Abstract

The use of non-invasive techniques for facial rejuvenation is gaining popularity worldwide. There are many substances both natural and synthetic, which may be used to restore or enhance appearance and hyaluronic acid is evolving as an ideal option. Its non-allergenic state makes it a favourable and easily utilised material for injection. Hyaluronic acid has numerous beneficial properties when injected into the skin, including: hydration, space filling, lubrication, shock absorption, modulation of inflammatory cells and scavenging of free radicals. These properties enable cosmetic surgeons to use hyaluronic acid to rejuvenate the face effectively, safely and with predictable aesthetic results. There are a plethora of commercially available preparations of hyaluronic acid, each with its own clinical indications and advantages. There are also several methods of injective hyaluronic acid fillers, each depending on the area, type and nature of the defect. This chapter provides an overview of the key principles of hyaluronic acid and highlights the most important clinical principles in the use of this molecule to rejuvenate the face.

Introduction

The popularity of non-invasive cosmetic procedures for facial rejuvenation has dramatically increased in recent years. In the United States, it is estimated that one in four cosmetic procedures now involves the use of soft-tissue augmentation with injectable fillers. In 2008, nearly 1.6 million procedures using soft-tissue fillers were performed in the United States, a 144 percent increase over the 650,000 performed in 2000 [1]. According to the Procedure Survey conducted by the American Society for Dermatologic Surgery (ASDS) in 2007, soft tissue filler injections ranked among the top 5 procedures, with soft tissue augmentation procedures showing a 130 per cent increase between 2005 and 2007 [2]. A more recent survey conducted by the American Society for Aesthetic Plastic Surgery (ASAPS), concluded that the most commonly performed non-surgical procedure in the United States was the injection of botulinum toxin-type A. The injection of hyaluronic acid (HA) fillers ranked fifth [3]. In 2008, more than two-thirds of soft-tissue augmentation procedures used hyaluronic acid-based fillers, making their use the third most performed cosmetic procedure in the United States [1].

For many years, surgical techniques dominated the facial rejuvenation process. However,
in recent times practice has been moving consistently towards non-invasive cosmetic procedures thanks to both clinician choice and patient request. Indeed, non-surgical cosmetic procedures now account for the majority of all cosmetic procedures performed in the United States and in Europe. The increasing availability of such procedures and their convenience as a result of minimal ‘downtime’ are propelling this trend [4,5]. The use of injectable fillers for the restoration of facial volume can significantly help to rebalance facial disproportion and, by reducing rhytides and volume loss, can produce a younger and healthier appearance. Facial augmentation using soft tissue biodegradable fillers is gaining popularity worldwide as such products offer more vivid results than facial creams and chemical peels, as well as being less invasive and more subtle than facial surgery [4,5].

The first surgical soft tissue augmentation was a fat transplantation performed by Neuber in 1893 [6]. Since this first procedure, paraffin was used but was found to be associated with formation of extensive granuloma and was subsequently abandoned [7]. Pure silicone was also tried but this similarly produced severe facial distortion and latent granuloma formation [8]. Popularisation of the use of dermal bulking agents started with the introduction of the injectable bovine collagen in the early 1980s. As some patients were allergic to these products, test injections became mandatory three weeks prior to the main procedure. Recent alternative agents include acellular human dermis (Dermalogen®) and cultured fibroblasts (Isologen®); these seem to be associated with less immunological intolerance and a longer duration of action. Autologous fat, another important part of the filler armamentarium has been used extensively. However, the newer generations of fillers are becoming more favourable because the aesthetic results and duration of fat autotransplantation may be variable and difficult to manage for clinicians and patients alike. Reports on fat-grafting technique are still anecdotal and clear evidence on the ‘effective take’ of fat is lacking [8].

