** Immediate visual improvement was observed in all lesions. The procedure was well tolerated. Adverse events were limited to transient pinpoint bleeding at the injection site.

**CONCLUSION:** Microinjection of low viscosity HA offers a valuable technique for the treatment of discrete depressed acne scars.


**OBJECTIVE:** To differentiate a non-infectious inflammatory reaction following hyaluronic acid injection for facial rejuvenation from other reported complications, and describe appropriate treatment.

**METHODS:** Using a review of the literature and information available from the manufacturer, recommendations for management of non-infectious hyaluronic acid reactions are made. RESULTS: Patients who are afebrile with a normal white blood cell count and negative cultures, who appear to have an infectious process following hyaluronic acid injection are in fact having an inflammatory response. The inflammation may worsen with...
antibiotic therapy. Treatment should be systemic and/or local steroids, which may need to be for up to 6 months. CONCLUSION: After reviewing the literature, non-infectious inflammatory reaction following hyaluronic acid injection is exceedingly rare with only one other reported case. Erythematous skin in the week following injection without other infectious markers, such as fever or elevated serum white blood cell count, is an inflammatory reaction and should be treated with steroid therapy.


BACKGROUND: Hyaluronidase (Hylase Dessau(R)) is a hyaluronic acid-metabolizing enzyme, which has been shown to loosen the extracellular matrix, thereby improving the diffusion of local anesthetics. Lower eyelid edema is a common post-interventional complication of cosmetic procedures performed in the lid region, such as the injection of hyaluronic acid fillers for tear-trough augmentation. The purpose of this study was to validate the efficacy of hyaluronidase in the management of lower eyelid edema. METHODS: We performed a retrospective analysis with 20 patients with lower eyelid edema. Most patients (n = 14) presented with edema following hyaluronic acid injection (tear-trough augmentation), whereas the minority (n = 6) were treated due to idiopathic edema (malar edema or malar mounds). Patients were treated by local infiltration of approximately 0.2 ml to 0.5 ml of hyaluronidase (Hylase Dessau(R)) 20 IU to 75 IU per eyelid. Photographs were taken prior to and seven days after infiltration. RESULTS: Hyaluronidase was found to reduce effectively and rapidly or resolve eyelid edema after a single injection. No relevant adverse effects were observed. However, it must be noted that a hyaluronidase injection may also dissolve injected hyaluronic acid fillers and may therefore negatively affect tear-trough augmentations. While the effects of a treatment for edema due to tear-trough augmentation were permanent, malar edema and malar mounds reoccurred within two to three weeks. CONCLUSION: The infiltration of hyaluronidase is rapid, safe and currently the only effective option for the management of eyelid edema. No relevant adverse effects were observed.


BACKGROUND: Hyaluronic acid (HA) dermal fillers are effective and safe for correction of facial rhytides. A new volumizing HA filler, 20 mg/ml HA dermal filler (Juvederm(R) Voluma(R), Allergan Inc., Irvine, CA), is the only HA filler with a FDA indication for facial volumization due to age-related facial volume loss. OBJECTIVE: Evaluate the biological properties, including biochemical, biophysical and rheological, of this new 20 mg/ml HA dermal filler and discuss the importance of these properties in clinical applications. METHODS AND MATERIALS: A systematic search of the computerized bibliographic databases Medline, Embase, Embal, Biosis, SciSearch, Pascal, HCAPlus, IPA, and Dissertation Abstracts with key term "Voluma." Four articles on the biological properties of this new 20 mg/ml HA dermal filler were suitable for inclusion in this review. RESULTS: Biological analysis of elasticity and viscosity values of this new 20 mg/ml HA dermal filler demonstrated intermediate properties in three studies and high in one study compared to other HA dermal fillers. This 20 mg/ml HA dermal filler retained the highest elasticity and viscosity values at temperature of 37 degrees C. Histology demonstrated that this 20 mg/ml HA dermal filler has an intermediate pattern of distribution within the superficial and deep reticular dermis. CONCLUSION: This 20 mg/ml HA dermal filler demonstrated volumizing ability, and maintaining viscosity and free-flowing characteristics for easy injection, tissue lifting, and
molding. We hope future research incorporates biological properties analysis of this HA dermal filler in clinical trials.


BACKGROUND: Hyaluronic acid (HA) fillers and poly-L-lactic acid (PLA) fillers are frequently used to correct facial wrinkles. AIM: To compare the efficacy and safety of a novel injectable poly-L-lactic acid (PLA) filler and a well-studied biphasic HA filler for the treatment of moderate to severe nasolabial folds. METHODS: In this multicentre, randomized, evaluator-blinded, comparative study, subjects were randomized for injections with PLA or HA into both nasolabial folds. Efficacy was determined by calculating the change in Wrinkle Severity Rating Scale (WSRS) relative to baseline. Local safety was assessed by reported adverse events. RESULTS: At week 24, mean improvement in WSRS from baseline was 2.09 +/- 0.68 for the PLA side and 1.54 +/- 0.65 for the HA side. Both injections were well tolerated, and the adverse reactions were mild and transient in most cases. CONCLUSIONS: PLA provides noninferior efficacy compared with HA 6 months after being used to treat moderate to severe nasolabial folds.

52. Iannitti, T., et al. (2013). "A new highly viscoelastic hyaluronic acid gel: rheological properties, biocompatibility and clinical investigation in esthetic and restorative surgery." Int J Pharm. Nowadays there is an increased demand for safe and effective volume enhancing fillers to achieve soft tissue augmentation in order to overcome tissue defects and aging-associated skin changes. In the present study we characterized the rheological and biological properties of Variofill(R), a new highly viscoelastic hyaluronic acid gel, by investigating the local effects following subcutaneous implantation in the rat to detect the host-tissue reactions and biodegradation over 18 months. We also investigated, for the first time, the application of Variofill(R) in esthetic and restorative surgery in two medical case reports. In the first case report we successfully performed Variofill(R) treatment to improve facial scars in a patient previously involved in a car crash. In the second case report we carried out a novel procedure involving a high-dose (1000ml) injection of Variofill(R) into the dermis and subcutis of the abdominal quadrants in order to allow a classic reconstructive procedure of the abdominal wall in a patient presenting a wide incisional hernia.

53. Iannitti, T., et al. (2014). "Experimental and Clinical Efficacy of Two Hyaluronic Acid-based Compounds of Different Cross-Linkage and Composition in the Rejuvenation of the Skin." Pharm Res. BACKGROUND: In the field of aesthetic medicine there is an increasing demand for safe and effective hyaluronic acid (HA) fillers to counteract the aging process. METHODS AND AIMS: We designed a study to evaluate the safety and histological biocompatibility of Aliaxin(R) Global Performance, a cross-linked HA filler and ViscoDerm(R) Skinko E, a product composed of non-cross-linked HA and a complex including vitamins, antioxidants, amino acids and minerals injected into the skin of guinea pigs. Then, we translated our findings into the clinical setting, administering a combination of these compounds to patients seeking a facial rejuvenation procedure targeting moderate-to-severe wrinkles affecting the nasolabial folds. RESULTS: The animal study showed that the two compounds did not induce any significant inflammatory reactions and increased collagen and elastic fibers in the skin. In the clinical setting, injection of Aliaxin(R) Global Performance, followed by ViscoDerm(R) Skinko E, resulted in a higher improvement in nasolabial fold hydration, trans-epidermal water loss
and wrinkle aesthetic appearance, if compared with a protocol based on Aliaxin(R) Global Performance alone. CONCLUSION: In summary, we show evidence on the safety and mechanism underlying two new HA-based compounds of different cross-linkage and composition, proposing that they can be safely used in combination in patients seeking facial rejuvenation procedures with long-lasting efficacy.


The use of hyaluronic acid fillers for treatment of rhytides (wrinkles) is widespread in aesthetic dermatology and is considered a safe procedure; however, complications can occur especially if the injections are carried out by an inexperienced person and/or with a lack of anatomical knowledge. The two cases presented here exemplify this problem. In conclusion, both cases demonstrate complications after uncritical injection of hyaluronic acid fillers into "risk" or "expert" regions. While the patients in these two cases recovered completely, the injection of filler substances can also lead to the risk of potentially permanent side effects, such as granuloma, necrosis with scar tissue formation and even blindness. The frequency and severity of complications often show a direct correlation with the qualification or expertise of the person treating and hence injection treatments should be performed solely by physicians.


The use of fillers for camouflage after surgical rhinoplasty or during medical rhinoplasty process represent an attractive technique which allows to avoid or to delay surgical time often dreaded by the patients. This technique apparently quite simple, must be applied carefully in order to avoid possible complications that can sometimes be very serious. Through their seven years of experience, the authors have selected absorbable type of products: hyaluronic acid or calcium hydroxylapitate, both approved by ANSM. Preference is given to microcannulas (27G) over needles and injection techniques through multiple tunnels fitted with small fragmented boluses. Due to possible Tyndall effect and skin necrosis risk, a one-shot injection with a lot of product should be avoided. Calcium hydroxyapatite is preferred for the dorsum area while hyaluronic acid is recommended for the tip. The authors also relate the major encountered complications and describe the appropriated treatments. Nevertheless the strict application of the described technique represents the best way to prevent adverse complications.


During the last decade cosmeticfacial procedures have become part of the professional work of both dentists and maxillofacial surgeons. A shift has taken place from invasive surgical treatment towards minimally invasive treatments. Besides the use of botulinum toxin type A, non-permanent wrinkle fillers can be an alternative to invasive surgical treatment. Since botulism was first described in the 18th century, the neurotoxin has continued to develop, as a result of which Botox, now available in synthetically produced form, can safely be employed in healthcare. The frequency with which patients visit dentists and maxillofacial surgeons offers the professional group the possibility to inform patients about cosmetic facial treatments and to carry them out according to diagnosis.


A 38 Year-old-female presented with diplopia and bilateral lower eyelid swelling 1.5 months after hyaluronic acid filler injection of tear trough deformity. Comprehensive eye examination showed an inferior oblique muscle restriction on the right eye. Diplopia and bilateral lower eyelid puffiness were treated by injection of hyaluronidase which resulted in disappearance of both diplopia and bilateral lower eyelid puffiness.


**BACKGROUND:** Use of dermal fillers for soft tissue augmentation has become an integral part of aesthetic practices. Dermal fillers temporarily remove the appearance of rhytids and reduce the depth of skin folds. Even with the most experienced of injectors, adverse effects can and do occur ranging from mild bruising to severe injection necrosis. **AIMS:** Physicians should be able to treat the severe complication of vascular necrosis and detect impending necrosis after injection of a dermal filler, especially with hyaluronic acid fillers. **MATERIALS AND METHODS:** Case report of a patient who was followed for 6 months from time of injection of hyaluronic acid filler to complete healing of wound. **RESULTS:** Complete wound healing was achieved with early recognition and institution of treatment. **DISCUSSION:** We review a case report of injection necrosis and methods used to prevent and treat this complication. **CONCLUSION:** Early recognition of vascular necrosis with specific protocol for treatment after injection necrosis with hyaluronic acid fillers improves the outcome of wound healing.


**BACKGROUND:** Increasing volume is an important part of facial rejuvenation since volume loss is common and typically age-related. HA E Volume is a moderately firm gel designed to be injected into the subcutaneous tissue for volume enhancement. **OBJECTIVE:** To assess the efficacy, patient satisfaction, and safety of HA E Volume in patients with bilateral volume loss of the cheeks. **MATERIALS AND METHODS:** This was a multi-center, six-month, open-label study. Subjects received HA E in the cheeks at baseline, and a touch-up injection was optional three weeks later. Global aesthetic improvement, cheek thickness (caliper measurements), changes in volume using three-dimensional (3-D) photo analysis, adverse events and injection site reactions were evaluated at each visit. Optimal correction was defined as results obtained three weeks after last injection. A subject satisfaction questionnaire was performed three weeks after the last injection. **RESULTS:** Investigators evaluated the great majority of subjects as much or very much improved in terms of aesthetic improvement of their cheeks at week 3 and at mounts 3 and 6 (89.3%, 90.9%, and 76.4%, respectively). After six months, 65.8 percent of the correction achieved at week 3 (optimal correction) was maintained in terms of cheek thickness (caliper assessments), confirmed by 67.7 percent of the volume maintained based on 3-D volume analyses. The majority of subjects (92.1%) were satisfied or very satisfied with their aesthetic outcome. A
good tolerability profile was observed. CONCLUSIONS: Treatment with HA E Volume in cheeks led to good aesthetic improvement, sustained results confirmed by caliper and 3-D volume assessments, and high subject satisfaction.

62. Khan, F., et al. (2012). "Hyaluronic acid filler for a depressed scar." Dermatol Online J 18(5): 15. The use of filler for depressed scars has been documented but is rare in the literature. We present a case of a patient treated with hyaluronic acid fillers at the site of a long-standing depressed scar.

