Introduction

The products available to facial plastic surgeons for soft tissue augmentation have rapidly grown over the last decade. It is important to understand what options are available and their indications. These products have revolutionized how the aging face is approached.

Pathogenesis of Wrinkles

Rhytids or wrinkles are a large complaint in patients who are evaluated for facial rejuvenation. They vary in their depth and etiology. It is traditionally known that deeper wrinkles are due to repeated and habitual contraction of the mimetic muscles. For example, transverse forehead wrinkles are due to habitual repetitive motion of the frontalis muscle, oblique/vertical glabellar wrinkles from the corrugator muscles, and transverse glabellar wrinkles from the procerus muscles. More superficial wrinkles are due to sun exposure (photoaging). Other factors that contribute to rhytid formation and the aging face include fat atrophy (subcutaneous layer) with subsequent laxity of static suspensory ligaments. This causes deepened nasolabial folds or extension of the NF folds (Marionette lines), ptotic malar pads (decreased malar eminence), and jowling (atrophy of buccal fat pads). Decreased water content of skin, decrease in collagen to elastin ratio (less collagen more elastic makes for more elastic skin), gravity, and skeletal changes (decreased height of maxilla and mandible) are also contributing factors.

The etiology of skin changes are divided into those from aging, UV exposure, and those related to cutaneous disease. UV exposure causes thickened skin with degraded elastin fibers (aka elastosis) and decreased in mature collagen. UVA rays are a more definite source of photoaging and can be found in sunlight, florescent light, and tanning beds. UVB, if combined with UVA, causes elastosis occurs sooner. Cutaneous disorders like Ehlers-Danlos syndrome, progeria, or cutis laxa all lead to premature skin changes and aging.

We have discussed surgical options of managing the aging face (forehead/brow lifts, face lifts, blepharoplasties, and neck lifts etc) but there is an increasing trend toward minimally invasive techniques to include soft tissue augmentation using implants and injectable fillers. There are four pillars of facial rejuvenation which include:
I. Ensuring adequate skeletal framework and support
II. Tightening and repositioning the investing musculofacial aponeurotic system (eg: SMAS/platysmal complex)
III. **Replace of soft tissue volume loss**
IV. Redraping and removing excess skin

The primary focus of soft tissue augmentation is for replacement of soft tissue volume.

**History**

Soft tissue augmentation dates back to 1800’s with Neuber’s report of fat grafting using small pieces of fat from the upper arm to reconstruct face defects in TB osteitis patients. Afterwards, various other materials were tried and failed including: paraffin, vegetable oil, mineral oil, and beeswax. In 1950, Peer reported fat augmentation had an average loss of 45% in weight by the first year post implantation. These results begged for the development of an “ideal implant”. In 1962, Dow Corning’s “medical grade” silicone was widely being used. However, silicone was found to be a controversial substance given its potential adverse effects profile (especially with impure sources of silicone). Twenty years later, dermal fillers came to the scene and changed the game starting with Bovine collagen fillers in 1980’s. Collagen fillers have been a mainstay for decades and it has only been recently (in the 2000’s) that other fillers rose to eclipse collagen injection, the first of which was hyaluronic acid (HA) fillers. They revolutionized dermal fillers in that they were steps closer to the “ideal” (refer below). Although the first HA injectable was invented in 1989, FDA approval and wide spread use did not occur until the 21\textsuperscript{st} century. We have since seen the advent of other more refined HA fillers and semi-permanent fillers like Radiesse and Sculptra being explored as of late.

**The “Ideal” Implant**

Success of an implant/filler is predicated upon its proximity to meeting the criteria of an “ideal” implant. Most articles and texts refer to the following as components of that category: shows biocompatibility, painless, causes minimal inflammation, and is non-immunogenic, carcinogenic, or teratogenic. Further, it is biodegradable or easily-retrievable, predictable, adjustable to the patient’s anatomy, persistent (long-lasting) but not necessarily permanent, and gives a natural appearance.

**Types of Soft Tissue Augmentation**

There are various schemata used to classify kinds of implants and fillers used. In general, fillers are divided into permanence (absorbable/non-permanent vs non-absorbable/permanent) and source (human vs non-human vs synthetic). Further, most fillers have a location and skin depth for which the work best. Knowing this is key along with correctly identifying the depth of the defect to be corrected. The use of implants is variable and dependent of patient and physician preference.