Hyaluronic Acid (Hyaluronan; HA) is a naturally occurring linear polysaccharide and is a polymer of dimeric N-acetyl glucosamine and glucuronic acid arranged in macromolecular chains [9,10]. Hyaluronic acid is naturally present in the skin as part of the extracellular matrix, is a constituent of joint fluid, the vitreous of the eye, the nucleus of intervertebral discs and the umbilical cord. Its chemical structure is well preserved across a number of species from Ascaris slime to mammals. The structure of HA is identical in all vertebrates except for subtle differences in protein and nucleic acid contaminants. The substance demonstrates no antigenic properties in any bodily tissue of any species and thus, presents a low potential for allergic or immunogenic reactions. Due to its viscoelastic properties it acts as a ground substance of the dermis. Its functions include that of space filling, lubrication and shock absorption, alongside modulation of inflammatory cells and scavenging of free radicals [11]. HA is extremely hydrophilic: hydrogen bonding between adjacent carboxyl and N-acetyl groups to the extent that it can retain up to 1000 times its weight in water, meaning that one gram of HA can bind up to 6 litres of water [12]. In the skin and in the connective tissue, the levels of HA naturally decrease with age, resulting in dermal dehydration, reduced elasticity and movement with the formation of rhytides (wrinkles), representing the rationale for the use of HA as a dermal filler [13].

HA was first isolated from bovine vitreous by Meyer and Palmer in 1934 [14]. Mammalian HA is principally synthesised by fibroblasts with the enzyme hyalurcan synthetase, which resides on the cell surface. Formed HA is then extruded via the cell membrane into the extra-cellular space. Commercially available preparations of Hyaluronic acid are usually produced through extraction from rooster combs or by recombinant production from different strains of Streptococcus bacterium (e.g., Streptococcus zooepidemicus), each with unique rheological properties [15]. Endogenous HA has a half-life of approximately 24 hours, before it is enzymatically broken down by hyaluronidase and free radicals, followed by hepatic degradation to water and carbon dioxide [16]. The naturally occurring breakdown of HA by hyaluronidase represents an important feature of the HA fillers, as well as a major advantage over the collagen fillers, because HA which is injected excessively, in a superficial plane or inaccurately can easily be treated by intralesional injection of
hylauronidase. Commercially available preparations of hyaluronidases are available and principally used to treat over-injection of hyaluronic acid [17].

Research and development in Hyaluronic Acid (HA) has crossed many areas of biomedicine. The therapeutic utilisation of hyaluronic acid started in ophthalmic surgery and progressed to orthopaedic surgery, as an adjuvant lubricant for joints in patients with osteoarthritis [18]. The use of HA was brought to the attention of plastic surgeons via tissue engineering routes. It was extensively researched with a view to the production of dermal regeneration templates for reconstructive surgery. There are a considerable number of ongoing research projects dedicated to HA, with significant international collaborations.

The duration of the cosmetic effect of injected HA is determined primarily by its susceptibility to enzymatic degradation by the fibroblasts, resulting in the formation of shorter HA chains, which are then ingested by macrophages and keratinocytes. Supplementation of HA injection with oral antioxidants theoretically increases the duration of HA fillers but this has not been proven. In order to reduce its solubility and produce a more viscous and stable compound that can remain in the skin for longer, HA has been progressively bioengineered (principally through alcohol esterification) to form more stable polymers with higher resistance to enzymatic degradation. Bioengineered HA retains its biocompatibility but allows for a prolonged dissolution rate and an increased half-life [5]. Furthermore, the degree of esterification and cross-linking can be varied to alter its viscosity and thus, expands the range of cosmetic uses. The viscoelastic property of HA is determined by the length of the molecular chain, the concentration, the cross linking and the particle size.

Commercially available HA fillers are differentiated by many features, including their particle size, type of crosslinking agent, degree of crosslinking, percentage of cross-linked HA and the amount of free (un-modified) HA present. All these physical and chemical properties will influence the clinical characteristics of each type of HA filler and impact on clinical indications, ease of injection, degree of tissue filling, longevity, post-treatment appearance and side effects. HA have many natural advantages over other commercially available soft-tissue fillers, including: biocompatibility, non-antigenicity/immunogenicity, non-toxicity, ease in administration, low cost and reversibility. Further to this, it has a good safety profile with predictable results and requires minimal recovery time.