63. Kim, D. W., et al. (2011). "Vascular complications of hyaluronic acid fillers and the role of hyaluronidase in management." J Plast Reconstr Aesthet Surg 64(12): 1590-1595. Skin necrosis following the inadvertent arterial injection of hyaluronic acid (HA) is a serious complication. It is not clear whether or not subcutaneous injections of hyaluronidase decrease skin necrosis in HA-induced vascular complications. We had four cases of HA-induced vascular complications, two of which were treated with hyaluronidase the next day. All of the patients had skin necrosis and scarring. We performed an animal study with rabbit ears in which HA filler was injected into the auricular arteries of both ears. Five rabbits each received a subcutaneous injection of 750 IU of hyaluronidase 4 and 24 h after the filler injection. The hyaluronidase-treated ears in the 4-h intervention group had significantly smaller necrotic areas (p<0.05), while the 24-h intervention group had no differences in the area of necrosis. Hyaluronidase reduced the vascular complications of HA fillers when used early, but there was no benefit to hyaluronidase injection after 24 h.

64. Kim, E. G., et al. (2014). "Severe visual loss and cerebral infarction after injection of hyaluronic acid gel." J Craniofac Surg 25(2): 684-686. We report a case of a 23-year-old man with cerebral infarction and permanent visual loss after injection of a hyaluronic acid gel filler for augmentation rhinoplasty. The patient was admitted to the hospital with complaints of loss of vision in the right eye, facial paralysis on the right side, and paralysis of the left limbs with severe pain during augmentation rhinoplasty with filler injection. Brain magnetic resonance imaging and computed tomography showed ophthalmic artery obstruction and right middle cerebral artery infarction. Acute thrombolysis was performed to treat the infarction; however, the patient's condition did not improve. Intracerebral hemorrhage in the right temporal/frontal/occipital/parietal lobe, subarachnoid hemorrhage, and midline shifting were observed on brain computed tomography after 24 hours after thrombolysis. Emergency decompressive craniectomy was performed. After the surgery, the patient continued to experience drowsiness, with no improvement in visual loss and motor weakness. Three months later, he could walk with cane. This case indicates that surgeons who administer filler injections should be familiar with the possibility of accidental intravascular injection and should explain the adverse effects of fillers to patients before surgery.

65. Kim, H., et al. (2014). "The efficacy, longevity, and safety of combined radiofrequency treatment and hyaluronic Acid filler for skin rejuvenation." Ann Dermatol 26(4): 447-456. BACKGROUND: Recent advances in hyaluronic acid (HA) fillers and radiofrequency (RF) devices have been made in the context of skin rejuvenation and cosmetic surgery. Moreover, combination regimens with both techniques are currently being developed. OBJECTIVE: The present study was designed to examine the clinical and histologic effects of a new needle that incorporates an RF device for HA injections. METHODS: A new intradermal needle RF device (INNOfill; Pacific Pharma, Korea) was assessed in the present study. In the animal arm,
procollagen production was measured by using enzyme-linked immunosorbent assay, the filler volume was quantified by incorporating a dye with filler, and the filler distribution was assessed through the changes in tissue structure. In the human arm, the efficacy of the combination regimen was assessed by using the wrinkle severity rating scale (WSRS).

RESULTS: In the animal study, RF treatment increased procollagen production in a time-dependent fashion. The total volume was significantly increased with the RF treatment when compared with the filler injections alone, and lasted for up to 7 weeks after treatment. Additionally, the filler distribution was reduced in animals treated with RF when compared with the untreated group. In the human study, the nasolabial folds of subjects treated with RF before filler injections exhibited a significantly greater change in the WSRS score from baseline when compared with the nasolabial folds treated with filler injections alone.

CONCLUSION: A new device incorporating RF treatment before HA filler injection may represent a biocompatible and long-lasting advance in skin rejuvenation.


Hyaluronic acid (HA) fillers have many favorable characteristics that make it a popular injectable filler device. Its minimal immunogenicity and relative ease of use has helped HA become the most commonly used injectable filler today. A brief history of injectable fillers, the various injection techniques, and legal ramifications are discussed. A review of the most recent literature compares the efficacy and safety of HA to other injectable filler substances.


Hyaluronic acid (HA) is biocompatible, easy to use and reversible. HA fillers are considered to be safe, although some complications can occur. At this time, hyaluronidase is used off-label for correction. A 41-year-old woman presented to our clinic for focal erythematous plaque on hyaluronidase injection site. She got the injection for correction of HA filler excess. The skin lesion continued for 7 days. Histopathologic findings were nonspecific. On intradermal skin test, allergic reaction to hyaluronidase were confirmed. Adverse effects of this hyaluronidase are uncommon with local injection site reactions most frequently reported. Allergy to hyaluronidase should be included in the differential diagnosis when focal erythema and swelling occur after hyaluronidase injection.


We report a case of unilateral blindness and panophthalmoplegia after hyaluronic acid injection into the dorsum of the nose in a healthy young woman. Microspheres of hyaluronic acid are popular fillers for facial rejuvenation. While ocular side effects from injections in the nose and face have been reported following turbinate injection, rhinoplasty and infraorbital nerve block, ocular side effects from injection into the dorsum of the nose are extremely rare. We presume that the symptoms were due to obstruction of the branches of the ophthalmic artery. Under high injection pressure, the microspheres travelled to the ophthalmic artery and were propelled by the blood flow to the central retinal artery and the anterior and posterior long ciliary arteries, leading to her symptoms. Alternatively, there are several arterio-venous anastomotic channels in the nasal mucosa that aid heat exchange.
These may have been the conduit for reflux of the filler into the arterial side of the regional circulation. Physicians must remain aware of serious complications during cosmetic injections to this region.


The authors experienced a case with ocular ischemia with hypotony following injection of a dermal filler for augmentation rhinoplasty. Immediately after injection, the patient demonstrated a permanent visual loss with typical fundus features of central retinal artery occlusion. Multiple crusted ulcerative patches around the nose and left periorbit developed, and the left eye became severely inflamed, ophthalmoplegic, and hypotonic. Signs of anterior and posterior segment ischemia were observed including severe cornea edema, iris atrophy, and chorioretinal swelling. The retrograde arterial embolization of hyaluronic acid gel from vascular branches of nasal tip to central retinal artery and long posterior ciliary artery was highly suspicious. After 6 months of follow up, skin lesions and eyeball movement became normalized, but progressive exudative and tractional retinal detachment was causing phthisis bulbi.


In this study, we developed a composite filler comprising cross-linked hyaluronic acid (HA) and human collagen (COL) derived from the human umbilical cord with the aim of improving its biocompatibility and longevity compared with commercially available fillers. After HA/COL composite fillers were made in two different ratios (10:1 and 5:1), the physical properties of the fillers were evaluated. The interior morphologies and in vivo weight change of these hydrogels were also characterized at 1-16 weeks after injection into mice. To evaluate their biocompatibility and durability in vivo, we injected the composite fillers into nude mice subcutaneously. The variations of injected gel weight were measured and compared with the commercial dermal fillers (Restylane and TheraFill). The composites showed improved or similar physical properties (complex viscosity of 19-22 x 10^5 cP, and injection force of 10-12 N) over the commercial dermal fillers. Sixteen weeks following the injection, the ratio of remaining composite filler weight to initial weight (75.5 +/- 16.9%; 10:1) was shown to be greater than that of the commercial fillers (43.2 +/- 8.1%, Restylane; 12.3 +/- 5.3%, TheraFill). In addition, immunohistochemical analysis with angiogenesis-related markers such as isolecitin and vWF revealed newly formed blood vessels and cellular influx into the composite filler, which were not observed in the other fillers. These results clearly suggest that the HA/COL composite filler is a superior candidate for soft tissue reconstruction. The filler we developed may be a suitable candidate as an injectable dermal filler for tissue augmentation in humans.


Hyaluronic acid (HA) fillers are increasingly used for midface augmentation, which can be performed for facial rejuvenation. Previous study proved that radiofrequency (RF) treatment prior to HA filler injection may provide synergistic and long-lasting effects for the reduction of nasolabial fold wrinkles. Here, we report a case in which the efficacy of two different treatments using RF and HA filler and HA filler alone was assessed using a split-face design. In conclusion, the intradermal needle RF with HA filler may be a more safe and effective method than HA filler alone for correcting midface volume deficit. Appropriate volume loss
replacement should correct the flattening and furrowing of the central area of the mid-cheek, which is a consequence of the aging process. Also, it will provide a more youthful appearance. Hyaluronic acid (HA) fillers are an established intervention for correcting facial volume deficiency. In a previous study (1), radiofrequency (RF) was used to overcome the short duration of HA fillers and resulted in a good outcome.


Perhaps the most significant change in facial rejuvenation in the last 10 years has been the introduction of nonsurgical treatments for the relaxation of facial wrinkles and for the restoration of lost volume. Fillers such as paraffin and silicone have been used in the past for volume restoration, but only recently have new fillers been developed whose safety and efficacy have been supported by clinical research. The introduction of hyaluronic acid (HA) fillers in 2003 began the filler revolution and paved the way for development of biostimulatory and permanent materials. There is an abundance of high-level evidence-based studies comparing the HA fillers, calcium hydroxylapatite, and poly(methyl methacrylate) with collagen and other HA formulations, but there is only limited high-level data evaluating poly-L-lactic acid.


SUMMARY: Soft-tissue fillers have been applied throughout the face; however, the literature has largely ignored the injection of fillers into the nasal anatomy. This Special Topic article reviews proper filler choice and injection technique for the nose based on the senior author's (R.J.R.) experience. Discussion includes indications for soft-tissue filler injection into the nose as well as specific technical pearls based on filler material, anatomic area, and potential complications. The application of soft-tissue fillers to rhinoplasty has certainly broadened the nasal surgeon's armamentarium. While major structural changes of the nose are best accomplished through surgical alteration of the osseocartilaginous framework, soft-tissue fillers offer an excellent method to augment areas or refine irregularities. These often subtle alterations require precise preinjection nasal analysis.


INTRODUCTION: Despite the debates on penile girth enhancement (PGE), demands for enhancement are increasing. Recently, various fillers have been widely used for soft tissue augmentation with proven efficacy and safety. AIMS: To identify the feasibility and efficacy of PGE by injection of filler. METHODS: Fifty patients with subjective small penis who visited Korea University Guro outpatient clinic were enrolled and prospectively followed. Restylane Sub-Q (Q-med, Upssala, Sweden) was injected into the fascial layer of penile body via 21G cannula with "Back & Forth Technique" and homogenized with a roller. MAIN OUTCOME MEASURES: From April 2006 to February 2008, 50 patients were enrolled and 41 patients were followed until 18 months after PGE. Changes in penile girth at midshaft were measured by tape line at 1 and 18 months. Patient’s visual estimation of residual volume (Gr 0-4), patient’s satisfaction (Gr 0-4), and any adverse reactions were also evaluated. RESULTS: Mean injected volume was 20.56 cc (18-22). Compared with basal girth of 7.48 +/- 0.35 cm,
maximal circumference was significantly increased to 11.41 +/- 0.34 cm at 1 month (P < 0.0001) and maintained as 11.26 +/- 0.33 cm until 18 months. In patient's visual estimation, two patients complained the decrease as Gr 3 with focal depression at 1 month. At 18 months, all patients answered as Gr 4 without asymmetry. Patient's and partner's satisfaction score was 3.71 +/- 0.46 and 3.65 +/- 0.48 at 1 month and 3.34 +/- 0.53 and 3.38 +/- 0.49 at 18 months. There were no inflammatory signs or serious adverse reactions in all cases. CONCLUSIONS: Considering the property of material, methods, and follow-up results of 18 months, PGE using filler is a very effective and safe technique for penile augmentation.

77. Kwon, S. G., et al. (2012). "Ischemic Oculomotor Nerve Palsy and Skin Necrosis Caused by Vascular Embolization After Hyaluronic Acid Filler Injection: A Case Report." Ann Plast Surg. ABSTRACT: Hyaluronic acid filler injection is widely used for soft tissue augmentation. However, there could be disastrous complications by direct vascular embolization. We present a case of ischemic oculomotor nerve palsy and skin necrosis after hyaluronic acid filler injection on glabellar. Blepharoptosis, exotropia and diplopia developed suddenly right after the injection, and skin necrosis gradually occurred. Symptoms and signs of oculomotor nerve palsy were continuously improved through steroid therapy. Skin defects healed with minimal scars through intensive wound care. Percutaneous filler injection of periorbital areas should be performed carefully by experienced surgeons, and the possibility of embolization should be considered promptly if symptoms develop.

78. Lambros, V. (2011). "A technique for filling the temples with highly diluted hyaluronic acid: the "dilution solution"." Aesthet Surg J 31(1): 89-94. BACKGROUND: Hollow temples are a common sign of aging, contributing to the upper face appearing "pinched" and the brows appearing short and ptotic. Many treatments have been described for this area, including fat injections and implants. However, traditional injection techniques have not proven entirely satisfactory in correcting the problem without resulting irregularities. OBJECTIVES: The author describes a technical refinement wherein diluted hyaluronic acid (HA) fillers are injected into the temple. METHODS: Thus far, a series of 40 patients has been treated over 18 months with the author's technique, which involves diluting the HA filler by a ratio of approximately two to one (diluent to filler) and injecting the temple as evenly as possible. As the saline component absorbs, the filling material is distributed more evenly in the temple than with undiluted filler. RESULTS: Patients experienced improved results, with a smoother appearance to the brow. There were no instances of complications requiring dissolution of the product with hyaluronidase. Irregularities proved minor and easily correctable; no intravascular complications were noted in this series of patients. Clinical photographs demonstrate improvement in the "pinched" upper face and an apparent elongation of the brows. The author estimates, based on prior experience, that duration of effect will be approximately two to three years. CONCLUSIONS: Dilution of the HA fillers administered for brow treatment results in a more even distribution of the product and a lower morbidity than previously described techniques, making temple treatment far easier than in the past.

