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Rheomodulation of Calcium Hydroxyapatite: Implications for Cosmetic Treatment and Prevention of Complications

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Introduction

Hyaluronic acid (HA) dermal fillers are the most widely used injectable category worldwide for the treatment of cosmetically relevant volume depletion of the face. Their varied physical properties and reversibility make them highly versatile, safe, and capable of delivering outstanding cosmetic outcomes in the right hands. Unfortunately, an overreliance on HA dermal fillers as a treatment modality has led to overuse, resulting in unnatural outcomes. Heavily publicized on social media and via celebrity commentary, this trend has swung the pendulum toward "filler fatigue", a growing tendency among cosmetic patients to avoid HA dermal fillers in their treatment plans, whether or not such a caution is warranted.

This presents an opportunity for dermatologists who perform cosmetic procedures to consider widening their scope of treatment to include biostimulators, if they have not already done so. While biostimulators do not fully replace HA gels, which remain important tools for focal revolumization, contouring, and structural support, they introduce a distinct mechanism of action that provides both revolumization and skin quality improvements to patients in a progressive manner. As of 2025, the two major biostimulators available in Canada are poly-L-lactic acid (Sculptra®) and calcium hydroxyapatite (Radiesse®). In this article, we will build on the outstanding article by Dr. Malika Ladha on calcium hydroxyapatite (CaHA)[1] by outlining the clinical and safety implications involved in adjusting product rheology through dilution and hyperdilution of CaHA. We invite you to review her article, as we sought to avoid duplicating its content.

CaHA: From "Filler" to Skin Quality Treatment

CaHA has been commercially available in Canada for several years under the brand name Radiesse® (Merz Aesthetics, Canada). It is supplied in a 1.5 cc syringe containing 30% CaHA and 70% carboxymethylcellulose (CMC) carrier gel.[2] The Radiesse+® formulation contains lidocaine for increased patient comfort during treatment. According to the product monograph, it is classified as an injectable implant indicated for subdermal implantation in correcting moderate to severe facial wrinkles and folds, restoring and/or correcting the signs of facial fat loss (lipoatrophy) in people with human immunodeficiency virus, and for rejuvenating the hands.[2] As of 2025, it is also approved for treating moderate to severe wrinkles of the décolleté, albeit in a hyperdilute form (see below). Prior to the development of high-concentration, highly cross-linked, high-G' HA gel dermal fillers, CaHA stood alone as a very high-G' product, making it well-suited for supraperiosteal injections aimed at structural revolumization of the zygoma, mandible (**Figure 1**), and chin.

Injection yields immediate revolumization, largely from the CMC carrier gel, which will recede over the following weeks. During this time, CaHA microspheres come in physical contact with dermal fibroblasts, stimulating the production of type I and type III collagen, elastin, proteoglycans, and other components of the extracellular matrix.[3]

Effect of "Dilution" and "Hyperdilution" on Rheology of CaHA

By diluting CaHA (1:1 with diluent, yielding 3 mL) or hyperdiluting it (any dilution beyond 1:1, such as 1:2 with diluent yielding 4.5 mL or 1:3 with diluent yielding 6.0 mL) and administering it via subdermal injection, this mechanism of action can also be harnessed to improve skin quality. The diluent typically includes 0.5 mL of lidocaine, with the remaining volume made up of normal saline. This preparation is carried out using 3, 5, or 10 mL syringes and connectors, the process of which is described in detail in Dr. Ladha's article.[1]

One of the most critical concepts to grasp when using CaHA as a biostimulator (rather than a traditional filler) is that rheomodulation occurs rapidly, even with small amounts of diluent.[4] Common sense may suggest that doubling the volume with a 1:1 dilution would simply halve the product's G' and "stiffness": this is not the case. Diluting CaHA at a 1:1 dilution producing 3 mL total, reduces its G' by more than tenfold (**Figure 2**). At this concentration, CaHA can still provide both modest revolumization as well as improvement in skin quality of the treatment area. In contrast, hyperdiluted CaHA (e.g., 1:2, 1:3 or greater), yields a product with negligible G' that behaves more like a liquid than a gel, provides negligible revolumization, yet improves skin quality.