**Dermal (intra-dermal) Fillers**

Dermal fillers have undergone the most rapid growth over the past several years. As there continues to be a dramatic rise in the number of ‘non-invasive’ cosmetic procedures performed, dermal fillers are being utilized more. In statistics published by the American Society for Aesthetic Plastic Surgery (ASAPS) in 2008, Botox injections led in the number of non-invasive procedures performed and were the number one procedure being performed world-wide, followed by laser hair removal. In a very close third place was the use of dermal fillers, specifically hyaluronic acid. When considering the following fillers, understand that the pursuit of the “ideal” implant/injectable has driven the advent of one filler to the next.
Collagen

Collagen fillers were the first dermal fillers available, specifically, bovine collagen (Zyderm). It was initially reported by Knapp in 1977. Its main clinical advantage is its ability to correct superficial wrinkles and its smooth flow profile (ease of injections). A primary limitation of bovine collagen is its duration profile of only 1-4 months persistence. Bovine collagen has a short lived effect and is rapidly resorbed. In attempts to counteract this, another form of Bovine collagen cross-linked with glutaraldehyde (Zyplast) was created. Cross-linking involves adding a polymer chain to a molecule and is done to slow degradation. Even with this, Zyplast still requires repeat treatments for a longer effect.

Another limitation of bovine collagen is its antigenicity. Bovine collagen is harvested from cowhide and goes through a purification process followed by enzymatic degradation, and sterilization. Despite this there is still a potential for type IV allergic hypersensitivity, although rare at 1.5-3% incidence. To this regard, use of Bovine collagen requires a test injection (volar forearm); the site is inspected in 48-72 hours and at 1 month. Erythema, induration, or signs of irritation in 6 hours is a positive result and bovine collagen cannot be used. Further, given a 1.3-6.2% false negative rate, it is recommended another test be placed at 2-4 weeks. Treatment is essentially delayed until 2-4 weeks AFTER a second negative test. To circumvent this, autologous injectable collagen (Autologen), was developed. However, the main disadvantage of Autologen is the skin must be obtained from the donor-recipient and must be shipped for processing before it can be used.

Preparations of bovine collagen contain local anesthetic (0.3% lidocaine) unlike human collagen and are painless. Complications and adverse reactions are: transient erythema, edema, ecchymosis, local skin necrosis, local granulomatous reaction, and abscess formation. Complications are rare (4/100,000) but can last for up to two years.

A newer collagen made of porcine collagen (Evolence) has become available in the US and FDA approved (2008, 2009). Its benefits include: no need for skin testing. Clinical results show greater duration than bovine or human collagen – upwards of 18 mos post implantation.

Hyaluronans (Hyaluronic acid; HA)

For several years, collagen was the material to beat. However, the advent of hyaluronic acid changed all that and brought the facial plastic world closer to the “ideal” implant. To understand this, one must understand the characteristic of this injectable. HA is a glycosaminoglycan. It is a naturally occurring, ubiquitous substance in mammalian connective tissue making it extremely biocompatible, non-immunogenic or antigenic naturally. It is hydrophilic and, with water, it is able to occupy a larger volume compared to its mass and withstand compression. In its native state it has a short life span but when cross-linked it can persist from 6-18 months or even more. Persistence for HA increases with: higher concentrations of HA (delays degradation), increased percentage of cross-linking, increased types of cross-linking, and high fluid retention (water-binding) capacity. Injection technique is also important. There is a higher de novo collagen synthesis if injected into the deep dermis. Lastly, it has the ultimate reversibility in that hyaluronidase can be injected to break the cross-links of previously injected HA. The HA becomes resorbed in hours by surround interstitial fluid. Various forms of HA have been FDA approved as of the 21st century.

In a pivotal, multicenter study by Baumann et al, HA was compared to bovine collagen in a double-masked, RCT. 439 patients were studied, all with at least moderate to severe and symmetrical
nasolabial folds. Each patient was injected with bovine collagen on one side and an HA filler on the other side. The evaluating investigator and the patients were blinded as to which formulation was used on either side. The patients were evaluated for up to 24 weeks. 81-90% of the HA filler maintained a clinically significant improvement from baseline at 6 mos or more. Up to eighty-eight percent of patients preferred the side which the HA filler had been injected.

**Restylane (NASHA = Non Animal Source HA)**

Was the first HA on the market. Although, hyaluronic acids were first developed in 1989, Restylane was not FDA approved until 2003.