**Indications**

The hallmark of the aging face is the loss of subcutaneous volume. This is commonly associated with increase in facial vasculature, alterations in pigmentation, increases in number and depth of lines and rhytides of the skin and decreased tissue elasticity and hydration. Histologically, this is associated with a thinning of the epidermis and dermal atrophy with loss of elastic tissues and dermal collagen. Aging adversely affects the skin by reducing viscoelasticity and dermal volume, resulting in the formation of rhytides. HA dermal fillers have a role in addressing these deficits and may be used alone, or in combination with other nonsurgical products such as botulinum toxin or operative interventions [5,19]. The treatment for age related facial changes can be multiple, encompassing skin care products, energy based therapies (lasers, light sources, radiofrequency, etc.), fillers and toxins. HA fillers play a major role in the correction of changes associated with aging, especially those of the mid and lower half of the face, including cheeks, peri-orbital regions, naso-labial folds, vertical lip lines, marionette lines around the mouth and lips as well as the lips themselves. The concept of the ideal filler has been debated for years. A filler should be easy to inject, long lasting, well tolerated and without any adverse reaction. To date, the HA fillers are the only injectable products that fulfil the majority of these criteria. The indications for hyaluronic acid injection are summarised in Box 1.
- Loss of vermilion bulk and projection (pout)
- Loss of lip fullness
- Loss of lip eversion
- Volume replacement of marionette line
- Volume replacement of the deep mental groove
- Volume replacement of the anterior jowl line
- Blunting of nasolabial folds
- Malar atrophy

**Box 1: Indications for hyaluronic acid injection.**

The primary indications for HA fillers are volume enhancement for photo-aging rhytides, deep nasolabial folds, lip rhytides, marionette lines, lip filling and contouring, chin and cheek augmentation and treatment of tear trough lines. Generally HA is not ideal for superficial rhytides, instead it is more suited for deep folds and volume augmentation. However, smaller molecular preparations have been shown to have good effect with superficial rhytides. After a full pre-treatment assessment and pre-treatment photographs, the correct product should be selected. The greater the viscosity of the gel, the better its ability to resist shear and exert a deformational force on surrounding tissue to correct a defect. The pay-off for such qualities is palpability and firmness to touch. Superficial injections have, as expected, a higher risk of visibility. This has led to various HA products being used for different areas of the face due to difference in residence time, persistence, injectability and the need for local anesthetic. The differences between the various HA agents are due to the source derivation (animal vs bacteria), cross-linking (the method used to create cross linking and the degree of cross linking present), the concentration of HA, the amount of free HA (non-cross-linked) and the particle size and uniformity of structure [20]. Different manufacturing processes result in varying firmness of the gel and so different amounts of swelling caused by the accumulation of water. As a result of this variability, a wide range of HA fillers are now commercially available and particular fillers have a better theoretical application to different parts of the face (Table 1). For example, a viscous filler with a larger ‘granule’ size would be best suitable for injecting into the cheeks more than a lip because of its risk of palpability (Figure 1).