79. Lazzeri, D., et al. (2012). "Blindness following cosmetic injections of the face." Plast Reconstr Surg 129(4): 995-1012. BACKGROUND: Complications following facial cosmetic injections have recently heightened awareness of the possibility of iatrogenic blindness. The authors conducted a systematic review of the available literature to provide the best evidence for the prevention and treatment of this serious eye injury. METHODS: The authors included in the study only the
cases in which blindness was a direct consequence of a cosmetic injection procedure of the face. RESULTS: Twenty-nine articles describing 32 patients were identified. In 15 patients, blindness occurred after injections of adipose tissue; in the other 17, it followed injections of various materials, including corticosteroids, paraffin, silicone oil, bovine collagen, polymethylmethacrylate, hyaluronic acid, and calcium hydroxyapatite. CONCLUSIONS: Some precautions may minimize the risk of embolization of filler into the ophthalmic artery following facial cosmetic injections. Intravascular placement of the needle or cannula should be demonstrated by aspiration before injection and should be further prevented by application of local vasoconstrictor. Needles, syringes, and cannulas of small size should be preferred to larger ones and be replaced with blunt flexible needles and microcannulas when possible. Low-pressure injections with the release of the least amount of substance possible should be considered safer than bolus injections. The total volume of filler injected during the entire treatment session should be limited, and injections into pretraumatized tissues should be avoided. Actually, no safe, feasible, and reliable treatment exists for iatrogenic retinal embolism. Nonetheless, therapy should theoretically be directed to lowering intraocular pressure to dislodge the embolus into more peripheral vessels of the retinal circulation, increasing retinal perfusion and oxygen delivery to hypoxic tissues. CLINICAL QUESTION/LEVEL OF EVIDENCE: Risk, V.


A foreign body granuloma is a non-allergic chronic inflammatory reaction that is mainly composed of multinucleated giant cells. Foreign body granulomas may occur after the administration of any dermal filler. Factors such as the volume of the injection, impurities present in the fillers, and the physical properties of fillers affect granuloma formation. The formation of granulomas involves five phases: protein adsorption, macrophage adhesion, macrophage fusion, and crosstalk. The clinical and pathologic features of granulomas vary depending on the type of filler that causes them. Foreign body granulomas can be treated effectively with intralosomal corticosteroid injections. Surgical excisions of granulomas tend to be incomplete because granulomas have ill-defined borders and moreover, surgical excisions may leave scars and deformities.


In the aging process, upper periorbital can be divided broadly into two groups. Group 1 is characterized primarily by soft tissue ptosis of the upper eyelid, which requires surgical excision. The patients in group 2, show volume depletion of the soft tissue and bony resorption of the orbit, characterized by deflation of the upper eyelid as well as sunken, hollow, and skeletonized orbits. Currently, structural fat grafting is the only means for adding volume the depleted upper periorbit. It is, however, an invasive procedure associated with fairly significant morbidities, long downtime, and hence poor patient acceptance. The advent of safe hyaluronic acid (HA)-based dermal filler has, in the authors' opinion, revolutionized treatment for this group of oculoplastic patients. In the current series, 36 patients with volume depletion of the periorbit were treated with HA dermal fillers to restore the smooth arc of the upper periorbit. The average volume required ranged from 0.2 to 0.6 ml of filler. Despite the relatively small volume required, the upper periorbital aesthetics of the patients were successfully and dramatically transformed. At this writing, the longest follow-up period has been 3.5 years, with the patient still maintaining periorbital volume. No significant
morbidities occurred. Given the multiple risks and the resistance of patients to structural fat grafting compared with HA dermal fillers, the authors believe that this nonsurgical technique for adding volume to the periorbit should become the method of choice for this group of oculoplastic patients.


For volume restoration of the face, hyaluronic acid is conventionally injected through long, large-bore, 18-gauge needles because of the higher viscosity subtypes required. These hyaluronic acids are either more highly cross-linked or larger in particle size than the less-viscous subtypes. The microdepot injection technique involves using the 31-gauge BD insulin syringe (Becton-Dickinson, North Ryde, NSW Australia) to deposit small amounts of filler (0.05-0.1 mL) throughout the area of volume loss. The procedure is extremely well tolerated, requiring only topical and ice anaesthesia. Using this method, volume restoration can be achieved naturally and progressively over a period of time. Fractional filling every 3-4 months is continued until the desired level of volume correction is attained. Patients undergoing fractional filling followed over a 12-month period did not indicate any observable compromise in filler longevity, even when highly viscous hyaluronic acid fillers were injected through small-bore, 31-gauge insulin syringes.


BACKGROUND: Pronounced nasojugal groove (tear trough deformity) is one of the landmarks of aging. Hyaluronic acid filler can be used for attenuating the nasojugal sulcus but irregular lumpness and overcorrection are common adverse reactions. OBJECTIVES: We evaluated the effect of Restylane Vital(R) with its specialized injector on volume correction and skin tone of nasojugal groove. SUBJECTS AND METHOD: Ten Korean women were enrolled in this study. Subjects were randomized to be injected a stabilized hyaluronic acid-based gel of nonanimal origin (NAHSA injector, Restylane Vital(R), Q-med) on one side of nasojugal groove, with the other side paired as control. The treatment was performed in one session. Outcome assessments included standardized photography, mexameter, and spectrometer for skin tone, global evaluation by blinded investigators, and patients' self-assessment. An assessment was made before treatment, immediately after treatment, and 1, 3, and 6 months after the treatment. RESULTS: All patients reported a high degree of satisfaction. Duration of overall effect varied among the patients. Correction of the nasojugal groove with a Restylane Vital(R) injector causes minimal tissue trauma and allows exact placement of hyaluronic acid. Restylane Vital(R) injector offers more predictable results and a lower incidence of adverse effects than more commonly used techniques. CONCLUSIONS: Hyaluronic acid filler intradermal injection with special injector is a safe and effective method for correction of nasojugal groove.


Reversal of the visible signs of facial aging with the use of injectable products as an alternative to surgery has become more popular, with nearly 5 million procedures performed in the United States in 2012. Volume augmentation products, such as hyaluronic acid (HA), calcium hydroxylapatite (CaHA), and poly-L-lactic acid (PLLA), are often used in combination
with one another and with neurotoxins for facial rejuvenation because of the complementary modes of action. This article presents 2 case reports involving patientspecific combinations of 2 different HA products, injectable PLLA, and CaHA with incobotulinumtoxinA or abobotulinumtoxinA. The combination of HA, CaHA, PLLA, and neurotoxins has resulted in outstanding outcomes for many patients, with no clinical evidence of increased adverse events secondary to combination therapy.

Injection of synthetic fillers for soft tissue augmentation is increasing over the last decade. One of the most common materials used is hyaluronic acid (HA) that is safe and temporary filler for soft tissue augmentation. We present a case of 54-year-old female who experienced vascular occlusion and nasal alar necrosis following HA injection to the nasolabial folds. She suffered from pain, necrosis, infection, and alar loss that finally required a reconstructive surgery for cosmetic appearance of the nose. The case highlights the importance of proper injection technique by an anesthesiologist, as well as the need for immediate recognition and treatment of vascular occlusion.

PURPOSE: To evaluate the efficacy of hyaluronic acid gel fillers as a nonsurgical alternative for the management of upper eyelid margin asymmetry in cases of relative retraction. METHODS: This is a retrospective study of 8 patients with upper eyelid margin asymmetry relating to relative upper eyelid retraction treated with hyaluronic acid gel injection to affect upper eyelid lowering. Digital photographs were used to quantitatively assess outcomes by comparing pretreatment and posttreatment differences between marginal reflex distance (MRD1) in the right and left eyelids. Image J was used for photographic analysis, and Student paired t test was performed. RESULTS: Eight patients (2 male; mean age, 50.9 years; range, 30-69 years) were injected with hylauronic acid gel in the upper eyelid. The etiology of upper eyelid margin asymmetry included Graves eyelid retraction (n = 3), asymmetry following reconstructive surgery (n = 1) and aesthetic surgery (n = 1), contralateral Horner syndrome (n = 1), Bell palsy (n = 1), and contralateral involutional ptosis (n = 1). The average volume injected in the upper eyelid was 0.2 ml (range, 0.1-0.4 ml). One of 8 patients was injected bilaterally. Average follow-up was 5.7 months (range, 2-12 months). Two of 8 patients requested repeat injection within a 6-month period for undercorrection. No overcorrections were noted, and no patient requested reversal with hyaluronidase. There was a statistically significant improvement in symmetry with mean pretreatment MRD1 difference of 1.53 mm (range, 0.78-3.36 mm) and mean posttreatment MRD1 difference of 0.70 mm (range, 0.02-2.03 mm), p = 0.007. At 4 to 8 months' follow-up, 8 of 8 demonstrated persistent improvement in asymmetry with statistically significant reduction in MRD1 difference when compared with pretreatment with average follow-up MRD1 difference of 0.74 mm (range, 0.11-1.65 mm), p = 0.018. CONCLUSION: This pilot study suggests that upper eyelid injection with hyaluronic acid gel filler may be an effective nonsurgical alternative to improve upper eyelid margin asymmetry in cases of relative upper eyelid retraction.

With the proliferation of dermal fillers in the aesthetic workplace have come instructions from various manufacturers regarding dermal placement. Determination of injection needle
location in the dermis has in large part been based on physician expertise, product and needle familiarity, and patient-specific skin characteristics. An understanding of the precise depth of dermal structures may help practitioners improve injection specificity. Unlike other dermal fillers that suggest intradermal and deep dermal injection planes, a new hyaluronic acid with a cohesive polydensified matrix may be more appropriate for the superficial dermis because of its structure and its high degree of integration into the dermis. To that end, the authors designed a small study to quantify the depth of the superficial dermis by means of ultrasound and histology. Using ultrasound resources, the authors determined the depths of the epidermis, the dermis, and the reticular dermis in the buttocks of six patients; the authors then extrapolated the depth of the superficial reticular dermis. Histologic studies of two of the patients showed full integration of the product in the reticular dermis. Following determination of injection depths and filler integration, the authors describe a technique ("blanching") for injection of the cohesive polydensified matrix hyaluronic acid into the superficial dermis. At this time, blanching is appropriate only for injection of the cohesive polydensified matrix hyaluronic acid known as Belotero Balance in the United States, although it may have applications for other hyaluronic acid products outside of the United States.


Although the benefits of adding lidocaine are recognized in terms of relieving the pain experienced upon injection, it would appear beneficial to establish the impact of lidocaine within the Stylage(R) range, the only one to incorporate both an anaesthetic (lidocaine) and an antioxidant in the form of mannitol in its crosslinked gel of HA. A clinical follow-up was carried out at 11 centres over a period of 6-8 months, depending on the practitioner, and involved 84 patients. The aim of this study was to determine fact from fiction with regards to the benefits of adding local anaesthetic to a filler : 1.Does this addition offer a real benefit in relation to the basic gel? 2)Could it be the cause of other incidents directly linked to lidocaine? 3. Could it have an impact on the durability of the result?


In this roundtable discussion, the physicochemical properties and potential clinical applications of two new ranges of hyaluronic acid fillers are reviewed. These fillers display enhanced tissue integration after implantation due to novel manufacturing processes, and one of the ranges is customized for specific clinical applications by variation of filler gel calibration and cross-linking.


OBJECTIVE: The primary objective of this study is to examine the use and persistency of small gel particle hyaluronic acid (SGP-HA) filler (Restylane(R); Medicis Aesthetics Inc, Scottsdale, AZ) in the treatment of temporal fossa volumization over a 12-month follow-up, and determine local adverse events (AEs). STUDY DESIGN: This is a US Food and Drug Administration-approved, blinded, prospective, single-center, open-label trial enrolling 20 subjects undergoing subcutaneous injection of SGP-HA for rejuvenation of the temples. Primary outcomes were measured using a standardized grading system&mdash;the Hollowness Severity Rating Scale (HSRS)&mdash;at each visit by the treating investigator, a
blinded physician assessment of randomized photos using the HSRS, and patient questionnaires over a 12-month period. AEs were monitored by the investigator and via patient diaries. RESULTS: At weeks 4, 12, and 24, and month 12, all graders (ie, investigator, blinded physician assessor, and patients) reported improvement overall in hollowness. At baseline, temporal fossa hollowness was measured as moderate to severe. At week 4 to month 12, temporal fossa was graded at none or only mild hollowness. No touch-ups were necessary at week 4 on all subjects. All AEs were mild or moderate and resolved within 2 weeks. CONCLUSION: Our study demonstrates clinically significant efficacy and safety in the use of Restylane for temple augmentation and, thus, facial rejuvenation.