On-label Indication of Hyperdilute CaHA in Canada: Treating the Décolleté

In 2025, Radiesse® received an on-label indication for the treatment of moderate to severe chest wrinkles. Though dilution and hyperdilution of CaHA have long been common practice, this marks the first Health Canada-approved indication for the use of hyperdilute CaHA.

In the trial leading to approval,[5] 117 patients were enrolled and received 1–3 treatments of CaHA diluted at 1:2 (1.5 mL CaHA combined with 3.0 mL diluent, totalling 4.5 mL of product per treatment) injected across the décolleté area. Over 80% of the treatments were performed via cannula (25G, 50 mm), through three port sites. Sixteen weeks after the final treatment, the responder rate was 78.4%. Patients initially rated as severe (4/5 on the photonumeric scale; very severe [5/5] were excluded) achieved the best outcomes, with 89.3% demonstrating at least a 1-grade improvement.

Based on the author's experience, the ideal candidates for this treatment present with primarily textural, crêpe-like skin changes (**Figure 3**). Though deep etched-in rhytides can be softened, they may be more effectively addressed when combined with highly cohesive, low G' HA gels superficially injected with a needle during the same session. As the décolleté is susceptible to significant photodamage, pairing 1:2 CaHA injections with intense pulsed light, vascular

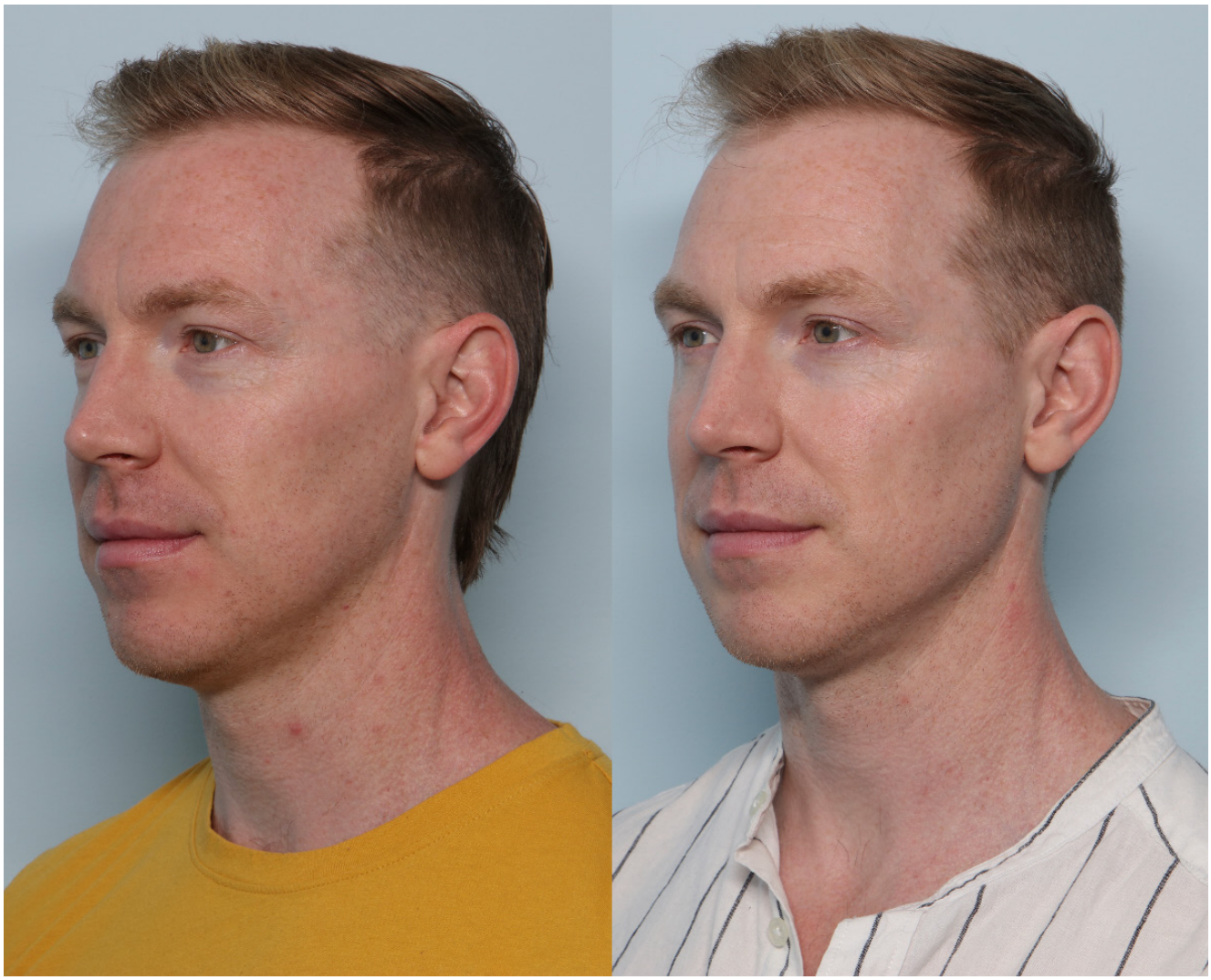

Figure 1. Jawline definition enhancement observed 3 months after administering 1.5 mL of CaHA per side to the mandible. For the horizontal segment of the mandible, 0.5 mL of CaHA was injected on bone using a needle, while the remaining 1.0 mL was injected subdermally via cannula to both the vertical and horizontal segments of the mandible; *photo courtesy of Vincent Richer, MD, FRCPC.*

laser, or laser resurfacing offers a high-yield combination approach, providing significant clinical improvement in one treatment visit.

Adverse Events with CaHA and the Mitigating Effects of Hyperdilution

When discussing the side effect profile of dermal fillers and biostimulators with patients, we group them into three categories: **1)** expected or probable local effects of treatment, **2)** nodules, and **3)** vascular compromise.

- **Local effects:** Treatment may cause pain from needle insertion, a sensation of pressure/sharpness from cannulas, purpura/ecchymosis, edema, and tenderness to touch.

These effects can be mitigated with gentle technique, patient distraction (verbal, vibratory, other), use of anesthetics (topical or injected at cannula port sites), avoidance of alcohol or medications/supplements that promote bruising when not medically necessary, and using acetaminophen instead if needed. We tend to