<table>
<thead>
<tr>
<th>Preparations</th>
<th>Company</th>
<th>Indications</th>
<th>Duration of Effect</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hylaform®/Hylaform Plus®</td>
<td>Genzyme</td>
<td>Moderate to severe facial lines and rhytides</td>
<td>3-4 months</td>
<td>Good safety profile No skin test necessary - can be used at the initial consultation</td>
<td>Results may be short-lived, lasting approximately 3 months. Cannot be used in patients with hypersensitivity to avian proteins (eggs). With Hylaform plus, superficial injection may lead to skin discoloration</td>
</tr>
<tr>
<td>Restylane®/Restylane-L®</td>
<td>Medicis Aesthetics</td>
<td>Moderate to severe facial rhytides and folds, nasolabial folds or parentheses lines Lip augmentation</td>
<td>6-12 months</td>
<td>Good safety profile Predictable results No skin test necessary - can be used at the initial consultation Relatively long duration of effect Easily injected through small-gauge needles Restylane-L contains lidocaine local anaesthetic</td>
<td>Rare immunologic reactions Higher incidence of bruising, pain, and post-procedure swelling Relatively expensive</td>
</tr>
<tr>
<td>Product</td>
<td>Company</td>
<td>Description</td>
<td>Duration</td>
<td>Safety Features</td>
<td>Additional Notes</td>
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<tr>
<td>Perlane®/Perlane-L®</td>
<td>Medicis Aesthetics</td>
<td>Moderate to severe facial rhytides and folds, nasolabial folds or parentheses lines</td>
<td>6-12 months</td>
<td>Good safety profile&lt;br&gt;Predictable results&lt;br&gt;No skin test necessary - can be used at the initial consultation&lt;br&gt;Relatively long duration of effect&lt;br&gt;Perlane-L contains lidocaine local anaesthetic</td>
<td>Rare immunologic reactions&lt;br&gt;Higher incidence of bruising, pain, and post-procedure swelling&lt;br&gt;Relatively expensive</td>
</tr>
<tr>
<td>JUVÉDERM® Ultra</td>
<td>Allergan, Inc</td>
<td>Juvéderm® ULTRA 2 for superficial facial lines around the lips, corners of the eyes&lt;br&gt;Juvéderm® ULTRA 3 for nasolabial folds and lip augmentation&lt;br&gt;Juvéderm® ULTRA 4 for deep facial folds and rhytides&lt;br&gt;Juvéderm® ULTRA SMILE for lip augmentation and fine perioral rhytides&lt;br&gt;Juvéderm® HYDRATE restores hydration to the face, neck, décolletage and hands</td>
<td>3-12 months</td>
<td>Good safety profile&lt;br&gt;Predictable results&lt;br&gt;No skin test necessary - can be used at the initial consultation&lt;br&gt;Lidocaine 0,2% (no in Juvederm® Hydrate)</td>
<td>Only short term complication results are available&lt;br&gt;Rare immunologic reactions</td>
</tr>
<tr>
<td>JUVEDERM® Vycross™ technology</td>
<td>Allergan, Inc</td>
<td>Juvéderm® VOLUMA® for volume restoration of the cheeks, cheekbones, and chin&lt;br&gt;Juvéderm® VOLIFT for severe facial wrinkles and folds&lt;br&gt;Juvéderm® VOLBELLA for the lip area and fine lines</td>
<td>Up to 18 months</td>
<td>Lidocaine 0,2%&lt;br&gt;Good safety profile&lt;br&gt;Predictable results</td>
<td>No skin test necessary - can be used at the initial consultation</td>
</tr>
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**Table 1:** Hyaluronic Acid Fillers [13,23,24].

**Figure 1:** Granulomas following injection of thick viscous filler in the upper lip.
A new generation of dermal filler is now available and it is characterized of new technology: Vycross™ (Allergan, Inc, Irvine, CA). Its patented Vycross™ technology incorporates short chain HA together with long chain HA to provide more efficient crosslinking than other dermal fillers [21].

In Vycross™ dermal fillers the more efficient crosslinking results as a longer product duration and the elastic modulus (G' or gel hardness) of ~160 Pa is lower than that of other fillers, [22] this provides a smoother and softer gel that is easy to inject.

Conversely, a softer product with a smaller particulate size would not give the volume enhancement needed in the deep tissue planes. It is for this reason that practitioners should be familiar with the range of products so that bespoke treatment may be offered to the patients, tailored to individual need. See Box 2 for a summary of some of the factors involved when choosing an appropriate HA filler.

- Concentration of hyaluronic acid
- Type and degree of cross-linking (solubility)
- Ratio of cross-linked to non-cross-linked molecules
- G prime (stiffness)
- Duration of action
- Design and size of the syringe
- Presence of lidocaine
- Cost

Box 2: Factors to consider when choosing a hyaluronic acid agent.

Pre-Treatment Evaluation

Pre-treatment evaluation requires a comprehensive knowledge of the filler materials available and the potential treatment effects, an understanding of the aetiology of rhytides and an appreciation for patient expectations. Fine, superficial rhytides better respond to therapy at the intradermal level. Deep, substantial rhytides typically have a subcutaneous or muscular component and are better corrected through subcutaneous filling. Often a rhytide will have both a superficial and deep component, such as the naso-labial fold, and both of these components need to be addressed to obtain optimal results [5]. The identification of patients’ expectations is a key element and should include prior experience with fillers, their understanding of the longevity of the treatment and the necessary time for recovery. Patients of all ages are selecting soft tissue augmentation, either as a precursor to or a substitute for cosmetic facial surgery, but there is a trend toward the use of injectable devices in younger patients (aged 35-50 years) for facial rejuvenation.