Loss of volume in the temple can result in a gaunt, wasted appearance. Dermal filler augmentation of the temples can counteract volume loss and achieve a more balanced and youthful appearance. Although the temporal fossa is a critical area for volume restoration of the aging face, published information is limited. The authors retrospectively describe the treatment of 20 female patients who sought facial rejuvenation and received small gel particle hyaluronic acid (SPG-HA) injections for temporal fossa augmentation. The authors discuss a rationale for their choice of dermal filler and provide a detailed, illustrated injection technique guide for restoring volume in the temporal fossa region with SPG-HA. There is a need for prospective, controlled studies investigating safety, efficacy and persistency of hyaluronic acid fillers in this area of the face.


PURPOSE: To describe one surgeon’s experience with the use of hyaluronic acid gel (Perlane) as a tear-trough filler over an 18-month period and to assess patient satisfaction with the procedure. METHODS: Consecutive, interventional case series involving case note review, masked grading of clinical photographs, and patient satisfaction survey. RESULTS: A total of 198 eyes of 100 patients were treated, with a mean follow-up of 5.1 months. Patients were principally female (87%), white (89%), and middle-aged (mean age = 47.8 years). Eight percent had previous lower eyelid blepharoplasty, and one had thyroid orbitopathy. The gel was placed preperiosteally, deep to orbicularis, anterior to the inferior orbital rim, with a mean volume of 0.59 ml per eye. The injection procedure was tolerable in 95% of patients without local anesthetic. Side effects described by patients included bruising (75%), swelling (26%), blue discoloration (4%), and lumpiness (33%). However, only 7% required dissolution with hyaluronidase. Eight percent requested additional hyaluronic acid gel within 3 months. Mean downtime was 1 day. Most patients (85%) described marked or moderate satisfaction with the treatment, 5% were ambivalent, and 10% were dissatisfied. CONCLUSIONS: This series confirms the effective use of hyaluronic acid gel (Perlane) in tear-trough rejuvenation. It has high patient tolerability, minimal complications, and high patient satisfaction. However, bruising, persistent lumpiness, or lack of perceived effect can lead to dissatisfaction in approximately 10% of cases.


Recent advancements, including more versatile facial fillers, refined injection techniques and the adoption of a global facial approach, have contributed to improved patient outcome and increased patient satisfaction. Nine Canadian specialists (eight dermatologists, one plastic
surgeon) collaborated to develop an overview on volume restoration and contouring based on published literature and their collective clinical experience. The specialists concurred that optimal results in volume restoration and contouring depend on correcting deficiencies at various layers of the facial envelope. This includes creating a foundation for deep structural support in the supraperiosteal or submuscular plane; volume repletion of subcutaneous fat compartments; and the reestablishment of dermal and subdermal support to minimize cutaneous rhytids, grooves and furrows. It was also agreed that volume restoration and contouring using a global facial approach is essential to create a natural, youthful appearance in facial aesthetics. A comprehensive non-surgical approach should therefore incorporate combining fillers such as high-viscosity, low-molecular-weight hyaluronic acid (LMWHA) for structural support and hyaluronic acid (HA) for lines, grooves and furrows with neuromodulators, lasers and energy devices.


**BACKGROUND:** An 18-month persistence study reported nasolabial fold (NLF) improvements using a small gel-particle hyaluronic acid (SGP-HA) dermal filler lasted up to 18 months after one retreatment. **OBJECTIVE:** To evaluate the efficacy and persistence of SGP-HA for the correction of NLFs for up to 36 months. **METHODS & MATERIALS:** Subjects completing the 18-month persistence study were permitted to enroll in an 18-month extension trial. Most required second retreatments to achieve optimal correction of their NLFs. Subjects were followed for up to 36 months after their initial treatment. The primary efficacy measure was a 1-point improvement from baseline Wrinkle Severity Rating Scale (WSRS) score as determined by a blinded evaluator at different time points. **RESULTS:** The study enrolled 52 subjects. Forty subjects required a second retreatment for optimum NLF correction. Mean retreatment volume was less than 50% of the initial treatment volume. Twenty-six subjects completed the study. Blinded assessments revealed that 94% to 100% of subjects maintained WSRS scores of 1 point or more higher than baseline throughout the study. **CONCLUSIONS:** Participants in the 18-month extension of an 18-month SGP-HA persistence study continued to demonstrate improvement of NLFs up to 36 months after a second retreatment. The mean volume of SGP-HA required for optimum NLF correction decreased substantially with each retreatment. Subjects reported no treatment-related adverse events after the second retreatment.


**BACKGROUND:** This pilot study compared a monophasic hyaluronic acid dermal filler with a biphasic filler for the correction of nasolabial folds. **METHODS:** Participant- and assessor-blinded, randomized clinical trial involving participants with moderate to severe nasolabial folds. Split-face design comparing a monophase hyaluronic acid (HA) filler (mono-HA) with a biphasic HA filler (bi-HA). Injection with touch-up after 1 month. Wrinkle improvement was measured before and after injection and after 1, 2, 4, and 7 months, using the Wrinkle Severity Rating Scale and the Global Aesthetic Improvement Scale as outcome criteria. An optional treatment was offered at the end of the study, with participants allowed to choose one of the products. **OBJECTIVE:** Evaluation of efficacy and safety of both products. **RESULTS:** Both products showed immediate, good results after injection and touch-up and demonstrated good durability over time. Participant preference for optional treatment at the end of the study favoured mono-HA. Both products were well tolerated, without serious
adverse events. CONCLUSION: The effect after injection of mono-HA and bi-HA is generally comparable, although there was a trend in favor of mono-HA. Materials and funding for this study were provided by Teoxane, Geneva, Switzerland.


OBJECTIVE: To describe findings in patients who received dermal fillers and later developed peri-ocular mass lesions. DESIGN: Retrospective case series. PARTICIPANTS: Patients who presented with peri-ocular masses secondary to dermal filler use. METHODS: Retrospective chart review. RESULTS: Three patients with remote filler injection (hyaluronic acid and polyalkylimide), not volunteered on initial history, presented with peri-orbital swelling and/or inflammation that was suspicious in each case for more serious pathology. CONCLUSIONS: It is important for the injecting physician, the ophthalmologist, and the patient to recognize this complication to permit appropriate investigation and management.


BACKGROUND: Hyaluronic acid-based dermal fillers have gained rapid acceptance for treating facial wrinkles and deep tissue folds. Although their space-filling properties are well understood, this study evaluates the cellular and molecular changes in skin, as a secondary effect, following injection of a commercially available, 24-mg/ml, cross-linked hyaluronic acid-based filler (HYC-24L+) in a rodent model. METHODS: Sprague-Dawley rats, aged 2 to 4 months, were injected intradermally with 20 μl of HYC-24L+ using a linear threading technique and followed to 12 weeks after injection. Untreated skin and saline injection were used as study controls. Enzyme-linked immunosorbent assay and reverse-transcriptase polymerase chain reaction methods were used to investigate changes in the expression of several extracellular matrix proteins and genes over time. RESULTS: HYC-24L+ significantly increased the protein expression levels of collagen types I and III in rat dermal tissue for up to 12 weeks. The ratio of collagen type III to type I protein, however, remained unchanged, suggesting maintenance of collagen homeostasis. A significant increase in dermal elastin after HYC-24L+ injection was also observed. Gene expression analysis confirmed that several genes associated with extracellular matrix production and assembly were also transiently up-regulated, and that these changes temporally preceded those observed at the protein level. CONCLUSION: In addition to its well-understood space-filling function, as a secondary effect, the authors demonstrate that HYC-24L+ stimulates the production of several extracellular matrix components, including dermal collagen and elastin.


PURPOSE OF REVIEW: To review the current literature regarding aesthetic enhancement using facial neuromodulators and fillers and to present advanced techniques using facial injectables for periocular rejuvenation. RECENT FINDINGS: The authors provide a summary of traditional periocular locations for the injection of neuromodulators and dermal fillers. The authors also present novel and advanced techniques utilizing injectables in the periocular region. SUMMARY: Minimally invasive procedures with little-to-no recovery time are continuing to increase in popularity. Neuromodulators and hyaluronic acid gel fillers have been shown to be well tolerated and efficacious nonsurgical alternatives in periocular rejuvenation.

IMPORTANCE Iatrogenic occlusion of the ophthalmic artery and its branches is a rare but devastating complication of cosmetic facial filler injections. OBJECTIVE To investigate clinical and angiographic features of iatrogenic occlusion of the ophthalmic artery and its branches caused by cosmetic facial filler injections. DESIGN, SETTING, AND PARTICIPANTS Data from 44 patients with occlusion of the ophthalmic artery and its branches after cosmetic facial filler injections were obtained retrospectively from a national survey completed by members of the Korean Retina Society from 27 retinal centers. Clinical features were compared between patients grouped by angiographic findings and injected filler material. MAIN OUTCOMES AND MEASURES Visual prognosis and its relationship to angiographic findings and injected filler material. RESULTS Ophthalmic artery occlusion was classified into 6 types according to angiographic findings. Twenty-eight patients had diffuse retinal and choroidal artery occlusions (ophthalmic artery occlusion, generalized posterior ciliary artery occlusion, and central retinal artery occlusion). Sixteen patients had localized occlusions (localized posterior ciliary artery occlusion, branch retinal artery occlusion, and posterior ischemic optic neuropathy). Patients with diffuse occlusions showed worse initial and final visual acuity and less visual gain compared with those having localized occlusions. Patients receiving autologous fat injections (n = 22) had diffuse ophthalmic artery occlusions, worse visual prognosis, and a higher incidence of combined brain infarction compared with patients having hyaluronic acid injections (n = 13). CONCLUSIONS AND RELEVANCE Clinical features of iatrogenic occlusion of the ophthalmic artery and its branches following cosmetic facial filler injections were diverse according to the location and extent of obstruction and the injected filler material. Autologous fat injections were associated with a worse visual prognosis and a higher incidence of combined cerebral infarction. Extreme caution and care should be taken during these injections, and physicians should be aware of a diverse spectrum of complications following cosmetic facial filler injections.


BACKGROUND: Numerous hyaluronic acid (HA) fillers seem to have similar characteristics, although manufacturers insist that monophasic and biphasic HA fillers are different in many ways. Little information regarding this is available in the literature. OBJECTIVES: To determine characteristics of monophasic fillers vs. biphasic fillers. MATERIAL AND METHODS: We tested three different (two biphasic and one monophasic) HA fillers both in vitro and in vivo. In the in vitro assay, cell toxicity, resistance to enzyme degradation, syringeability and morphology of particles were tested. In vivo, the efficacy and safety were investigated in the dorsal skin of hairless mice. RESULTS: There was no cell toxicity in any of the three HA fillers. Resistance to enzymatic degradation and syringeability were better in the two biphasic HA fillers than in the monophasic filler. In particle morphology test, gel type monophasic HA filler was also found as a particle type, although there was a slight difference. Volume assessment in animal skin was superior with the monophasic than with the two biphasic HA fillers. CONCLUSION: Biphasic HA fillers have some advantages in hyaluronidase resistance, syringeability and lower risk for overcorrection, while monophasic HA fillers may be more suitable for volume augmentation due to swelling capacity.

BACKGROUND: A variety of hyaluronic acid (HA) fillers demonstrate unique physical characteristics, which affect the quality of the HA filler products. The critical factors that affect the degradation of HA gels have not yet been determined. OBJECTIVE: Our objective was to determine the characteristics of HA gels that affect their resistance to the degradation caused by radicals and enzymes. METHODS: Three types of HA fillers for repairing deep wrinkles, Juvederm Ultra Plus (J-U), Restylane Perlane (Perlane), and Cleviel, were tested in this study. The resistance of these HA fillers to enzymatic degradation was measured by carbazole and displacement assays using hyaluronidase as the enzyme. The resistance of these fillers to radical degradation was measured by the displacement assay using H2O2. RESULTS: Different tests for evaluating the degradation resistance of HA gels can yield different results. The filler most susceptible to enzymatic degradation was J-U, followed by Perlane and Cleviel. The HA filler showing the highest degree of degradation caused by H2O2 treatment was Perlane, followed by J-U, and then Cleviel. Cleviel showed higher enzymatic and radical resistances than J-U and Perlane did. Furthermore, it exhibited the highest resistance to heat and the lowest swelling ratio among all the fillers that were examined. CONCLUSION: The main factor determining the degradation of HA particles is the gel swelling ratio, which is related to the particle structure of the gel. Our in vitro assays suggest that the decrease in the swelling ratio will lead to a retarding effect on the degradation of HA fillers.


PURPOSE: To investigate the clinical manifestations and visual prognosis of retinal artery occlusion resulting from cosmetic facial filler injections. DESIGN: Retrospective, noncomparative case series. METHODS: Setting. Institutional. Study Population. Twelve consecutive patients with retinal artery occlusion caused by cosmetic facial filler injections. Main Outcome Measures. Filler materials, injection sites, best-corrected visual acuities, fundus fluorescein angiography and optical coherence tomography findings, and associated ocular and systemic manifestations. RESULTS: Seven, 2, and 3 patients had ophthalmic, central retinal, and branch retinal artery occlusions, respectively. Injected materials included autologous fat (7 cases), hyaluronic acid (4 cases), and collagen (1 case), and injection sites were the glabellar region (7 cases), nasolabial fold (4 cases), or both (1 case). Injected autologous fat was associated with worse final best-corrected visual acuity than the other materials. All patients with ophthalmic artery occlusion had ocular pain and no improvement in best-corrected visual acuity. Optical coherence tomography revealed thinner and less vascular choroids in eyes with ophthalmic artery occlusion than in adjacent normal eyes. Concomitant brain infarction developed in 2 cases each of central retinal artery occlusion and ophthalmic artery occlusion. Phthisis developed in 1 case of ophthalmic artery occlusion. CONCLUSIONS: Cosmetic filler injections into the glabellar region or nasolabial fold can cause retinal artery occlusion. Iatrogenic ophthalmic artery occlusion is associated with painful blindness, a thin choroid, brain infarction, and poor visual outcomes, particularly when autologous fat is used. Ophthalmic examination and systematic brain magnetic resonance imaging should be performed in patients with ocular pain after such injections.


