



Synthetic Fillers in Facial Cosmetic Surgery-Different Categories Discussion of Rheologic Properties

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ABSTRACT

Introduction: The pursuit of facial rejuvenation and aesthetic enhancement has evolved significantly over time. Early techniques, such as fat transplantation in the 1890s, paved the way for modern dermal fillers (DF), which have become a cornerstone of minimally invasive cosmetic procedures. Today, filler injections are among the most popular treatments for soft tissue augmentation, facial volumization, and body contouring. This review explores the development of dermal fillers, their current applications, and the key physical properties that differentiate them.

Materials and Methods: A comprehensive literature review was performed using scientific databases (PubMed, Scopus) to identify peer-reviewed articles, clinical studies, and manufacturer data on dermal fillers. The analysis focused on:

- Historical evolution of filler materials.
- Chemical compositions and physical properties.
- FDA-approved clinical applications.
- Reported efficacy and safety profiles.

Results: Dermal fillers have undergone significant advancements, offering improved safety, durability, and natural results. Their versatility allows for tailored treatments in facial rejuvenation and beyond, making them indispensable in aesthetic medicine.

Conclusion: As DF technology continues to evolve, understanding their properties ensures optimal patient outcomes. Their integration into cosmetic practice underscores their importance in meeting the growing demand for non-surgical aesthetic solutions.

Keywords: Dermal fillers; Synthetic fillers; Hyaluronic acid; Temporary dermal fillers.

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Introduction

Today, the desire for cosmetic facial surgeries to rejuvenate and regenerate facial volume as a result of aging, facial muscle movements and gravity has increased. Among these, non-surgical rejuvenation methods have a special place. Surgical procedures require hospitalization and their recovery time is long, while non-surgical procedures can be performed in the office. These methods yield significant improvement with less risk and less cost than most surgical alternatives [1]. The most popular non-surgical methods include the use of injectable fillers, fat transfer (minimally invasive), neuromodulators, and skin resurfacing techniques. This chapter discusses injectable fillers, their advantages and disadvantages, risks, and injection methods. Dermal fillers (DF) have been developed as an alternative to plastic surgery, in response to the increasing request for minimally invasive procedures. They have become an integral part of both aesthetic medicine and cosmetic surgery [2]. Dermal fillers (DFs) can be classified into three major types: temporary (non-permanent): (like hyaluronic acid) which are short-lasting fillers and need repeated injections after their resorption, semi-permanent fillers: (poly-L-lactic acid and calcium hydroxyapatite) which last longer but they will undergo some resorption as well, and permanent fillers: (polymethylmethacrylate and liquid silicone) which may be long lasting with only a single injection. DFs can also be divided into two categories: non-biodegradable and biodegradable. The non-biodegradable DFs include liquid silicone and PMMA (poly-methyl methacrylate) [3].

We mention some other non-biodegradable and biodegradable fillers in Table 1 [4]. By definition, permanent fillers are those non-biodegradable materials that after injection will stay in the body for longer than five years. They are neither digested nor used for tissue regeneration. Such products may contain polymethylmethacrylate microspheres (FDA approved in 2006), highly purified forms of liquid silicone, and hydrogel polymers. There is no FDA-approved indication for the use of liquid silicone or silicone gel for injection to fill wrinkles or augment tissues anywhere in the body [5]. In 1954 a filler which is a deep dermal semi-permanent was created by French chemists. It is a biocompatible, synthetic polymer and biodegradable [3]. However, DFs truly made their debut in the 1970s when various animal-derived collagens had been researched and tested for use on humans and therefore collagen injections and implants were introduced. Specifically, collagen derived from cows (bovine collagen) was developed

in the 1980s following the ban on liquid silicone and it was a hallmark of tissue augmentation for decades [3,6]. Collagen dominated the dermal filler market for 22 years, from its Food and Drug Administration (FDA) approval in 1981 until hyaluronic acid (HA) fillers entered the market in 2003 [3,4]. As bovine collagen is foreign to the human body, a sensitivity test was needed to ensure that the patient was not allergic to it. The incidence of preexisting hypersensitivity to bovine collagen is between 2% and 4% [7]. In 2004 FDA approved, Hylaform (Genzyme Biosurgery) is a HA-based DF derived from an avian source (rooster comb). Hylaform is indicated for the treatment of moderate to severe facial wrinkles and folds, such as nasolabial folds. It is not recommended for lip enhancement or augmentation. Its major disadvantage is its lack of longevity, as benefits generally last 3 to 4 months. Hylaform Plus is another form of Hylaform designed for mid to deep dermal injection to treat moderate to severe facial wrinkles and folds. It is equal to Hylaform, except for particle size, which is increased to 750µm [8].