Each patient has a different treatment needs, ranging from correction of fine lines and rhytides in younger patients to primary volume restoration in older patients and their needs must guide the treatment approach. Practitioners should aim to advise patients in the selection of the most appropriate rejuvenating treatment based on a variety of factors, specifically, patient age, motivating factors, timing, cosmetic area to be addressed and desired outcome. A series of steps need to be determined to formulate the most appropriate approach for volume restoration with injectable devices for satisfying patient treatment expectations.

Cosmetic medicine has developed rapidly over the years as a better understanding of the process of facial aging has led to a more targeted and efficient treatment approach. Facial aging is now established to be due to a number of different features. These include the involutional loss of dermis, resulting in loss of skin tone, gravitational changes due to loss of elasticity, remodelling of bony and cartilaginous structures, and sun damage causing photo-aging. More recently, the concept of volumetric loss in the face has further added...
to our understanding; fatty volume either migrates or is lost from the face. This occurs in predictable areas and a number of treatments now specifically address this issue either alone, or in combination with traditional rejuvenation techniques. Some of these factors are preventable - most notably the sun damage to the skin that alters dermal composition - but others are less so; gravitational changes are dependent on the environment and volumetric loss is somewhat unavoidable and largely determined by genetic variables. The overall effect of these processes gives us the features of the aging face; flattening of the forehead, brow, glabella and temporal concavity in the upper face, descent of the nasal tip and flattening of the cheek in the mid face and recession of chin, appearance of jowls, loss of lip fullness, and descent of oral commissures in the lower face. In addition the aging process is manifested in the form of rhytides throughout the face. Surgical procedures address laxity within the tissues and reposition the soft tissue of the face, on a ‘macro’ scale. Additional ‘micro’ adjustment can be made with fat transfer at the time of surgery, the so-called ‘volumetric’ facelift. Independent surgical fat transfer is still useful but does involve a hospital or clinic stay, and is quite clearly an invasive procedure. However, surgical fat transfer does not address the finest lines in the face. Rhytides caused by active muscle contraction can be ameliorated by the use of botulinum toxin. For established lines there is anecdotal evidence that repeated use of this modality may allow the reversal of superficial lines, although formalised studies into this are limited. There is also a trend amongst the younger population to undergo botulinum toxin treatments in order to prevent the formation of rhytides, particularly in the forehead area. That said, most treatments for established rhytides are aimed at volumetric replacement of soft tissue: dermal and/or deep tissue plane augmentation. As previously outlined, the ideal filler substance should be non-allergenic, non-carcinogenic, with minimal adverse sequelae, no associated migration and minimal inflammatory response. It should be reproducible, durable, simple and painless to administer, with minimal recovery time, user-friendly, easily stored and large amounts should be readily available. It should preferably have a long-lasting effect with slow degradation in the body.

There are advantages to temporary (rather than permanent) fillers; if the result is not to the patients liking, then it will be reversed over a period of time. Permanent fillers, while an attractive proposition, have two obvious drawbacks; misplacement of filler usually necessitates surgical removal, and the filler placement cannot subsequently be adjusted to account for ongoing age-related changes in the face. Finally, physicians must gain informed consent by counselling patients regarding the associated risks and benefits of injectable substance therapy [24].

Pearls

The injection of HA is generally carried out in the outpatient clinic setting, with the patient in an upright position for gravitational rhytides to be visible, with the head supported on a headrest to avoid sudden movements. Patients on anti-platelets or anti-coagulants are advised regarding the higher risk of bleeding and advised to stop such agents prior to procedures.

Anesthesia, where applied, is usually in the form of topical creams but injection local anaesthetic or nerve blocks may be required, especially for lip procedures which can otherwise be quite painful.