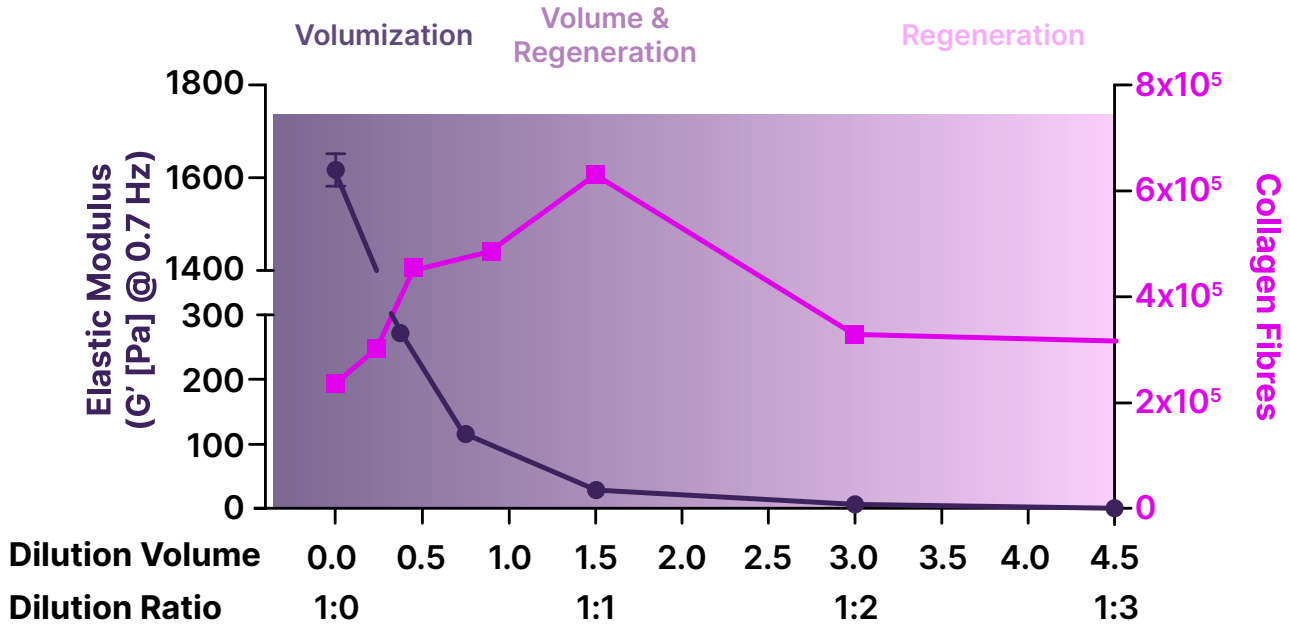

Figure 2. This graph highlights the rapid decline in elastic modiolus (G') as diluent is added to the syringe containing CaHA. Superimposed are in-vivo collagen measurements data, demonstrating the regenerative effect of CaHA when used as a biostimulator; *adapted from McCarthy et al. Dilutional rheology of Radiesse: implications for regeneration and vascular safety. J Cosmet Dermatol. 2024;23(6):1973-1984. doi:10.1111/jocd.16216.*

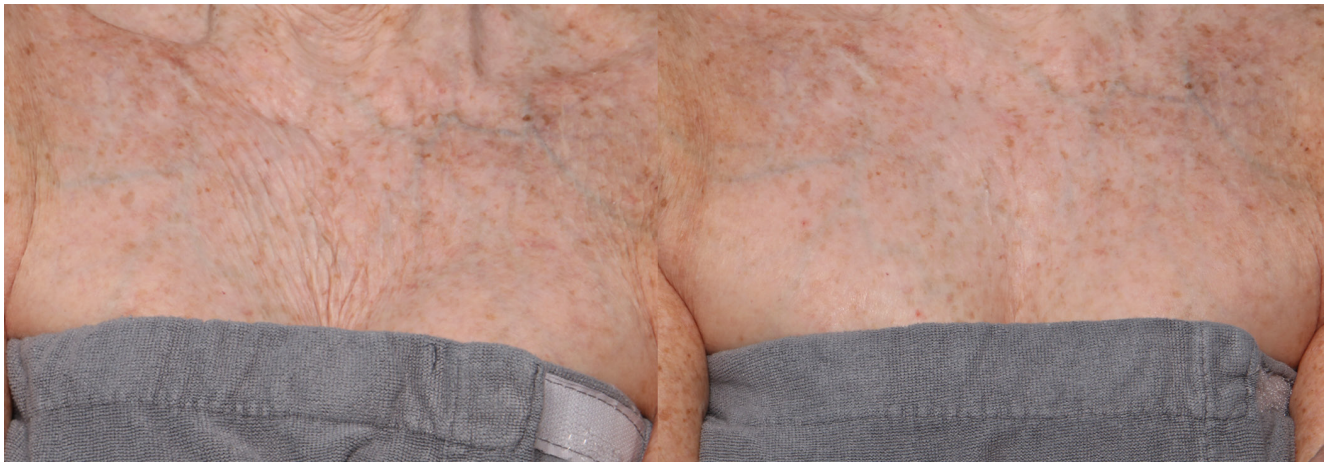

Figure 3. Improvement of crêpe-like texture of the décolleté observed 9 weeks after two treatment sessions, each using two syringes of CaHA (1:2 hyperdilution) per treatment; *photo courtesy of Vincent Richer, MD, FRCPC.*

overprepare patients by advising them to "expect a bruise" so they can plan their treatment around important social or professional engagements.

- **Nodules:** Nodules can present as product accumulation, focal biostimulation or "delayed-onset nodules" (DONs), the latter which are thought to have an immune or infectious origin, and may be described to patients as a foreign body reaction.