In 2004, a synthetic polymer (Poly-L-Lactic Acid) was introduced for restoring lost volume and to correct facial imperfections causing neocollagenesis around the filler particles. The best known PLLA filler which is currently on market is Sculptra (Galderma) [9]. The PMMA filler Bellafill (previously Artefill; Suneva Medical, Inc., Santa Barbara, CA) was approved by the FDA in 2006 for use in facial tissue around the mouth. Bellafill is a non-resorbable filler made from PMMA microspheres suspended in a collagen matrix that contains lidocaine. Bellafill was more recently approved in 2015 for the treatment of acne scars. In a manner similar to PLLA, PMMA stimulates neocollagenesis around the filler beads. As it contains bovine collagen, it also needs an intradermal skin test to detect the risk of a hypersensitivity reaction [10]. In 2008, the FDA approved Prevelle Silk (Genzyme Biosurgery), which is the same product as Hylaform, with the addition of 0.3% lidocaine hydrochloride. It can correct the moderate to severe facial wrinkles and folds like nasolabial folds [11]. DFs have been used for restoring lost volume and correcting various facial imperfections such as wrinkles or scars. For superficial wrinkles, a DF should be injected into the superficial dermis and in the case of deeper rhytides, a DF is injected into the deep dermis or subdermal level. Dermal fillers work by occupying space and indirectly by stimulating the dermis to increase elastin and collagen production [10]. Dermal fillers have some common and less common side effects.

Common side effects are bruising, redness, swelling, pain, tenderness, itching, and rash and non-common side effects are overcorrection, palpable nodules, granulomas, infection, and open wounds, soreness at the injection site, allergic reaction, and intravascular injection necrosis [12]. In this paper we examine various types of dermal fillers, discussing their advantages and disadvantages.

Filler types

Non-permanent fillers

Collagen replacements

Prior to the introduction of hyaluronic acids, these substances were known as gold standard and were made from bovine or human collagen. The first product approved by the FDA for soft tissue augmentation was bovine collagen [13]. Due to the possibility of allergies to these substances, it was necessary to perform allergy tests before injection [14]. Several collagen alternatives have been introduced: Zyderm, Zyplast, Cosmoderm, and Cosmoplast (INAMED Aesthetics, Irvine, CA). Zyderm and Zyplast are bovine collagen materials. Zyderm received FDA approval in 1981. Zyplast was more durable and received FDA approval in 1985 [15]. Cosmoderm and cosmoplast are products of human collagen derived from the culture of human fibroblasts [16]. These products have a shorter lifespan than bovine collagen and are less likely to be allergic to bovine collagen and are easier to use.

Hyaluronic acid

Hyaluronic acid is present in the skin dermis and provides a scaffold for collagen growth. Aging destroys hyaluronic acid and causes wrinkles on the skin. It binds to water molecules increases skin hydration and enhances its volume and elasticity. There is no need to perform allergy testing. The shelf life of this material is short. Recently, hylans have been added to hyaluronic acid to increase longevity. The lifespan of hyaluronic acid is between 6 and 9 months [17]. Hyaluronic acid is injected intradermally and if the desired result is not achieved, it can be destroyed by the enzyme hyaluronidase [18]. Restylane (Medicis Aesthetics, Inc., Scottsdale, Arizona) was the first filler based on hyaluronic acid to receive FDA approval in 2003. It is derived from the culture of streptococci binds strongly to water molecules and is ideal for medium to deep skin injections. The high cross-link of this material makes it last longer between 4 to 6 months (depending on the injection site). There are two other formulas of Restylane. Re-

stylane Fine Line has a smaller particle size and lower viscosity, which means that it is ideal for more superficial dermal injections. Restylane Perlane has larger particle size, higher viscosity, and longer results and is ideal for deep skin injections. Hylaform (Inamed, Santa Barbara, Calif.) And Hylaform Plus were approved by the FDA in 2004 [19]. Due to its higher cross-linking and lower hyaluronic acid, it has a slightly shorter shelf life than Restylane. There is a possibility of allergy to this substance and it is suitable for moderate dermal injections. Hylaform Plus has larger particles and is suitable for deep injections [18]. Captique (Allergan, Santa Barbara, Calif.) Was introduced in 2004 and received FDA approval and is a hyaluronic acid derived from bay bacterial fermentation. It is suitable for medium to deep injections [19]. Juve'derm (Allergan, Inc., Irvine, Calif.) Was approved by the FDA in 2006. A biocompatible substance that has 3 different formulas. Juve'derm 24 HV and Juve'derm 30 HV cross-links have higher links that are suitable for deep injections, and the Juve'derm 30 formula is better for superficial injections [20].

Cymetra

Cymetra (LifeCell Corporation, Branchburg, NJ) is a micronized form of human acellular dermal tissue called alloderm that contains collagen, proteoglycans, and all skin tissue components except cells. It is packaged in powder form and must be mixed with saline before injection. Its duration is between 3 to 6 months [21].