- Source: equine streptococci
- Cross-link: Cross-linked with BDDA; 80% cross-linked with 2% degree of cross-linking.
- Concentration: 20mg/mL
- FDA approved for up to six months correction for mid-dermal applications for deep wrinkles, lip augmentation, nasolabial fold correction, and for glabellar creases.
- Perlane (part of the Restylane family) boasts larger particles (delays degradation) and allows for deeper injections.

**Juvederm**

Competitor to Restylane. It received FDA approval June 2006.

- Source: equine streptococci
- Cross-link: Cross-linked with BDDE; 90% cross-linked with at least 6% (highest 11%) degree of cross-linking.
- Concentration: 24mg/mL; other formulations range from 18-30mg/mL
- Water binding capacity: Higher hydrophilic properties than Restylane.
- Possibly the longest persisting HA filler.
- FDA approved deep wrinkles and furrows, lip augmentation, nasolabial fold correction and nasojugal area.

**Hydrelle (formerly Elevess)**

Newest on the market. It is the FDA approved (2009) and, currently, the only HA filler to come standard with local anesthetic (0.3% lidocaine). Juvederm and Restylane are working on their preparations.

- Source: equine streptococci
- Cross-link: Cross-linked with BCDI (novel linker)
- Concentration: 28mg/mL.
- There have been case reports of allergic reactions.

The complications of HA fillers are very rare but do include skin discoloration due to the Tyndall effect. Given the hydrophilic properties of these fillers, blue reflection of the water in the area can cause a blue gray tinge.
Calcium hydroxylapatite (CaHA) fillers (Radiesse)

This is one of the emerging semi-permanent dermal fillers on the market. It was FDA approved in 2006 as a dermal and subcutaneous filler. It is the first dermal filler to receive two FDA indications - facial wrinkles (mod-severe wrinkles, folds such as nasolabial grooves) AND facial wasting from HIV-associated lipoatrophy. It is composed of 30% CaHA microspheres and 70% carboxymethylcellulose gel. It stimulates neocollagenesis formation around its particles in vivo and has a longer persistence than HA. It is not recommended for lip augmentation (pink body of the lips) to avoid palpability or nodule formation. Nodules can be reversed with slit incision as the filler becomes well-circumscribed from the collagen formation. There are no systemic or immunologic responses. It has demonstrated longevity of over one and up to two years. Many clinicians add lidocaine to Radiesse syringe for use making it painless. All of its materials are biocompatible. For many physicians, this is becoming the first line choice for soft tissue augmentation. Its complications include: nodule formation (but NOT granulomas), ecchymosis, and hematoma.

Poly-L-Lactic acid (PLLA; Sculptra)

This is a semi-permanent filler FDA approved in 2004 to treat HIV-associated lipoatrophy and later for wrinkles in 2009. It is a volume enhancer which causes controlled inflammation where fibroblasts leave collagen as the PLLA degrades. It is delivered via a depot method or a crosshatching linear method in the cheeks, temples, and lateral face and should not be used in the periobital or lips. Its main advantage is in that its persistence can last upwards of two years. It is intended for correction of shallow to deep nasolabial fold contour deficiencies and other facial wrinkles in which deep dermal grid pattern (cross-hatch) injection technique is appropriate (this corresponds to Wrinkle Assessment Scores of 2 to 4). The microparticles need to be placed in the deep dermis or subdermally. It needs to be appropriately diluted to prevent nodule formation, requires multiple treatments, and the patients must continue to massage the area for 5 days post-treatment.

Polymethylmethacrylate (PMMA, Artecoll, Artefill)

This is a synthetic filler with large particles (30-50 microns) that make it difficult to be phagocytized and relatively permanent. It has a controversial past as earlier forms were riddled with complications. However, the Artefill formulation has recently received FDA approval as of 2006. Its main advantage is that it can last possibly upwards of five years. Its particles become covered by large monocytes after 2 days, followed by fibroblasts at 2 months, and a fibrous capsule at 7 months. It has limited reversibility. Especially for earlier formulations, patients who had experienced misplacement in tissue or inflammatory reactions had no alternative aside from wide local excision. Further studies are being carried out over this filler.

