



## Therapeutic Pearls

# Novel Filler Technique: Hyaluronic acid and Calcium hydroxylapatite mixture resulting in favorable esthetic and longevity outcomes



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### What is known about this subject in regard to women and their families?

- Women lose volume in the face from decreasing fat, bone, and muscle, leading to a lack of structural support of the face.
- Multiple types of “fillers” have been designed to favorably enhance female features.

### What is new from this article as messages for women and their families?

- We present a novel approach that incorporates mixing hyaluronic acid and calcium hydroxylapatite to create an elegant, moldable compound that integrates nicely into the tissue while providing a long-lasting result.
- Generally, patients who identify as female desire more voluminous contour changes from fillers, which is a benefit of the combination of calcium hydroxylapatite and hyaluronic acid.

Hyaluronic acid (HA) fillers, which are commercially available in >20 forms from various manufacturers, and calcium hydroxylapatite (CaHA) filler, commercially available as Radiesse (Merz, Inc.), are injectable filling agents that have been approved by the U.S. Food and Drug Administration for cosmetic injection since 2003 and 2006, respectively (Kontis and Rivkin, 2009).

HA is a linear glycosaminoglycan with repeating disaccharide units; it is naturally present in the human body as part of the extracellular matrix. When used for esthetic purposes, HA is a viscoelastic hygroscopic gel or particulate synthesized from bacteria. The gel is composed of particles that range in size and concentration, depending on the product.

In general, the smaller the particle size, the shorter the longevity of the gel in tissue due to greater surface area exposure to enzyme and free radical degradation. HA polymers are crosslinked, usually with 1,4-butanediol diglycidyl ether, divinyl sulfone or 2,7,8-diepoxyoctane, to increase product longevity within the tissue. Injection of HA primarily has a direct filling effect on tissue (Quan et al., 2013), but there is limited evidence to show that HA gel may insert between collagen bundles, stretching collagen fibers and thereby triggering fibroblasts to produce new collagen (Quan et al., 2013). In general, HA fillers last between 4 and 24 months, depending on crosslinking, particle size, monophasic versus biphasic gel state, volume and location of injection, and host metabolism (Quan et al., 2013).

CaHA is a synthetic biodegradable compound composed of microspheres that contain calcium and phosphate, the same minerals found in human bone. The microspheres measure 20 to 45  $\mu\text{m}$  in diameter and are suspended in a glycerin-sodium carboxymethyl-

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**Fig. 1.** Calcium hydroxylapatite mixed with hyaluronic acid filler.

cellulose aqueous gel that dissolves between 1 and 3 months after injection. Injection of CaHA initially results in mechanical expansion of tissue, largely due to the volume of the carrier gel. However, the microspheres induce an inflammatory response that has a biostimulatory effect leading to fibroplasia, beginning at approximately 1 month, and eventual collagen synthesis. Therefore, volume seen from CaHA injection is initially largely due to the volume of the carrier gel, which dissolves within the first 3 months, and subsequently due to the volume created from biostimulation of collagen (Herrmann et al., 2018). In general, CaHA fillers last between 10 and 14 months, depending on the amount injected and host metabolism.

For 2 decades, the primary author has treated thousands of esthetic patients with HA, CaHA, or both fillers during the same treatment session. However, for >3 years, the primary author has been injecting HA (either Restylane Defyne, Juvederm Ultra Plus, or Revanesse Versa) combined with CaHA. The mixture consists of 1 mL of HA mixed with a 1.5 mL CaHA. The two fillers are mixed using a LeurLock connector system that enables the two products to be blended together into an evenly milky-white substance that is easy to inject through a 26 g or 27 g needle (Fig. 1). During the integration process, the combination product is mixed back and forward no less than 20 times. This process is performed immediately before injection because CaHA can precipitate and cannot sit for longer than a few minutes after being mixed. When injected, the HA–CaHA mixture is an elegant, moldable compound that integrates nicely into the tissue, including the temples, mid-face, nasolabial folds and marionette lines, chin, and jawline. The HA–CaHA mixture provides the patient with a smooth, even, highly supportive lift that achieves a very high level of patient satisfaction both in terms of esthetic appearance and longevity (Fig. 2).

In our case the patient was treated with the HA–CaHA mixture of 1.5mL CaHA and 1.0mL HA along the zygomatic arch (at the level of the periosteum), as well as along the melolabial crease and marionette lines (in the dermal and subdermal planes). In addition, she received a total of 147.5 U abobotulinum toxin within the frontalis, corrugator, procerus, orbicularis oculi, depressor anguli oris, and mentalis muscles.

The purpose of combining CaHA with HA is two-fold. First, the combination takes advantage of CaHA's high G' and HA's smooth texture to create a silky, milky-white gel that substantially lifts the tissue, but is smoother, more malleable, and easier to inject than CaHA alone. Second, volume loss over time seems to be less obvious when CaHA and HA are combined. This observation might be due to the fact that, although CaHA's carrier gel degrades relatively rapidly within 3 months, HA degradation takes place slowly and evenly over time, so HA remains present in the tissue to lessen the perceptible volume loss due to CaHA's carrier gel degradation. Additionally, as HA slowly degrades, CaHA's biostimulatory effect leads to delayed collagenesis, shifting the volumization effect from the HA filler to the CaHA filler. Of note, another benefit of combining CaHA with HA is that the HA portion of the combination increases the reversibility of the filler if hyaluronidase is used to treat complications, such as nodules or intravascular occlusion.

The authors acknowledge that mixing CaHA with HA changes the rheologic characteristics of each filler, and further study is needed to evaluate the rheologic and biostimulatory properties, as well as the longevity of the combination. They also acknowledge that not all HA fillers can be mixed with CaHA.

The primary author of the current article has used the HA–CaHA combination in over 250 cases with no adverse events (i.e. nodules, granulomas, vascular occlusion).



**Fig. 2.** (A) Immediately prior to the procedure. (B) Immediately after the procedure. (C) One week after the procedure. (D) Seven months after the procedure. (E) Nearly one year after the procedure.

This technique was only recently reported by [Chang et al. \(2020\)](#), who noted favorable outcomes. The primary author of the current article has used this technique in >175 cases with no adverse events (i.e., nodules, granulomas, vascular occlusion). Every patient injected with the HA–CaHA mixture has been highly satisfied with their immediate and long-term outcomes. Every patient seen in follow-up has requested the same HA–CaHA mixture, except for one who opted for one syringe of filler rather than the two-syringe HA–CaHA combination due to cost. This technique was only recently reported by Chang et al who also noted favorable outcomes. Of not HArmonyCa by Luminera is a HA–CaHA combination filler currently approved in certain countries outside the United States.

Although every patient's cosmetic goals are unique, generally the author finds that patients who identify as female desire more voluminous contour changes from fillers, such as anterior projection of the medial molar eminence. On the other hand, patients who identify as male generally prefer a more subtle and less voluminous change. As detailed by [Wieczorek et al. \(2015\)](#), sexual dimorphism lends to men requiring a flatter and wider cheek area rather than the fuller, rounder appearance that requires more fillers, as desired by female patients. It is important to always clarify the patients' goals and expectations, but in the authors' experience, the volume and properties afforded by the combination of HA–CaHA mixture has been an advantage in the female population specifically. High satisfaction on the part of the authors and their patients, as well as excellent esthetic and longevity outcomes, prompted the authors to publish this unique technique.

#### Conflicts of interest

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#### Study approval

The author(s) confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies.

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