Semi-permanent fillers

Sculptra

Sculptra (Dermik Laboratories, Berwyn, PA) is a synthetic poly-L-lactic acid. It is in powder form and should be mixed with saline 2 hours before consumption. Subcutaneous injections are suitable for repairing deep and large defects. Over-correction should not be done. The duration of this substance is 18 to 24 months depending on the injection site [18].

Hydroxyapatite fillers

Radiesse (BioForm Medical, San Mateo, CA) is a filler containing calcium hydroxyapatite particles. It is a sticky substance and is suitable for deep dermal and subdermal injections. This substance does not cause allergies. This material is very durable due to the carrier material that decomposes in 6 to 8 weeks. Simultaneously with this process, collagen is made in place and the volume of the area is maintained [22]. The injected

filler is palpable for 2 to 3 months until the particles decompose and collagen appears in place. Radiance FN contains hydroxyapatite in a degradable gel carrier [23]. This material is not FDA-approved and has a long shelf life. Therefore, over-correction should not be done [21].

Permanent fillers

ArteFill

ArteFill (Artes Medical, San Diego, CA) is an FDA-approved product composed of 20% polymethylmethacrylate microspheres and 80% bovine collagen as a delivery agent [24]. Because of bovine collagen, allergy testing is needed. The delivery agent degrades after about 4 months, but microspheres are permanent and become encapsulated by inflammatory reactions, which are responsible for 50 to 70 percent of permanent correction and volume maintenance. Overcorrection should not be performed and the patient may need several touch-up injections spaced 3 to 4 months apart for optimal results [13].

Injectable silicone

Silicone refers to polymers of silicon. Small volumes of Silicone are injected in a grid-like fashion spaced at 1 to 3mm into the deep dermis called micro-droplet technique. Several injections spaced four weeks apart are required to gain final results. Encapsulation occurs around particles and is permanent. Silikon (Alcon Laboratories, Fort Worth, TX) is an injectable silicone for facial augmentation. AdatoSil (Bausch & Lomb, Rochester, NY) is another injectable silicone that is more viscous than Silikon [25].

Mesogel

Pistor in 1958 introduced mesotherapy as a noninvasive rejuvenation medical procedure. In fact, nutrients, hormones, vitamins, enzymes, and others is injected intradermally, Increasing both hydration and fibroblast activation [26]. Different injection techniques can be used in mesotherapy: (i) the intra-epidermal technique; (ii) the popular technique, in which reagents are injected into the dermo-epidermal junction; (ii) the nappage method, in which injections penetrate to a depth of 2–4mm and are delivered at an angle of 30–60; and (IV) point-by-point injection into the deep dermis [27]. Gao F et al and others have demonstrated that hyaluronic acid injected into the skin can stimulate fibroblasts to express collagen type 1 (Col-1), matrix metalloprotease-1 (MMP-1), and inhibitor of matrix metalloproteinase-1 (TIMP). Hyaluronan oligosaccharides promote excisional wound healing through enhanced angiogenesis [28]. Booster therapy with HA is a safe and well-tolerated procedure, and results in improvement in skin elasticity and relative increase in skin hydration [29]. Clinical experience of skin rejuvenation by HA-based mesotherapy suggests this technique is safe inasmuch as it is performed by a trained physician, who follows safe-injection practices with appropriate aseptic techniques to prevent the risk of infection related to inadequate safety measures. Furthermore, several studies suggest it can improve skin hydration, firmness and viscoelastic properties [30]. This study objectively demonstrated the efficacy and the tolerance of a non-cross-linked HA filler in sustainably improving skin elastic parameters and complexion radiance. In particular, we showed that intradermally microinjected HA (mesogel) might be of value to improve suppleness of ageing skin, inasmuch as injections are performed by a trained physician with appropriate

Table 1. Examples of biodegradable fillers and non-biodegradable fillers.

Biodegradable Fillers	Non-Biodegradable Fillers
Hyaluronic Acid	Polymethylmethacrylate microspheres with bovine collagen
Bovine Collagen	Silicone
Poly-L-Lactic Acid (PLLA)	Polymethylmethacrylate Microspheres Sus-pended In Carboxyglu-conate Gel
Calcium Hydroxyapatite	Polymethylmethacrylate Silicone Suspension
Dextran Beads In Hyaluronic Acid	Acrylic Hydrogel Particles Suspended In Hy-aluronic Acid
	Polyacrylamide Gel

aseptic measures [31].

Conclusion

Cosmetic surgery is the gold standard for people who need it, but with dermal fillers, we can achieve long-lasting corrections with fewer side effects that's why in the last 5 years, dermal fillers have become popular in the US and also in many other countries. It is important to know the different groups of dermal fillers and know each usage and the area in which they can be used. The longevity of the aesthetic-enhancing effects depends on the type and amount of filler, and injection technique utilized and, treatment location. Case selection and understanding the facial anatomy, aesthetics, and techniques to get a good result in minimally invasive procedures like using dermal fillers are also important factors to get a good result.

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Conflict of Interest

There is no conflict of interest to declare.

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