A nodule of product accumulation refers to visible and/or palpable CaHA below the skin. It may appear clinically as a nodule, or simply be palpated without affecting the cosmetic outcome. Such nodules typically become evident once edema/bruising from the procedure subside. They may result from excessive product deposition during needle injections or from overlapping passes when fanning with a cannula. Additionally, fibrous septae within the dermis and subcutis may segregate the product, even when distribution feels uniform during injection. Depending on the severity of the cosmetic concern and the patient's level of distress, watchful waiting and massage may be performed at this phase. A published strategy includes injecting normal saline followed by vigorous massage or the use of a focal vibration tool to promote resolution of this situation.[6] The putative mechanism is product dispersion (CaHA and CMC gel). To minimize the risk of product accumulation nodules, dilution or hyperdilution of CaHA is a sound strategy: the significantly lowered G' of the product alters its physical properties, making it behave more like a liquid than a gel.

A nodule may also appear weeks to a few months following an otherwise unremarkable treatment recovery. Although considered "late onset," these nodules are not clinically inflammatory and appear distinct from the DONs observed with HA dermal fillers. We hypothesize these nodules represent focal biostimulation: localized accumulation of collagen and elastin in an area of prior focal product accumulation that was previously clinically unnoticed. In our experience, saline injection for resuspension has been ineffective in this scenario. A published algorithmic approach recommends using intralesional triamcinolone acetonide as a second-line option,[7] and we have found that injecting a very small amount of triamcinolone acetonide (2 mg/cc) to be effective in this scenario (n=3). Generous massage immediately after CaHA-CMC treatment is a viable strategy to minimize the risk of both product accumulation and focal biostimulation nodules.

- **Vascular compromise:** The adoption of CaHA into clinical practice has been limited by valid concerns regarding vascular compromise, given the absence of an injectable reversal enzyme. Published protocols for managing vascular events with CaHA[8] focus on restoring tissue oxygenation through other means (massage, aspirin, hyperbaric chamber) similar to approaches used for vascular events that occur with HA. Interestingly, these protocols also recommend injecting hyaluronidase, with the aim of increasing tissue permeability to oxygen.

Vascular events associated with CaHA have been reported primarily with the undiluted product. Experimental models of occlusion have examined the occlusive potential of dilute and hyperdilute CaHA, suggesting that the odds of a vascular occlusion, especially with hyperdilute CaHA, is greatly reduced.[9] In clinical practice, the author limits CaHA use to areas with a lower risk of vascular occlusion (avoiding the nose, forehead, and nasolabial fold) and employs subdermal cannula injections to further mitigate risk.

Common Off-label Uses of CaHA

One of the most common indications for CaHA in the author's practice is revolumization and improving elasticity in the lateral cheek—covering the preauricular region, extending from inferior to the zygoma, down to the mandible, and lateral to soft tissue that may be contributing to the development of a jowl. CaHA diluted 1:1 is injected via cannula using a fanning technique, often through a single port site, with contralateral access to optimize injection ergonomics. Patients notice some immediate revolumization from the CMC carrier gel, followed by the biostimulating effects of CaHA over 6–12 weeks, resulting in subtle volume and increased elasticity (**Figure 4**). We encourage