Hyaluronic acid (HA) fillers have become the material of choice for soft-tissue augmentation. HA fillers are longer lasting, less immunogenic and can be broken down by hyaluronidase. These advantages make HA fillers the most common of the temporary fillers on the market. However, early and delayed complications, ranging from minor to severe, can occur following
HA-filler injection. We evaluated and treated 28 cases of HA-filler-related complications that were referred to our hospital over a period of 5 years from July 2004 to October 2009. Twenty-eight patients were included in our study; 82.1% of the patients were female and 17.9% were male. Complications were roughly classified as nodular masses, inflammation, tissue necrosis and dyspigmentation. Affected locations, in descending order of frequency, were the perioral area, forehead, including glabella, nose, nasolabial fold, mentum, including marionette wrinkles, cheek area and perioral wrinkles. The most disastrous complication was alar rim necrosis following injection of the nasolabial fold. We propose two 'danger zones' that are particularly vulnerable to tissue necrosis following filler injection: the glabella and nasal ala. Although there is no definite treatment modality for the correction of HA-filler complications, we have managed them with various available treatment modalities aimed at minimizing patient morbidity.

104. Park, T. H., et al. (2012). "Clinical outcome in a series of 173 cases of foreign body granuloma: improved outcomes with a novel surgical technique." J Plast Reconstr Aesthet Surg 65(1): 29-34. BACKGROUND: Soft-tissue filler injections have become popular, and injections of even illegal materials are widespread. Complications such as foreign body granuloma often occur in such cases, and appropriate treatment is mandatory but no optimal treatment has been established. METHODS: We treated 173 patients who underwent surgical excision of foreign body granulomas via direct approach to the lesion (n = 121) or injection therapies (n = 52) at Kangbuk Samsung Hospital over a period of 7 years from April 2004 to February 2011. A retrospective chart review found that 104 patients had a history of treatment failure at other hospitals. Among these 104 patients, 83 had a history of prior injection therapy and 21 patients had a history of prior surgical therapy. Patient satisfaction was evaluated at our hospital on a scale of 1-5 using an in-house questionnaire. Comparisons between patients receiving injection therapy and patients receiving surgical therapy were made using the Mann-Whitney test. RESULTS: Patients who underwent surgical therapy via direct approach to the lesion reported statistically higher satisfaction scores 4(3-4) than those who underwent injection therapy 3(2-3) (p < 0.001). CONCLUSIONS: Our novel surgical technique results in better outcomes and patient satisfaction in cases of severe foreign body granuloma.

105. Park, T. H., et al. (2012). "Clinical experience with complications of hand rejuvenation." J Plast Reconstr Aesthet Surg 65(12): 1627-1631. PURPOSE: Prominent signs of ageing of the hands have recently been treated with permanent or longer-lasting injectable dermal fillers. However, few previous studies have described the long-term complications of such hand rejuvenation. The purpose of our report was to share our experience of 15 cases with long-term complications following hand rejuvenation using various medical fillers. PATIENTS AND METHODS: We performed a retrospective review of the management of 15 patients who presented with complications from the injection of synthetic fillers for hand rejuvenation at a tertiary medical centre over a period of 10 years from March 2002 to January 2011. RESULTS: Injected materials included polymethylmethacrylate (PMMA) microsphere filler, calcium hydroxyapatite filler, hyaluronic acid filler, poly-l-lactic acid (PLLA) filler and other medical fillers. Of the total study sample of 15 patients, nine underwent surgical excision, six patients with a history of PMMA or PLLA filler injection received intralesional steroid therapy and three patients with a history of hyaluronic acid filler injection received injection therapy using hyaluronidase. CONCLUSIONS: Hand rejuvenation complications can be successfully treated according to our proposed algorithm.
   a. BACKGROUND: A monophasic, highly crosslinked hyaluronic acid dermal filler offers further treatment options for deep lines. OBJECTIVE: To investigate the efficacy and tolerability of Belotero. METHODS AND MATERIALS: A total of 149 patients received injections. Efficacy was assessed on the Wrinkle Severity Rating Scale (WSRS) and the Global Aesthetic Improvement Scale (GAIS). Adverse events were recorded at each evaluation session. RESULTS: Mean WSRS improved significantly (P<0.001) by 1.9 score points without any decline throughout the 12-week period. Improvement was found in 89.9 percent of patients on the (GAIS), 59.7 percent of whom were designated as very much/much improved. Investigator and patient satisfaction was stated in more than 90 percent of cases as excellent/good. Adverse events, exclusively localized to the injection area, occurred in 85.9 percent of patients immediately after injection and declined to 12.8 percent in week 2. None were serious. CONCLUSION: The findings indicate the benefit of the highly cross-linked, monophasic hyaluronic acid dermal filler, especially in the treatment of patients with deep and extremely deep folds. Overall, the filler appears to be well tolerated. This evaluation raised no major safety concerns.

   Facial aging is a three-dimensional process, and facial rejuvenation procedures intended to reverse the effects of aging need to address this by combining products that relax hyperkinetic musculature, volumize/fill, and recontour/lift the whole face. In line with the desire of patients to achieve an overall youthful facial appearance, we report for the first time three cases where patients have been successfully treated across the whole face with a novel, three-step approach, layering incobotulinumtoxinA and two dermal fillers (calcium hydroxylapatite and a monophasic hyaluronic acid filler with CPM Technology) injected at three separate treatment visits. The results suggest that this layering approach based on an understanding of the underlying causes of facial aging, where different products are used in combination to treat the entire face, can enable patients to achieve the desired outcome of a return to the characteristics of a more youthful face.<br><br> <em>J Drugs Dermatol.</em> 2013;12(9):978-984.

   Hyaluronic acid (HA)-based injectable fillers three-dimensionally restore the natural contours of the lips and perioral area, thereby reducing some signs of aging lips. To evaluate the short-term aesthetic impact of treatment with the HA dermal filler Juvederm(IR) VOLBELLA(R) with Lidocaine, formulated utilizing VYCROSS() technology, for enhancement or correction of asymmetry of the lips, evaluated using a patient-centric approach. Sixty-two subjects were enrolled in this study, conducted at two sites in Germany. Primary endpoints were satisfaction with improvement, look and feel of the lips, assessed by subject and physician at first visit and 4 weeks post-treatment. Immediately after injection at first visit, 83.6% of subjects were Extremely Satisfied, Very Satisfied or Satisfied with improvement in the lips, which increased to 94.1% and 93.0% of subjects with/without top-up treatment at follow-up, respectively. After injection at first visit, 61.7% of subjects rated the look and feel of their lips
as Extremely Natural or Very Natural, which increased to 75.0% and 93.0% of subjects with/without top-up treatment, respectively. The HA dermal filler was associated with minimal discomfort, bruising or swelling of the lips; almost two-thirds of subjects (62%) returned to social engagements on the same day. The high degree of subject satisfaction with aesthetic improvement in the lips, as well as the natural look and feel, indicates that this HA dermal filler represents an effective treatment option for patients requiring lip enhancement.

Macrolane is an injectable, biocompatible, soft-tissue filler that has been available in the UK since 2008 and is promoted for use in breast augmentation. There are few data available on the long-term effects of this relatively new product and concerns have been raised about the implications for breast imaging, in particular breast screening. In this context we present a spectrum of imaging appearances and complications encountered to date.

The use of fillers for nonsurgical rhinoplasty has advanced in both materials and methods, and continues to gain popularity in North America. This technique is most often used for secondary revisions, although reports of fillers used in primary rhinoplasty in selected patients have been recently described. The present report details the use of a hyaluronic acid dermal filler in a young Middle Eastern man for a post-traumatic crooked nose deformity. Primary correction of the patient's right-sided nasal bone deviation using hyaluronic acid as a soft tissue filler was achieved with excellent results and patient satisfaction. The current use of fillers in nasal contouring is reviewed.

BACKGROUND: Data regarding several hyaluronic acids (HAs) used identically for facial tissue augmentation have heretofore been unavailable. OBJECTIVES: This prospective, split-face, randomized, two-armed study sought to determine the long-term safety and effectiveness of three HAs (HA-1 (Belotero Basic/Balance), HA-2 (Restylane), and HA-3 (Juvederm Ultra 3/Juvederm Ultra Plus XC) in the treatment of nasolabial folds (NLFs). METHODS: Twenty participants in Arm A received HA-1 in one NLF and HA-2 in the other. In Arm B, 20 participants received HA-1 in one NLF and HA-3 in the other. Injection was at visit 2, with follow-up visits at 1, 6, 9, and 12 months. Mean volume of HA was slightly <1.5 mL/NLF. RESULTS: Adverse events were unremarkable across all HAs, with injection site erythema being the most frequent adverse event. Mean pretreatment NLF severity rating for both arms was 2.3; at 12 months, mean posttreatment severity rating was 1.5 for HA-1/HA-2 and 1.6 for HA-1/HA-3. Although not statistically significant, participants tended to show a preference for HA-1. CONCLUSION: All three HAs provided essentially equivalent results, except for 4-week evenness results, which favored HA-1. Injection volumes of the three HAs were also similar.

The dermal extracellular matrix (ECM) provides strength and resiliency to skin. The ECM consists mostly of type I collagen fibrils, which are produced by fibroblasts. Binding of fibroblasts to collagen fibrils generates mechanical forces, which regulate cellular morphology and function. With aging, collagen fragmentation reduces fibroblast-ECM binding and mechanical forces, resulting in fibroblast shrinkage and reduced function, including collagen production. Here, we report that these age-related alterations are largely reversed by enhancing the structural support of the ECM. Injection of dermal filler, cross-linked hyaluronic acid, into the skin of individuals over 70 years of age stimulates fibroblasts to produce type I collagen. This stimulation is associated with localized increase in mechanical forces, indicated by fibroblast elongation/spreading, and mediated by upregulation of type II TGF-beta receptor and connective tissue growth factor. Interestingly, enhanced mechanical support of the ECM also stimulates fibroblast proliferation, expands vasculature, and increases epidermal thickness. Consistent with our observations in human skin, injection of filler into dermal equivalent cultures causes elongation of fibroblasts, coupled with type I collagen synthesis, which is dependent on the TGF-beta signaling pathway. Thus, fibroblasts in aged human skin retain their capacity for functional activation, which is restored by enhancing structural support of the ECM.


Dermatological procedures which are considered as being minimally invasive, such as those using injectable fillers based on hyaluronic acid, revolutionized aging treatment, especially of the face. By promoting the replacement of lost volume and attenuating grooves and wrinkles, they ensure a more youthful appearance and certain functional recovery of facial aesthetics. The authors review some of the main physicochemical characteristics of these dermal fillers, highlighting the product line Stylage(R), the manufacture of which includes mannitol.


INTRODUCTION: Hyaluronidase (HA) degrades hyaluronic acid, allowing flexibility in the use of hyaluronic acid-based fillers commonly used in facial correction. Potentially differing properties of available hyaluronidases and fillers may influence their interaction, leading to important differences in ultimate cosmetic results. This study examines the physical properties of various fillers after exposure to commonly available hyaluronidases in vitro to better inform their in vivo clinical use. METHODS: Four commonly used HA fillers were exposed to varying concentrations of Vitrase (ovine testicular hyaluronidase) and Hylenex (human recombinant hyaluronidase) in vitro. The gross properties of these fillers were then observed to evaluate time- and dose-response; photographs were obtained to allow visual comparison at 1 minute and 5 minutes post-exposure. RESULTS: At a concentration of 0.1 mL Vitrase to 0.2 mL filler, Restylane dissipated most followed by Juvederm; Belotero most retained its form. Hylenex at the same concentration showed similar results, again affecting Restylane most and Belotero least. Response to treatment with both hyaluronidases increased substantially over time, increasing progressively from exposure to 5 minutes post-exposure. When exposed to Hylenex at 15 U and 30 U to 0.2 mL filler, Belotero retained its form most, followed by Juvederm, Juvederm Voluma, and then Restylane. The effects on filler structure increased with 30 U concentration vs 15 U concentration of Hylenex. DISCUSSION: Available hyaluronidases and HA fillers appear to have differing physical
properties that influence their interaction in a time and dose-dependent manner. Knowledge of the ways in which specific fillers interact with different hyaluronidases may help achieve desired cosmesis when aiming to adjust delicate facial fillers.


Soft-tissue augmentation with hyaluronic acid and calcium hydroxyl apatite are among the most widely used minimally invasive cosmetic treatments for the correction of contour deficiencies and wrinkles of the face without the risk, recovery time, and expense of a major surgery. Training and experience in the art and science of fillers is essential for the successful creation of a more youthful and natural appearance. An understanding of the different products, the injection techniques, the indications, and the potential complications of each filler are paramount to success.


