Collagen Stimulators
Poly-L-Lactic Acid and Calcium Hydroxyl Apatite

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KEYWORDS

• Collagen stimulators • Calcium hydroxyl apatite • Poly-L-lactic acid • Facial rejuvenation • Fillers

KEY POINTS

- Aging is a three-dimensional process, with changes in multiple tissues contributing to the overall effect.
- The role of volume loss in the clinical changes observed in the aging face is becoming widely appreciated. Mastery of volume replacement has become essential to the successful practice of aesthetic medicine.
- Lifting techniques alone, without addressing volume loss, can no longer adequately address the aging process in the face. This approach may actually exacerbate, rather than ameliorate, the aging process.
- Calcium hydroxyl apatite and poly-L-lactic acid, the so-called collagen stimulators, offer a unique and effective way to address this issue with natural-appearing results with long duration.

Videos of dorsal hand treatment with calcium hydroxyl appetite; and panfacial treatment with poly-L-lactic acid accompany this article at http://www.facialplastic.theclinics.com/

INTRODUCTION

Over the last decade, many studies of the structural changes observed in the aging face (in bone, fat pads, facial ligaments, muscle, skin) have increased our understanding that facial rejuvenation is far more complex and nuanced than simply filling lines and folds or cutting and lifting soft tissue and skin.[1–3] This, in addition to the many new products introduced to the marketplace over the same time period has fueled our evolution of panfacial rejuvenation and restoration using fillers.[4]

According to the American Society of Plastic Surgeons (ASPS), more than 1.7 million injections of soft tissue filler were performed in the United States in 2014 alone. This represents more than a 250% increase from just 14 years ago. Most of these injections used hyaluronic acid (HA)-based products, however close to a quarter of a million of these injections were carried out over the year using calcium hydroxylapatite (CaHA) (Radiesse, Merz Pharma, Frankfurt, Germany) and poly-L-lactic acid (PLLA) (Sculptra, Sinclair Pharmaceuticals, Galderma Laboratories, Fort Worth, TX, USA).[5]

The purpose of this article is to discuss current techniques used with CaHA and PLLA to safely and effectively address the changes observed in the aging face. The original US Food and Drug Administration (FDA) studies for aesthetic approval

Disclosures: None (A. Breithaupt); Speaker, Trainer, Consultant, and Advisory Board Member for Allergan, Merz, Galderma, and Valeant (R. Fitzgerald).
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Facial Plast Surg Clin N Am 23 (2015) 459–469
http://dx.doi.org/10.1016/j.fsc.2015.07.007
1064-7406/15/$ – see front matter

of most of the currently commercially available fillers, including these 2, looked at correction of the nasolabial fold by direct injection using a recognized and standardized grading chart and then subsequently gave approval for "subdermal implantation for the correction of moderate to severe facial wrinkles and folds, such as nasolabial folds." These 2 products also received FDA approval for restoration and/or correction of the signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus. More recently, in 2015, Radiesse was approved by the FDA for dorsal hand augmentation. On-label refers to use strictly as described in the studies carried out to garner FDA approval (and these are the only uses for which the product manufacturers may commercially promote their product). With time and experience, doctors may discover other advantageous uses of these products, and this is referred to as off-label use. Many of the techniques described in this article are off-label.

Much has already been written about the science behind these products. A brief review follows here.

The principal component of Radiesse is CaHA, a biomaterial with more than 20 years of safe and effective use for devices in orthopedics, neurosurgery, dentistry, otolaryngology, and ophthalmology, demonstrating its biocompatibility and low incidence of allergenicity.[6] Calcium hydroxylapatite is a synthetic analogue of the inorganic constituent of bone and teeth. The CaHA microspheres (25–45 μm) represent 30% of the final product and are suspended in a 70% gel carrier containing sterile water, carboxymethylcellulose, and glycerin. An immediate fill and lift is seen from the gel carrier, which dissipates over the next several weeks, while the CaHA remains at the site of injection. When this site is examined 3 months later, the CaHA microspheres are encapsulated by a network of fibrin, fibroblasts, and macrophages, with the CaHA acting as a scaffolding for fibroplasia and new collagen formation. At 9 months, the microspheres begin to absorb and can be found within macrophages.[7] The clinical result can last for 12 to 18 months. The glycerin helps the product flow from the syringe, but may cause pronounced transient swelling and edema. The patient should be made aware that this swelling is only temporary (24–72 hours).

One method used to help select the optimum product for a specific area (ie, soft product for lips, stiff product for chin) is to look at a given product's rheology. Rheology is the study of the flow characteristics of different products (eg, cement vs water); one rheological component that can be measured is referred to as G′. G′ is a measure of elasticity, meaning a material's stiffness or ability to resist deformation under pressure. Radiesse has a high G′ value, which is suitable for lifting soft tissue and contouring, making it an ideal agent, for example, for deep supra-periosteal injections along the malar eminence and zygomatic arch, the mandible, and the chin.[8] This can be done to replenish volume in areas of bony remodeling in an aged face, or to create bony prominence in patients with congenital skeletal hypoplasia.

The product can also be diluted and used to augment the dorsal hand.[9]

PLLA is a synthetic, biocompatible, and biodegradable polymer of lactic acid that has been used safely in various medical applications for more than 3 decades.[10] The product is supplied as a lyophilized powder in a sterile glass vial and includes nonpyrogenic mannitol, sodium carboxymethylcellulose, and PLLA microparticles (40–60 μm). The product must be reconstituted with sterile water before injection and this is discussed in more detail later. A transient fill as a result of the mechanical distention of the tissues is seen immediately after injection, but this resorbs over the next several days. The true mechanism of action of PLLA begins with a subclinical inflammatory tissue response after implantation, followed by encapsulation of the particles and subsequent fibroplasia. This fibroplasia volumizes the tissues and produces the desired cosmetic result. This mechanism of action enables the product to gradually and progressively restore "a little volume all over" yielding a subtle and natural-looking result. It is important for both the practitioner and the patient to note that the final result is not accomplished by the product, but by the host's reaction to the product, and that this process takes 3 to 4 weeks.[10]

The bioengineering definition of biocompatibility is "the ability to elicit an appropriate host reaction in a desired application."[11] In the application of tissue augmentation, this requires a predictable amount of inflammation. A predictable amount of inflammation (and therefore a predictable result) is easily achievable by avoiding overcorrection. A predictable amount of inflammation requires 3 things: (1) a predictable product (with a homogeneous particle size), (2) a predictable methodology (achieved over the last decade of use), and (3) a predictable patient (the absence of active autoimmune disease).[12] As experience has been gained with this product and technical issues have evolved, we have seen that most of the adverse events seen with early use (papules and nodules, especially around the eyes or lips), stemmed from suboptimal technique. Therefore, a few simple yet critical components of methodology unique to this product (product reconstitution, placement,