Liquid Silicone

Subcutaneous volume enhancers (fillers)

Autologous fat

This technique is a fundamental mode of facial volume filling for surgeons in the operative room. It is the filler of choice in combination with aging face surgery. It is the oldest form of soft tissue augmentation in literature. There are variable outcomes with this technique but harvest methods and placement techniques affect its outcome. Microlipoinjection using a low negative pressure suction from
manual syringes is least traumatic. Fat can be harvested from the lateral thighs, hips, abdomen, medial knees, or gluteal area. The fat is then separated from oil or serosanguinous fluid carefully and washed with sterile saline. It is injected into the subcutaneous tissue using blunt cannulas under lower pressure with deposition of fat on withdrawal to allow for precision placement of fat. After injection, the area is massaged to smoothen the field. It is indicated for: nasolabial grooves, marionette lines, midface, lips, glabellar furrows, and hemifacial atrophy. Overcorrection by 30-50% is recommended given its average loss of weight. Complications include: mild swelling and slight ecchymosis at the treatment sight. There is a case is one case report of blindness following injection of fat to the glabella.

**Autologous SMAS fascia**

As lip augmentation is very frequently requested. Autologous SMAS-fascia is a subcutaneous augmentation that can be placed in the lip and nasolabial groove with variable results. The only options for lip augmentation include fat, HA fillers, Allo-Derm, or alloplastic materials. It is harvested, rolled, and tunneled into place under the defect (as similar to Allo-Derm).

**Allo-Derm**

This is a homologous (donor), acellular dermal matrix that was first used clinically in the treatment of full-thickness burns. Since then, it has progressed and is being used for lip augmentation, for nasolabial and melolabial folds, and glabellar frown lines. Pieces are harvested into triangular shapes, rehydrated, rolled along its long axis and tunneled into the lips or under the aforementioned facial folds. Maximal swelling occurs 3 days post op and it is recommended that antibiotics are used for several days. Prophylactic acyclovir should be considered in patients with a herpes simplex history.

**Alloplastic material – ePFTE**

Expanded polytetrafluoroethylene (e-PFTE; Ultrasoft) is a highly biocompatible, inert, carbon-based material that has been used as vascular grafts for more than twenty ears. They are tunneled much like Allo-Derm or SMAS fascia but have it has a unique delivery system for tunneling and implantation using a trocar and cannula method. It is placed in the subcutaneous layer. A criticism of this material is that its microfibrillar structure allows for tissue ingrowth which causes the walls of the implant to harden and become more palpable. The thinner walled Ultrasoft was created to combat this and a saline filled implant (Fulfil) was created to compete with the softness HA fillers offer.

**Skeletal Onlay grafts/implants**

These are a reliable and safe option for soft tissue augmentation. These are considered when there are structural facial deficits and they are an indirect method of soft tissue augmentation. As ancestors of custom carved grafts, custom pre-formed implants are now manufactured from Silastic (silicone), ePFTE, and Porex. They most commonly involve structure deficits of the chin, mandibular angle, malar complex, and nasal dorsum. They are placed either above or below the periosteum in a sterile surgical field. Patients are to expect post op edema and anesthesia for three weeks. Capsule maturation occurs after six months. Alterations in bone volume adjacent to the implants are said to be clinically insignificant. Yet, they are reversible surgically should they need to be removed. The most challenging aspect of using this material is technique and identifying the appropriate implant size.
Metzinger et al did a five year retrospective review of Silastic midfacial malar implants. Sixty patients received malar implants and were followed from 24-60 months post op. Their technique involved facial analysis of the malar defect using a combination of the techniques proposed by Hinderer, Powell et al, and Predergast and Schoenrock. The appropriate size and shape implant was then chosen and carefully outlined on the patient. An intraoral, canine fossa approach is used to access the malar eminence and the implant was placed in a subperiosteal pocket. Post operatively, 85% reported an excellent result at 2 year follow up.

**Neuromuscular agents**

**Botox**

This is a physiologically active agent and its use makes for the most common non-invasive cosmetic procedure. Its effect on wrinkles and facial lines impinge on the fact that they are the result of underlying muscle contractions. Produced by Clostridium botulinum, there are A – G formulations, but BTX-A is the most potent at muscle paralysis in humans. It works by binding to pre-synaptic cholinergic terminals and preventing the release of Ach. Its effect is irreversible and only overcome by turnover and repair, absorption of the terminals it has inactivated, and sprouting new axonal terminals with new NMJs. Its effect lasts for 3-6 mos. The initial effects of Botox begin in 2-3 days but its maximal effect is noticed at 1-2 weeks post-injection. It can be used to treat various sites along the forehead/upper face. It is also use as a minimally invasive method of temporal browlift (injection of superolateral orbicularis leads to unopposed frontalis muscle action and lifts the brow). Complications are few but include: ptosis, temporary droop off the lower eyelid after treatment of crow’s feet. It does have immunogenic properties but is reversible.
Sources:


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