In recent years, injections with filler agents are often used for wrinkle-treatment and soft tissue augmentation by dermatologists and plastic surgeons. Unfortunately, the ideal filler has not yet been discovered and all of them may induce adverse reactions. Quickly biodegradable or resorbable agents may induce severe complications, but they will normally disappear spontaneously in a few months. Slowly biodegradable or nonresorbable fillers may give rise to severe reactions that show little or no tendency to spontaneous improvement. They may appear several years after the injection, when the patient does not remember which product was injected, and treatment is often insufficient. In this review, we discuss the most commonly used fillers, their most frequent adverse reactions as well as the characteristic histopathologic findings that allow the identification of the injected filler agent. In conclusion, histopathologic study remains as the gold standard technique to identify the responsible filler.


BACKGROUND: Hyaluronic acid (HA) fillers are frequently used for the correction of facial soft-tissue defects. OBJECTIVE: To compare the efficacy and safety of a novel monophasic HA filler (mono-HA), and a well-studied biphasic HA filler (bi-HA), in the treatment of moderate to severe nasolabial folds. METHODS: In this randomized, evaluator-blinded, split-face comparative study, subjects were randomized for injections with mono-HA or bi-HA on the left or right side of the face. Efficacy was determined by calculating the change in the Wrinkle Severity Rating Score (WSRS) relative to baseline. Local safety was assessed on the basis of subject diary entries which recorded erythema, swelling, induration, pruritus, irritation, mass, hematoma, pain, and dryness. RESULTS: At week 24, the mean improvement in the WSRS from baseline was 2.18 +/- 0.42 for the mono-HA side and 2.16 +/- 0.41 for the bi-HA side. Both fillers were well-tolerated and adverse reactions were mild and transient in most cases. CONCLUSIONS: Mono-HA has a non-inferior efficacy to bi-HA in the treatment of moderate to severe nasolabial folds.

Abstract Background: Hyaluronic acid (HA) fillers such as Restylane(R) are frequently used for the correction of facial soft-tissue defects. Objective: To compare the efficacy and safety of Elravie(R), a novel monophasic HA filler, and Restylane, a well-studied biphasic HA filler, in the treatment of moderate to severe nasolabial folds. Methods: In this randomized, evaluator-blinded, split-face comparative study, subjects were randomized for injections with Elravie(R) or Restylane(R) on their left or right side of the face. Efficacy was determined by calculating the change in the Wrinkle Severity Rating Score (WSRS) relative to baseline. Local safety was assessed on the basis of the subject diaries which recorded erythema, swelling, induration, pruritus, irritation, mass, hematoma, pain, and dryness. Results: At week 24, the mean improvement in WSRS from baseline was 2.18 +/- 0.42 for the Elravie(R) side and 2.16 +/- 0.41 for the Restylane(R) side. Both fillers were well tolerated and the adverse reactions were mild and transient in most cases. Conclusions: Elravie(R) provides non-inferior efficacy compared to Restylane(R) 6 months after being used to treat moderate to severe nasolabial folds.


Soft tissue augmentation is a process of implanting tissues or materials to treat wrinkles or soft tissue defects in the body. Over the years, various materials have evolved to correct soft tissue defects, including a number of tissues and polymers. Autogenous dermis, autogenous fat, autogenous dermis-fat, allogenic dermis, synthetic implants, and fillers have been widely accepted for soft tissue augmentations. Tissue engineering technology has also been introduced and opened a new venue of opportunities in this field. In particular, a long-lasting filler consisting of hyaluronic acid filler and living human mesenchymal cells called "injectable tissue-engineered soft tissue" has been created and applied clinically, as this strategy has many advantages over conventional methods. Fibroblasts and adipose-derived stromal vascular fraction cells can be clinically used as injectable tissue-engineered soft tissue at present. In this review, information on the soft tissue augmentation method using the injectable tissue-engineered soft tissue is provided.


A 24-month follow up of a previously reported case of successful hyaluronic acid filler use in steroid atrophy is presented. The patient had persistence of the volume and appearance of her scar with sustained satisfaction 24 months after hyaluronic acid treatment, without the need for repeat injection. This case suggests expansion of the use of hyaluronic acid fillers to include scar atrophy, as persistence of a desired cosmetic appearance for 2 years is demonstrated.


BACKGROUND: The blue hue of skin overlying injected hyaluronic acid (HA) fillers in certain cases has been hypothesized in the literature as related to the Tyndall effect. This investigation aims to understand the relevant optical concepts and to discuss the plausibility of this assertion. METHODS: Theoretic and physical aspects of relevant optical theories including the Tyndall effect, the Raleigh criterion and the Mie Solution are discussed, with simple examples. The physical properties of the system (both HA and subcutaneous tissue) are explored. Alternate concepts of dermal hue generation are discussed. RESULTS: The
Tyndall effect (and Rayleigh criterion) describe optical phenomenon that occur as light passes through colloidal solutions containing uniform spherical particles of sizes less than the length of a wavelength of visible light. HA fillers are complex, large, non-spherical, cross-linked hydrogels, and thus are not well characterized by these theories. Skin is a complex optical surface in which shorter wavelengths of light are selectively filtered at superficial depths. Light passing through to subdermal HA would have low blue light amplitude, minimizing what light could be preferentially scattered. Further, should blue hues be ‘generated’ subdermally, the same skin filters work in reverse, making the blue light poorly detectable by an external observer. CONCLUSIONS: The Tyndall effect is unlikely to cause dermal hue changes in HA filler instillation. Optical and perceptual processes explaining superficial vein coloration may better describe subdermal HA hue changes. Vein coloration is thought to be related to three processes: the reflective properties of the skin, the absorptive properties of blood and the perceptive properties of an observer’s eyes. Subdermal HA may simulate these phenomena by a number of undetermined, yet plausible mechanisms.


BACKGROUND: Pain management is an important objective in procedures involving dermal fillers composed of hyaluronic acid (HA). OBJECTIVE: To compare the 1-year clinical results of filling the nasolabial fold with 2 types of filler: large-gel particle HA and large-gel particle HA plus 0.3% lidocaine (HA+L). We compared the level of pain during treatment and 10 minutes after treatment and assessed the safety and efficacy profile, satisfaction, and histological findings (using reflectance confocal microscopy [RCM]). MATERIALS and METHODS: We performed a comparative, parallel-group, double-blind trial with an external observer (blinded to the type of treatment administered). The filler was applied to the nasolabial fold in 119 patients (HA in 62 patients and HA+L in 57). Patients were followed at months 3, 9, and 12. Pain was evaluated using a visual analog scale. Efficacy and satisfaction were evaluated using the Wrinkle Severity Rating Scale and the Global Aesthetic Improvement Scale. RCM images (n=32) were taken at baseline and at months 3 and 12. RESULTS: Pain: The severity of pain was decreased in patients treated with HA+L on application (P <.001) and 10 minutes later ( P=.008). Efficacy and satisfaction: No significant differences existed between the 2 groups at months 3, 9, and 12. RCM: Skin rejuvenation occurred with a 32% increase in the height of the dermoepidermal junction at month 12 (P <.001), which was similar in both groups. Adverse events: At month 3, the most common adverse events (AEs) were erythema (68%) and hematoma (11%). No AEs were recorded at months 9 or 12. CONCLUSION: The use of HA+L provides pain relief without affecting efficacy, satisfaction, safety, or the duration of results. RCM showed that the changes in the dermoepidermal junction represented a histological improvement in the skin with similar results in both groups.


BACKGROUND: Hyaluronic acid (HA) fillers such as Restylane((R)) are frequently used for the correction of facial soft tissue defects. OBJECTIVE: To compare the efficacy and safety of a novel HA filler, Emervel((R)) Classic, with those of Restylane in the treatment of moderate nasolabial folds. METHODS: This was a split-face, randomized and evaluator-blinded comparison study. Subjects were randomized to receive an injection of Emervel Classic or
Restylane on their left or right side. Efficacy was evaluated based on the change in Wrinkle Severity Rating Score (WSRS) from baseline. Local tolerability was assessed based on subject diary, which recorded the severity of erythema, oedema/swelling, bruising, pain/tenderness and pruritus during the first 3 weeks after injection. RESULTS: The interim results 6 months after injection are reported. At week 24, the mean improvement in WSRS from baseline was 0.83 +/- 0.51 for Emervel Classic, similar to that for Restylane (0.90 +/- 0.57). A similar volume of both fillers was injected. Most local tolerability events were mild and transient. Erythema, oedema/swelling and pain/tenderness were significantly less severe and disappeared faster with Emervel Classic than with Restylane (at least p < 0.05). CONCLUSION: Emervel Classic provides similar efficacy and better overall local tolerability compared with Restylane 6 months after treatment of moderate nasolabial folds.

124. Rzany, B., et al. (2012). "Full-face rejuvenation using a range of hyaluronic acid fillers: efficacy, safety, and patient satisfaction over 6 months." Dermatol Surg 38(7 Pt 2): 1153-1161. BACKGROUND: Full-face rejuvenation with dermal fillers in patients with multiple aesthetic indications is rarely studied. OBJECTIVE: To assess whether a new range of hyaluronic acid filler is suitable for full-face rejuvenation and to evaluate efficacy, safety, and patient satisfaction. MATERIALS AND METHODS: In this 6-month study, participants could receive five different fillers from the same range (HA(E) )for up to eight indications (periorbital lines, tear troughs, cheeks, cheek folds, nasolabial folds, upper lip lines, lips, and marionette lines). Outcomes included global aesthetic improvement, improvement in each indication, adverse events, local tolerability, and satisfaction. RESULTS: Seventy-seven participants with a mean age of 54.5 were enrolled; 48.1% had five or more indications treated. Mean total injection volume (baseline and touch-up) per participant was 6.7 mL. At month 6, 92.1% of participants remained at least improved over baseline, 79.7% of participants were satisfied or very satisfied with the durability of the results, and 63.0% of participants felt a lot or much better than before injection. No specific safety concerns were reported except expected injection site reactions. CONCLUSION: In participants with multiple indications, full-face rejuvenation using HA(E) provided effective, safe, satisfactory results.

125. Rzany, B., et al. (2012). "Correction of tear troughs and periorbital lines with a range of customized hyaluronic acid fillers." J Drugs Dermatol 11(1 Suppl): s27-34. BACKGROUND: The periorbital region is a challenging area for injectable filler. Overcorrection and/or the use of unsuitable fillers may lead to unwanted results. As evidence for this region is limited, most physicians follow a trial and error approach. OBJECTIVE: Assess the efficacy, patient satisfaction, and safety of the HA E filler range in periorbital rejuvenation. MATERIALS AND METHODS: This was a multi-center, six-month, open-label study. Subjects could receive HA E Touch, HA E Classic, and HA E Deep for the treatment of tear troughs and periorbital lines at baseline, and an optional touch-up three weeks later. Global aesthetic improvement for both indications, periorbital wrinkle assessments (Lemperle Rating Scale), 3-D volume analysis (for tear troughs only), adverse events and injection site reactions were evaluated at each visit. A subject satisfaction questionnaire was performed three weeks after last injection. RESULTS: Overall, HA E Classic and Deep were infected for tear troughs, and HA E Touch for periorbital lines. Mean aesthetic improvement in tear troughs was 1.5-2 grades for both products at each post-baseline visit, and results of the clinical evaluation were confirmed by results of 3-D volume analysis. Improvements of periorbital lines in both aesthetic outcomes and wrinkle severity were around 1.5 grades at week 3, and close to 1 grade at month 6. The majority of subjects were satisfied or very satisfied with their aesthetic outcome. Treatments of both indications were safe and well-tolerated, with only
mild and transient injection site reactions reported. CONCLUSIONS: This HA E filler range is suitable for rejuvenation of the periorbital region, which leads to safe results, long-lasting efficacy and high levels of patient satisfaction.


BACKGROUND: Demand for minimally invasive cosmetic procedures have led to an increased market of available products for facial rejuvenation. OBJECTIVE: To characterize trends in the usage of aesthetic products, specifically the use of botulinum toxins and dermal fillers, by United States physicians. METHODS: Data from the National Ambulatory Medical Care Survey was analyzed from 1993 to 2010 to evaluate the use of dermal fillers and neurotoxins in the United States outpatient setting. The types of physician specialties administering these products and their preferences in products were characterized. RESULTS: There were an estimated 100,000 annual cosmetic visits at which a dermal filler was administered from 1993 to 2010. From 2002 to 2010, there were 140,000 annual cosmetic visits for a dermal filler and 440,000 visits for a neurotoxin. While collagen was the most common filler used over the entire study period, its use declined eight percent annually. Hyaluronic acid fillers were preferred from 2002 to 2010, followed by calcium hydroxylapatite filler, representing 50 percent and 16.1 percent of visits, respectively. The leading neurotoxin was onabotulinumtoxin A, used at 87.1 percent of visits. Dermatologists were the leading specialty for the cosmetic use of both dermal fillers and neurotoxins. CONCLUSION: Providers' preference for cosmetic products appears to be influenced by their familiarity with them, with products that first came to market, such as the neurotoxin onabotulinumtoxin A and the hyaluronic acid fillers being used most frequently from 2002 to 2010.