Using a 27-30 gauge needle, the agent is injected into the middle to deep dermis, except in the red lips where it is more commonly injected intramuscularly rather than intradermally. Larger molecular HA will require larger gauge needles for injection. If injected subcutaneously the material is wasted as its bioavailability is very short due to quicker enzymatic degradation and the effect may be limited. The senior authors’ current practice involves using a layering technique where heavier gels are injected into the deeper layers
and lighter gels into the superficial layers. Constant movement of the needle is important in producing an even distribution of product, and avoiding intravascular injection [25]. Injection above the periosteum is favourable as it produces re-inflation of the natural fat pads, in the brow, malar, buccal, and mental areas. After injection, the area should be massaged by the practitioner (not the patient) to smooth out any irregularities. Care should be taken to avoid migration of the filler into an undesirable location. Ice packs may be used to decrease swelling and pain and the patient is advised to minimize movement of the injected area for the next couple of days, in order to reduce the incidence of bruising. Some physicians also advise abstinence from alcohol in the immediate post-procedure period, but evidence to support this is limited. Avoiding sun exposure within the first week may reduce the risk of skin redness and inflammation.

Combining HA filler treatment with injection of botulinum toxin is becoming increasingly popular because it extends the cosmetic response of the HA agent by immobilising the muscles and thus, increasing the biodegradation time. However, research is limited on the subject of concomitant injection and some authors prefer to inject botulinum toxin and fillers with a delay of at least one week, performing the former first.

Depending on the filler agent used and the depth at which it is injected, the effects of soft tissue augmentation will last from 4 to 12 months. It is difficult to be accurate in predicting the duration of effect and patients should be advised of this. However, a few guidelines may be reasonably mentioned. Most injections last at least three months and often up to six months, although there are anecdotal reports of longer duration and, indeed, some of the newer products claim up to 18 months of activity. On balance, it is probably best to advise patients to expect 4-6 months efficacy, and that treatments may be needed 2-3 times per annum. Concomitant treatment with botulinum toxin may prolong these effects [5]. There is some suggestion, although not proven as yet, that the repeated application of HA in the same area does, in fact, eventually provide a long-lasting result; whether this is due to the sustained increase of extracellular matrix, or whether this is the result of repeated scarring is not known. However it is to be point out that interval treatment times are dependent upon patient’s needs and perception of the cosmetic lasting effect; moreover, financial considerations should be contemplated. Many patients who claimed to be happy with their previous surgeon still chose to move to a different practice for a variety of reasons unrelated to their previous practitioner.

**Technical Points**

Anaesthesia is often obtained using a combination of topical, local and regional anaesthetic agents. Topical anaesthetic creams (benzocaine, lidocaine) should be applied 20 minutes before injecting local anaesthetic. Infra-orbital and mental nerve blocks provide the mainstay of regional anaesthesia. Local anaesthesia is usually delivered to the peri-oral area. More recent HA injectable filler are commercialized with local anaesthetic combined with the filler substance within the same syringe reducing discomfort for the patients and offering time effectiveness for the practitioners [5,13].

The depth of the filler injection is the key factor in obtaining an effective aesthetic result. Small-particle hyaluronic acid fillers (i.e.: Restylane, Juvaderm Ultra 2 and 3) are suited to injection into the superficial dermis and are ideal for correcting superficial rhytides, such as those of the forehead, periorbital and perioral regions. Hyaluronic acid with large-sized particles (i.e: Hylaform Plus, Juvaderm Ultra 4 and Voluma) is best used in the mid-dermis for the glabellar region, nasolabial folds and for atrophic scars (Figure 2). Layering fillers at different depths can improve the overall aesthetic result. These are the most commonly used techniques:
Linear threading

With this technique the fold is filled by a single puncture to the epidermis and injecting the HA agent along the track of the needle producing linear volume. The full length of the needle is used to create a channel in the middle of the rhytide or fold. The filler material is injected as the needle is slowly pushed forward so that the material is deposited along the entire length of the rhytide or fold. A retrograde injection technique may also be used, whereby the material is injected while the needle is being retracted. This technique is best used for the treatment of white-roll lip border and the nasolabial fold and it is the commonest technique used by the first author.

Serial puncture

With this technique the fold is filled by multiple injections of the agent, all in a row. This technique involves serial injections along the fine rhytide or fold. The injection site should be in close proximity such that the injected material congregates into a smooth, continuous line. No spaces should remain between the serially injected filler. This technique is optimal for the glabellar, philtral column enhancement, nasolabial folds and fine rhytides. It is commonly used in the periorbital and perioral areas by the first author.