AIM: Ha based dermal fillers in recent years aroused big interest in the area of cosmetic surgery for the rejuvenation of the dermis. There is not a ideal dermal filler (DF) for all applications and in commerce there are many types of DF that differ for their chemical-physical properties. So the aim of this paper is to correlate the rheological and physical properties of different DF to their clinical effectiveness. MATERIALS AND METHODS: In this frame the samples have been subjected to oscillation dynamic rheological and steady shear measurements. RESULTS: Our results demonstrate that the viscoelastic properties of different DF varie strongly also considering fillers of the same family. Furthermore it was found that the materials physical properties influence significantly the performance of dermal filler. In particular the clinical data appear to correlate with the concentration of the polymer and with the product between the concentration and the percent elasticity, so these should be crucial parameters for the clinical performance of DF. CONCLUSION: So rheological data can be a tool to have an indication on the efficacy and longevity of DF but it has to be considered that production technology, in-vivo-conditions, injector skills and experience influence them also significantly.


Full lips have always been associated with youth and beauty. Because of this, lip enhancement is one of the most frequently requested procedures in a cosmetic practice. For novice injectors, we recommend hyaluronic acid (HA) as the filler of choice. There is no skin test required; it is an easily obtainable, "off-the-shelf" product that is natural feeling when
skillfully implanted in the soft tissues. Hyaluronic acid is easily reversible with hyaluronidase and, therefore, has an excellent safety profile. While Restylane(R) is the only FDA-approved HA filler with a specific indication for lip augmentation, one can use the following HA products off-label: Juvederm(R) Ultra, Juvederm Ultra Plus, Juvederm Ultra XC, Juvederm Ultra PLUS XC, Restylane-L(R), Perlane(R), Perlane-L(R), and Belotero(R). We present our six steps to achieve aesthetically pleasing augmented lips. While there is no single prescription for a "perfect" lip, nor a "one size fits all" approach for lip augmentation, these 6 steps can be used as a basic template for achieving a natural look. For more comprehensive, global perioral rejuvenation, our 6-step technique can be combined with the injection of neuromodulating agents and fractional laser skin resurfacing during the same treatment session.


A new range of hyaluronic acid (HA) dermal fillers has been designed using Optimal Balance Technology, which centers around three main parameters: the degree of cross-linking, the size of gel calibration and the HA concentration. The five different products in the range (HA E Touch, HA E Classic, HA E Lips, HA E Deep and HA E Volume) have the same concentration of HA (20 mg/mL) and various degrees of cross-linking and gel calibration, in order to have distinctive physical properties adapted to their specific indications. HA E Classic, HA E Deep, HA E Lips and HA E Volume are available in two different formulations either with or without lidocaine. The efficacy, safety and patient satisfaction of the HA E range in various indications have been assessed in several classical studies. In this study, the rheological measurements of HA E Deep being the firmest gel within the range. Addition of lidocaine did not change the rheological properties of the HA E fillers. HA E fillers have three different degrees of gel calibration, with HA E Touch, HA E Classic and HA E Lips having the same smallest gel calibration and HA E Volume having the largest gel calibration within the range. Injection of all HA E fillers was smooth, regular, and required low extrusion force when using the Ultra Thin Wall (UTW)needle provided for each product. In summary, the HA E fillers have distinctive physical properties in terms of gel firmness and gel calibration, which were designed to adapt to their specific indications.


Many dermal fillers have been used for reducing facial skin lines and for providing lip augmentation, and hyaluronic acid (HA) is one of the most widely used agents. One of the main commercial forms of HA is Restylane (Q Med, Sweden) produced by microbiological engineering techniques. Although HA is non-immunogenic, hypersensitivity and Granulomatous foreign body reactions have been reported. Herein, we report three female patients (average age 56 years) who presented with firm nodular lesions of the lip and a history of injection with HA (Restylane, Q Med, Sweden). Histopathologically, all cases showed pools of amorphous hematoxyphilic material surrounded by bands of densely collagenized connective tissue with no inflammation or foreign body reaction. Histochemical stains confirmed the presence of acid mucopolysaccharides such as hyaluronic acid. We conclude HA (Restylane, Q Med, Sweden) is an inert filler that may persist at an injection site, resulting in a tumor-like nodule.
INTRODUCTION: Innovation in technology has resulted in the emergence of better, longer-lasting hyaluronic acid implants with fewer side effects. The new dermal implant Uma Jeunesse(R) was compared to Juvederm(R) in this split-face study. METHODS: Uma Jeunesse(R) is crosslinked with butanediol diglycidyl ether (BDDE) using a new crosslinking technology. Uma Jeunesse(R) and Juvederm(R) Ultra 3 were injected in a split-face study on 17 healthy volunteers, whose ages ranged from 33-58 years. There were 14 women and three men with medium to deep nasolabial folds. All subjects randomly received either Uma Jeunesse(R) or Juvederm(R)) Ultra 3 on one half of their face. Patients were followed up for 9 months. RESULTS: Juvederm(R) was easier to inject with lesser injection pain because of lidocaine, but late postinjection pain was much less with Uma Jeunesse(R) as compared to Juvederm(R). Overall rate of early and late complications as well as adverse events was lower with Uma Jeunesse(R) than Juvederm(R)) . After 9 months of follow-up, Uma Jeunesse(R) lasted in tissues for longer as compared to Juvederm(R)) even in patients injected for the first time (P<0.0001). Patient acceptability rate of Uma Jeunesse(R) was also much higher. Perception of pain during injection was lesser with Juvederm(R) probably because of the presence of lidocaine. CONCLUSION: The new dermal implant Uma Jeunesse(R) is a safe and patient-friendly product which resides in the tissues for longer with maintenance of aesthetic effect over and beyond 6 months, reaching 9 months in over 80% of patients, and Juvederm(R) injection is less painful.

The use of fillers in esthetic rejuvenation or reshaping has been well established and is one of toughest techniques for beginners due to segmental attachments and proximity to important anatomical structures in the infraorbital area making it difficult to achieve smooth esthetic results. To make filling easy, smooth, and repeatable, anatomical points were marked through specific surface measurements. Patients were injected with 0.5-1 mL of hyaluronic acid filler using the identified anatomical point. All patients treated have achieved restoration of the ogee curve with no bruising and minimal downtime with results lasting for 12-36 months. The results of the study suggest the use of single repeatable injection at the crucial point and if required at multiple identified anatomical points along the ligamental attachment to satisfy the esthetic outcome of the patient. Injection of filler at infraorbital points could instantly lift the face up, elevating the point of shadow and shifting the point of highest light reflection to the ideal malar point.

BACKGROUND: Penis enlargement is increasingly in demand. Methods for penis enlargement can be classified into surgical, nonsurgical (filling), and mechanical. Each method has shown only relatively successful results. A new formulation of injectable, stabilized, hyaluronic acid (HA)-based, nonanimal gel is available that may have applications for this use. OBJECTIVES: The authors propose a new technique for emicircumferential injection filling of the penis and assess the safety and efficacy of this procedure compared with lipofilling. METHODS: The authors retrospectively reviewed the charts of 83 patients who underwent penis enlargement with either their HA-injection technique or lipofilling between December 2007 and July 2011. Safety, efficacy, and patient satisfaction were assessed. RESULTS: The circumferential enlargement obtained from both techniques ranged from 3.2 to 4.5 cm, with
a decrement during erection. In all patients, the increase in penis length ranged from 1.8 to 3.6 cm. No complications were seen in patients treated with HA, whereas 8 patients treated with lipofilling developed granuloma, and another experienced fat necrosis. The vast majority (n = 72) of patients reported being "very satisfied" with the results. CONCLUSIONS: The ideal technique for penis enlargement should be nonsurgical, with a satisfactory and predictable result, a low rate of complications, and long-term stability. Emicircumferential enlargement with HA filler meets these requirements. However, results have been durable but not definitive, and repeated treatment (with associated costs) is necessary.


BACKGROUND: There have been few systematic investigations of the effectiveness, safety and tolerability of aesthetic lip augmentation using hyaluronic acid (HA) fillers. OBJECTIVES: Evaluate the effectiveness of small gel particle hyaluronic acid filler (Restylane Injectable Gel [SGP-HA]; Medicis Aesthetics Inc., Scottsdale, AZ) in lip augmentation using the Medicis Lip Fullness Scale (MLFS). Assess subjective improvement in lip appearance using the Global Aesthetic Improvement Scale (GAIS). PATIENTS, MATERIALS AND METHODS: Investigators treated 21 adults. The primary efficacy endpoint was an increase in lip fullness at least one grade on MLFS at eight weeks post-treatment. Adverse events were reported using patient diaries. RESULTS: Sixteen of 18 evaluable subjects (89%) had an improvement at least one grade on MLFS in both lips. MLFS and GAIS scores were consistent, suggesting clinically significant aesthetic improvement. Adverse effects were transient and mostly mild to moderate in severity. CONCLUSION: Lip augmentation with SGP-HA was well tolerated and resulted in clinically meaningful increases in lip fullness.


INTRODUCTION: Soft tissue augmentation by hyaluronic acid filler injections has become the most commonly done cosmetic procedure in the last 10 years. These are now being widely used for improvement of the nasolabial folds. The present study was done to evaluate the patient satisfaction after these injections. MATERIALS AND METHODS: The study was conducted on 10 consenting patients. Hyaluronic acid filler (22.5 ml cross linked), 1 ml on each groove was injected under an infraorbital block. Patient satisfaction was evaluated at 0, 14, 30, and 180 days. Photographic record was maintained. Any side effects experienced by the patients were recorded. RESULTS: All the patients were satisfied immediately after the procedure. More than 50% were not happy at 14 days. Majority of the patients were happy at 30 days and the satisfaction was maintained at 6 months. CONCLUSION: Fillers are a very safe and effective modality for improving the nasolabial fold. This could prove to be a very useful tool in dental practice. Setting the patient expectations before the procedure is performed can lead to satisfied and happy patients.


BACKGROUND: Hyaluronic acid (HA) gels are commonly injected into the skin to lift rhytides and to improve facial appearance. The different processes used in their manufacture and
formulation yield products with unique physical characteristics that play an important role in predicting their clinical performance. OBJECTIVE: The following rheologic evaluation was performed to objectively measure the physical characteristics of HA dermal filler products derived from similar bacterial sources and containing the same butanediol diglycidyl ether cross-linker, but formulated using different manufacturing techniques. The objective of this study was to evaluate the physical characteristics of two distinct families of HA products, thereby providing clinicians with a greater understanding of these products' attributes and the ability to optimize their use in the treatment of patients seeking facial rejuvenation.

MATERIALS AND METHODS: The physical properties of commercially-available dermal fillers containing HA were evaluated using rheologic testing methods under clinically-relevant conditions. Additionally, light microscopy was used to assess the particulate nature of each product. RESULTS: The gels tested demonstrated a broad range of elasticity, firmness and viscosity. Light microscopy confirmed the particulate nature of each product and revealed HA particles of varying size and distribution. CONCLUSION: This rheologic evaluation demonstrates that differences exist among the HA products tested including gel elasticity, viscosity, and the range and distribution of gel particle sizes. Understanding the distinct physical characteristics of different HA dermal fillers and how these characteristics may predict their clinical behavior can assist clinicians in achieving the desired results in patients seeking facial rejuvenation.


BACKGROUND: In nonsurgical facial rejuvenation, autologous fat and dermal fillers have become an effective method to achieve symmetry and balance of the midface. Nonsurgical techniques that target the dynamic anatomical relationships existing in the midface can improve rejuvenation outcomes in this commonly augmented region. OBJECTIVES: The authors described techniques for fat compartment and potential space volumization of the midface via a standardized and reproducible technique. They placed emphasis on access to anatomical spaces and compartments within the midface. METHODS: In 11 hemifacial cadavers, hyaluronic acid filler homogenized with red dye was injected via 3 midfacial ports that were anatomically designed to access the superficial fat compartments, deep fat compartments, or traverse the prezygomatic space. Specimens were dissected in a layered fashion to analyze relationships between the injected filler and midfacial anatomy. We have described 4 site-specific procedural techniques and created a video containing anatomical renderings of each targeted viaduct accompanied by technique demonstrations. RESULTS: We found that Beut techniques 1 through 4 can be performed through 3 midfacial viaducts. Port placement 1.5 cm inferolateral to the alar base in the nasolabial crease created a medial midface viaduct, suitable for access to the deep medial cheek fat, medial superficial fat compartment, premaxillary space, and adjacent superior nasolabial cheek compartment. Port placement within the nasojugal groove provided a middle midface viaduct to access the middle superficial fat compartment and medial suborbicularis oculi fat (SOOF). Port placement 1.5 cm inferolateral to the lateral canthus created a lateral midface viaduct to approach the pre-periosteal fat, prezygomatic space, lateral SOOF, and infraorbital fat compartment. CONCLUSIONS: Our findings indicate that anterior and lateral cheek projection, V-deformity correction, rhytid softening, and tear trough effacement can be achieved through the midfacial viaducts. Systematic assessment and site-specific nonsurgical rejuvenation of the midface may lead to increased safety, accuracy, and technique reproducibility in this commonly injected region.