Fanning

With this technique, the epidermis is punctured once, and then the needle is fanned out while injecting the agent, producing volume in a triangular shape. This is similar to linear threading, but before the needle is withdrawn, its direction is changed and a new line is injected. The fanning pattern of lines should be evenly spaced in a progressive clock-wise or anti-clockwise direction. This will result in an even filling and shaping. This technique is best used for deep malar injection.

Cross-hatching (Cross-radial)

With this technique multiple injections of linear threading can be combined within crisscross directions at right angles to provide volume in a square shape. In this technique, again the needle is inserted in a similar way to linear threading. A series of linear threading injections is made in the treatment area. The pattern of lines should be evenly spaced in a progressive grid so that the contour is evenly filled and shaped. This is analogous to fat transfer techniques and it is performed by the senior author for deeper volumetric adjustment. This technique is best used for the oral commissures, facial contours and the perioral area.
**Fern pattern**

This involves serial puncturing in a linear manner but is done perpendicular to the actual fold on either side of it, increasing dermal stiffness. This technique can be performed safely and effectively in the periorbital regions [26].

**Topical hyaluronic acid**

Topical HA is not cross-linked and it is therefore easily absorbed. It was first used as a vehicle for the delivery of other drugs to the skin, being particularly useful for sustained release and localized delivery. As the significance of HA in water retention in the dermis has come to light, topical pure HA has become a cosmetic product in its own right. In the superficial epidermis, it acts as a humectant contributing to moisture content and decreasing trans-epidermal water loss. Once absorbed into deeper dermis it increases turgidity within the dermis. It also assists in proliferation of dermal fibroblasts, promoting extracellular matrix production *in vitro*, although there is no clear evidence this occurs *in vivo*. Since non-cross-linked HA has a short half-life, this will need frequent application. As it may increase the water retention of the dermis, it is marketed as a plumping agent for the skin. It is worth noting that the potential benefits of topical hyaluronic acid are theoretical and at the time of writing the authors are not aware of any objective studies in this area and so cannot recommend its use.

**Post-Treatment Care**

The surgeon should immediately massage the injected area rather than the patient performing the massage. Cooling packs may help to prevent post-injection bruising and oedema. The patient’s head should be elevated by thirty degrees for the first 24 hours. Oral anti-histamines can be prescribed to reduce post-injection oedema and are especially useful in those with previous adverse reactions to dermal fillers [1,5]. Sun exposure, physical activity, alcohol intake should be avoided in order to reduce the risk of developing complications in the early post-treatment phase (up to seven days).

**Complications**

The most common adverse reactions to HA are due to the cross linking process used rather than the HA source or nucleic acid contaminants, though the exact reason for the reactions is still unclear [8,25]. In general, hyaluronic acid fillers have an excellent safety profile. Many complications can be avoided with careful injection technique or reversed by injection of hyaluronidase [1]. The most commonly reported complications include local bruising, purpura, erythema, tenderness, pruritus, oedema and hypersensitivity reactions irregularities secondary to nodule formation and delayed inflammatory reactions (Box 3) [5]. These are seen in up to 12% of patients. The incidence of these complications is much less frequent compared to injectable collagens and equally the volume of HA agent required is significantly less than that of collagen. Serious complications such as hematoma formation and significant swelling are reported to occur in up to 1:1600 cases. Rare side effects such as sterile abscesses, induction of sarcoid and even angioedema have also been reported [8,27].

<table>
<thead>
<tr>
<th>Local bruising</th>
<th>Purpura</th>
<th>Erythema</th>
<th>Tenderness</th>
<th>Pruritus</th>
<th>Oedema</th>
</tr>
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<tbody>
<tr>
<td>Irregularities secondary to nodule formation</td>
<td>Immediate hypersensitivity reaction</td>
<td>Delayed hypersensitivity reaction</td>
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**Box 3:** Complications of hyaluronic acid injection.
The surgeon should inform the patient that swelling may last up to 3 weeks but will usually last 1-2 days. Similarly, the lips may appear overcorrected due to swelling in the early post-injection period. Bruising may last over one week but can be ameliorated by cessation of aspirin and NSAIDs taken at least two weeks before the injection. Asymmetric animation may occur due to the residual effects of the local anaesthetic. All patients should be seen within two weeks after treatment. Hyaluronidase injections and massage may help to correct irregularities that are picked up during follow-up.

References