Objective: The aging nose presents as a drooping nasal tip secondary to atrophy of the underlying bony support with a relatively prominent dorsal hump. We hypothesized that low nasal tip projection in the Asian nose may be secondary to the retropositioned anterior nasal spine (ANS) as well. Therefore, we investigated how filler injection between the medial crura and the retropositioned ANS affects the nasal shape. Methods: Local anesthetic was injected on the ANS for analgesia and simulation for the following augmentation. To augment the retropositioned ANS, approximately 0.3 to 0.5 mL of injectable hyaluronic acid was injected between the footplates of the medial crura and the ANS. We evaluated 30 patients (29 women and 1 man) ranging from 21 to 71 years of age (36.5 +/- 7.2 years) before and after the augmentation. Results: Augmentation of the retropositioned ANS significantly decreased nasal width, but increased alar length, nasal tip protrusion, inclination of the nostril axis from the horizontal, and columellolabial angle (P < .0001). Conclusion: Our findings indicate that augmentation of the ANS elongates the pseudocolumella, lifts the medial crura, and affects the whole nasal shape. Consequently, augmentation of the retropositioned ANS with an injectable filler westernized the Asian nose. This temporary method may be useful to predict the results of ANS augmentation with other permanent fillers and to make a space to be filled with them.


**CONTEXT:** Facial fillers have revolutionized the field of cosmetic facial rejuvenation as it has become the prime sought-after rejuvenation procedure offering youthful, 3-dimensional look with minimal invasiveness. Fillers are expensive and need to be redone periodically hence a sound understanding of structural basis on which they are laid is important in reducing the quantity of filler required in each sitting as well as increasing the longevity of results. **AIM:** The aim of the following study is to analyse a novel method of facial filling "The pillars pyramids and tie beams (PPT)" technique and its advantages over the conventional methods. **SUBJECTS AND METHODS:** A novel technique of injecting the facial fillers was employed on 67 patients visiting our clinic. These patients were followed-up for a period of 3 years. **RESULTS:** We observed that the amount of filler material required in initial sitting remains the same, however the frequency of touch up visits is decreased and so is the amount of filler material required for follow-up injections. **CONCLUSION:** Facial contour remodelling is being revolutionised by the new filler materials for volume augmentation and no uniform consensus has been reached on the techniques currently used in clinical practice. We advocate this novel PPT technique of facial filling in facial rejuvenation to restore a youthful look as a primary goal.


**BACKGROUND:** Hyaluronic acid (HA) formulations are used for aesthetic applications. Different cross-linking technologies result in HA dermal fillers with specific characteristic visco-elastic properties. **OBJECTIVE:** Bio-integration of three CE-marked HA dermal fillers, a cohesive (monophasic) polydensified, a cohesive (monophasic) monodensified and a non-cohesive (biphasic) filler, was analysed with a follow-up of 114 days after injection. Our aim was to study the tolerability and inflammatory response of these fillers, their patterns of distribution in the dermis, and influence on tissue integrity. **METHODS:** Three HA
formulations were injected intradermally into the iliac crest region in 15 subjects. Tissue samples were analysed after 8 and 114 days by histology and immunohistochemistry, and visualized using optical and transmission electron microscopy. RESULTS: Histological results demonstrated that the tested HA fillers showed specific characteristic bio-integration patterns in the reticular dermis. Observations under the optical and electron microscopes revealed morphological conservation of cutaneous structures. Immunohistochemical results confirmed absence of inflammation, immune response and granuloma. CONCLUSION: The three tested dermal fillers show an excellent tolerability and preservation of the dermal cells and matrix components. Their tissue integration was dependent on their visco-elastic properties. The cohesive polydensified filler showed the most homogeneous integration with an optimal spreading within the reticular dermis, which is achieved by filling even the smallest spaces between collagen bundles and elastin fibrils, while preserving the structural integrity of the latter. Absence of adverse reactions confirms safety of the tested HA dermal fillers.


Non-surgical rejuvenation of the periorbital-cheek complex can be effectively and safely accomplished using a combination of two hyaluronic acid (HA) fillers with distinct viscosities. We present a series of 21 patients with mild to moderate tear trough deformities who were treated with concomitant injection of two dermal fillers (Restylane(R) and Perlane(R)). Procedural technique entailed micro-depot injections of the finer viscosity HA into the sub-muscular plane along the orbital rim followed by manual massage. Secondly, injections of the thicker, more firm HA were placed in the sub-muscular and/or deep dermal spaces in the upper malar and lateral zygomatic areas and in the medial aspect of the temporal fossa. On average 0.5 mL Restylane and 0.5 mL Perlane were used per side. Statistically significant improvement in modified Wrinkle Severity Rating Scale scores was seen at 20 weeks. Overall improvement in modified Global Aesthetic Improvement Scale scores occurred in 20 out of 21 patients. Mean patient satisfaction scores increased by 2 grades relative to baseline. Patients' self-reported overall mean improvement was 2.23, indicating moderate (26% to 50%) to good (51% to 75%) improvement. Side effects were limited to transient bruising and swelling. No patients required dissolution of injectant with hyaluronidase. Overall, this combination filler procedure was found to produce both statistically significant and clinically apparent improvement and was associated with an extremely high degree of patient satisfaction.


BACKGROUND: The effects of hyaluronic acid (HA) injection on tissue collagen anabolism are suggested to be related to the induction of mechanical stress, causing biochemical changes in skin physiology. OBJECTIVES: To ascertain the association between dermal mechanics modulated by a hyaluronic acid-based filler effect and metabolism. METHODS: Sixty females were randomised to receive a 0.5mL injection of HA gel or isotonic sodium chloride (control) in the arm. Skin biopsies were taken at baseline and after 1, 3 and 6 months. Protein and gene expression of procollagen, matrix metalloproteinases (MMP) and MMP tissue inhibitors (TIMP1) were measured blind by ELISA and qPCR, respectively. Injected volumes were measured by high-frequency ultrasound and radiofrequency analysis. Skin layer effects of
Injections were analysed by finite element digital modelling. RESULTS: One month after injection, the filler induced an increase in procollagen (p=0.0016) and TIMP-1 (p=0.0485) levels and relative gene expression of procollagen III and I isoforms compared with the controls. After 3 months, procollagen levels remained greater than in the controls (p=0.0005), whereas procollagen expression and TIMP-1 and MMP content were no longer different. Forty-three percent of the injected filler volume was found at 1 month, 26% after 3 months and 20% after 6 months. LIMITATIONS: The ultrasound imaging technique limited the scope of the investigation and precluded an evaluation of the action of the filler at the hypodermic level. CONCLUSIONS: Integrating both mechanical and biological aspects, our results suggest that mechanical stress generated by cross-linked HA plays a role in dermal cell biochemical response.


BACKGROUND: Volume loss and muscular hyperactivity are two major components of the aging process that contribute to the formation of the folds and wrinkles. Tear trough deformity is one of the most difficult depressions to correct surgically. PURPOSE: The aim of this study was to evaluate the results of ten patients submitted to periorbital filling with hyaluronic acid gel filler. METHODS: Between June and August, 2008, 10 patients have had their tears troughs treated with hyaluronic acid gel filler. The filler was introduced by a serial puncture technique and approximately 0.1 ml was injected at each pass. The filler was placed in the pre-periosteal tissue. Patients photographs before and after the procedure were reviewed to assess the outcomes. RESULTS: The mean volume per side needed to achieve correction was on the right side 0.61 ml (SD=0.25) and on the left side 0.65 ml (SD=0.26). The most common complications were bruising, erythema, local swelling, and pain at the injection site. The effect of treatment lasted up to 12 months. CONCLUSIONS: This pilot study showed that the treatment of tear trough deformity with hyaluronic acid gel filler was feasible, predictable and effective. All patients were very satisfied with their results.


BACKGROUND: Intradermal application of hyaluronic acid (HA) in varying chain length and cross-linking density is used routinely for hydrodynamic volume replacement of the extracellular matrix to reduce the clinical effects of aging. OBJECTIVES: In vitro data show that via receptors of the hyaladherin group hyaluronic acid has additionally direct or indirect effects on cells. In the case of native noncross-linked HA, it has been proved that the proliferative and metabolic activity of cutaneous fibroblasts can be increased. The aim of this study was to investigate whether these effects can be proved also for cross-linked HA and how these effects can be quantified for different preparations. MATERIALS AND METHODS: The effect on proliferative activity in cultures of native cutaneous fibroblasts and keratinocytes was investigated for noncross-linked HA, for noncross-linked HA with added glycerol, for HA that was stabilized in the carboxyl and hydroxyl groups per inner esterification, and for HA that was chemically cross-linked by 1,4-butanediol-diglycidylether, mixed in small particles in a biphasic compound with native HA, each in different concentrations (0.1, 1.0 and 10.0 mg/mL). RESULTS: HA that was stabilized in the carboxyl and hydroxyl groups per inner esterification induces the strongest proliferative effect on both cell types. Native noncross-linked HA and chemically cross-linked HA show a rather modest proliferative effect and on fibroblasts only, whereas noncross-linked HA with added
glycerol in high concentrations provokes a rather antiproliferative effect. CONCLUSIONS: The data show that HA does induce direct effects on cells depending on type and density of the cross-linkage. The practical relevance in terms of a metabolic filler effect needs to be verified in clinical studies.


In midface rejuvenation, hyaluronic acid (HA) fillers are commonly used as a versatile tool to improve appearance and to correct V-deformities and loss of volume. The induction of collagen as a major constituent of extracellular matrix (ECM) has been considered to be a basic effect of the rejuvenation procedure. Although commonly described as "dermal" soft fillers, histologic studies localized HA filler in the subcutaneous adipose tissue. Deep injection whenever possible lead to prolonged efficacy. Since volumizing HA filler induce mechanical stress not only to fibroblasts but adipocytes and deep injection itself causes minor trauma in the subcutaneous adipose tissue we suggest that the activation of adipose tissue-derived mesenchymal stem cells (ADMSC) is responsible for the observed clinical effects. We present a concept of filler action that discusses interactions of HA with adipocytes, ECM fiber network and ADMSC. Such a concept can explain the prolonged efficacy of deep midfacial filler placement and offers a new understanding to tailor HA fillers in the future.


Dermal fillers have been used for decades in soft tissue augmentation. Currently, filler implementation is among the most common minimally invasive procedures for rejuvenation and body sculpturing. There is a broad variety of filler materials and products. Despite immense experience, a number of controversies in this topic exist. Some of these controversies are addressed in this review, for example, who should perform filler injections, the difference between permanent and nonpermanent fillers, the off-label use of liquid silicone, and the role of pain reduction. Implementation of guidelines and restriction of filler use by trained physicians can improve safety for patients.


HA-HMDA hydrogels were developed by direct amide bond formation between the carboxyl groups of hyaluronic acid (HA) and hexamethylenediamine (HMDA) with an optimized carboxyl group modification in the preliminary experiment. However, these HA-HMDA hydrogels transformed into an unstable liquid form after steam sterilization, and were problematic for application to actual dermal filler. A new method to overcome the problem of the previously developed HA-HMDA hydrogels is to prepare them by adjusting the pH in this study. Not only are these improved HA-HMDA hydrogels prepared with lower amounts of cross-linking and activation agents compared to the previously developed hydrogels, but they also maintain a stable form after steam sterilization. These improved HA-HMDA hydrogels showed higher viscoelasticity and longer lasting effects than the previous ones, despite the fact that the amount of the HMDA used as a cross-linking agent as well as 1-ethyl-3-[3-(dimethylamino)propyl]carbodiimide (EDC) and 1-hydroxybenzotriazole monohydrated (HOBt) used as activation agents were substantially reduced. According to an in vivo test using a wrinkled mouse model, the improved HA-HMDA hydrogels exhibited significantly improved tissue augmentation effects compared to a positive control of Restylane, which is widely used for the tissue augmentation throughout the world.
Furthermore, histological analysis revealed excellent biocompatibility and safety of the improved synthesized HA-HMDA hydrogels.


BACKGROUND: Soft-tissue augmentation with fillers is an aesthetic procedure for restoring age-related volume loss. OBJECTIVE: To compare neocollagenesis and elastin production stimulated by Radiesse(R) (calcium hydroxylapatite; CaHA, Merz Pharmaceuticals GmbH) and a hyaluronic acid-based filler (HA; Juvederm(R) VOLUMA(R)). METHODS: Twenty-four women, aged 35-45, participated in this split-face, comparative study. Punch biopsies were taken 4 and 9 months after supraperiostal injection of each filler into the ipsilateral or contralateral postauricular area. Samples were analyzed for collagens type I and III, elastin, Ki-67, and inflammatory and angiogenic markers. RESULTS: At month 4, collagen type III was greater with CaHA vs HA (P=0.0052). By month 9, type I staining was higher with CaHA vs HA (P=0.0135), whereas type III was lower with CaHA than HA (P=0.0019). Staining for elastin, Ki-67 and angiogenesis was greatest with CaHA at both timepoints. Inflammatory markers increased most with HA treatment. CONCLUSIONS: CaHA resulted in more active, physiologic remodeling of the extracellular matrix than HA by stimulating a two-step process whereby collagen type I gradually replaced type III. Increased elastin stimulated by CaHA also indicates active remodeling. The results of this study suggest that, in the first 9 months after treatment, by reconstituting tissue homeostasis without inducing inflammation suggests CaHA has more desirable characteristics for a dermal filler than HA.