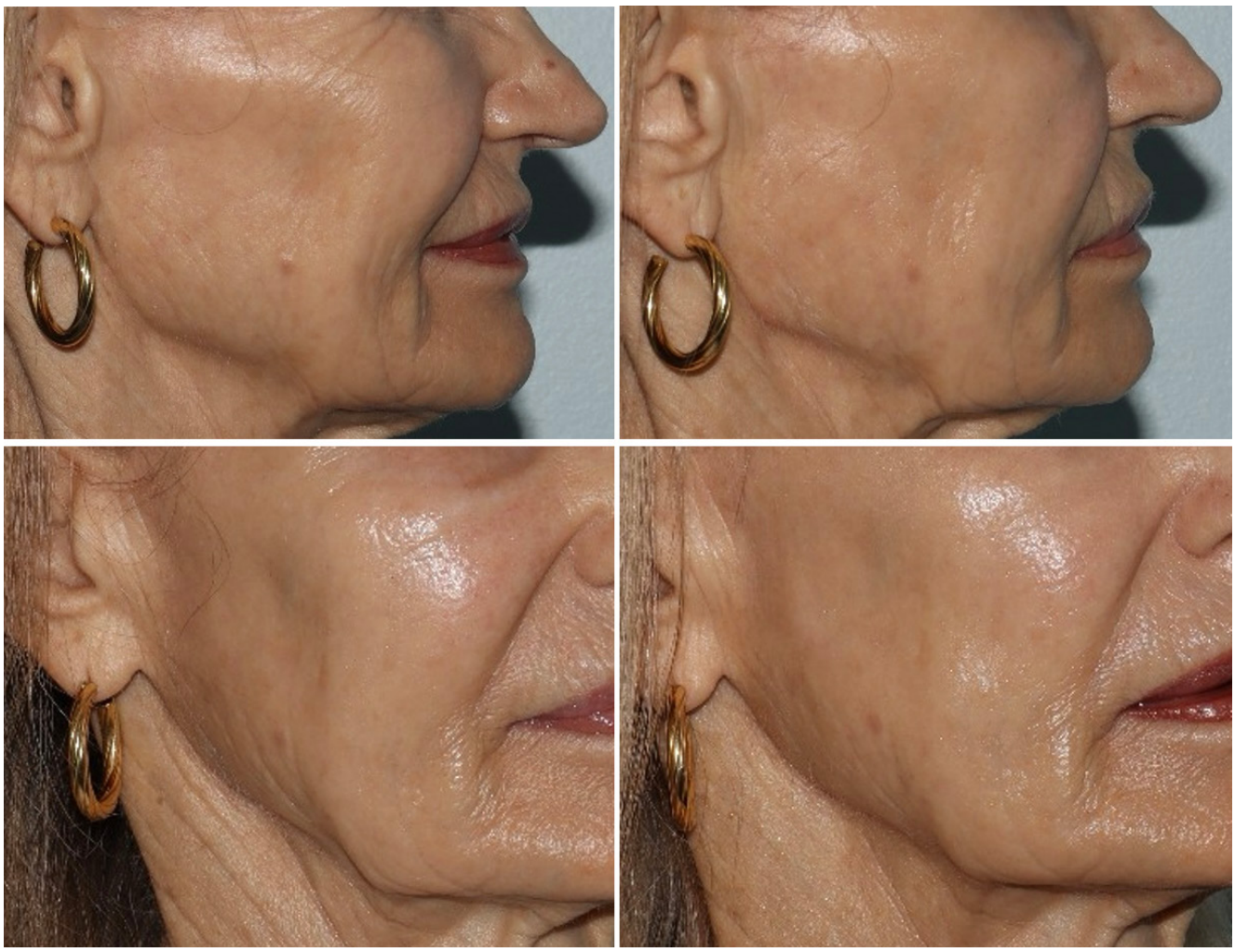

Figure 4. Lateral cheek revolumization and improvement in skin quality in a patient with severe volume depletion, observed 3 months after treatment with dilute CaHA (1:1),using one syringe per cheek. Note how the restoration of proportions subtly camouflages the jowl; *photo courtesy of Vincent Richer, MD, FRCPC.*

patients to touch their skin and pull it taut before the treatment, as the tactile improvement is often striking at their follow-up visit.

Hyperdilute CaHA has also become increasingly popular in the treatment of neck skin.[10] This anatomical site poses a challenge for treatment due to its particularly thin epidermis/dermis and minimal subcutaneous tissue. For patients with very thin skin, a hyperdilution of 1:3 (total reconstitution of 6.0 mL total) or greater is recommended. In younger patients with thicker skin, or those who show only a modest response after the 1:3 hyperdilution and experience no treatment-emergent issues, the author also considers using a 1:2 hyperdilution at this site. As was mentioned for the décolleté, the ideal candidates exhibit textural, crêpe-like skin changes, mild skin laxity, and minimal etched-in horizontal neck lines (**Figure 5**). Patients with severe laxity are better suited for surgical management, and horizontal lines may benefit from combination treatments such as HA injections. A challenge of treating this site is achieving even product distribution due to the ergonomics of treatment delivery. Multiple approaches are described in the literature; we recommend an approach that involves tracing down the midline and using three cannula port sites–two positioned laterally and inferiorly on the neck, and one at the midline between the chin and the thyroid cartilage (**Figure 6**).

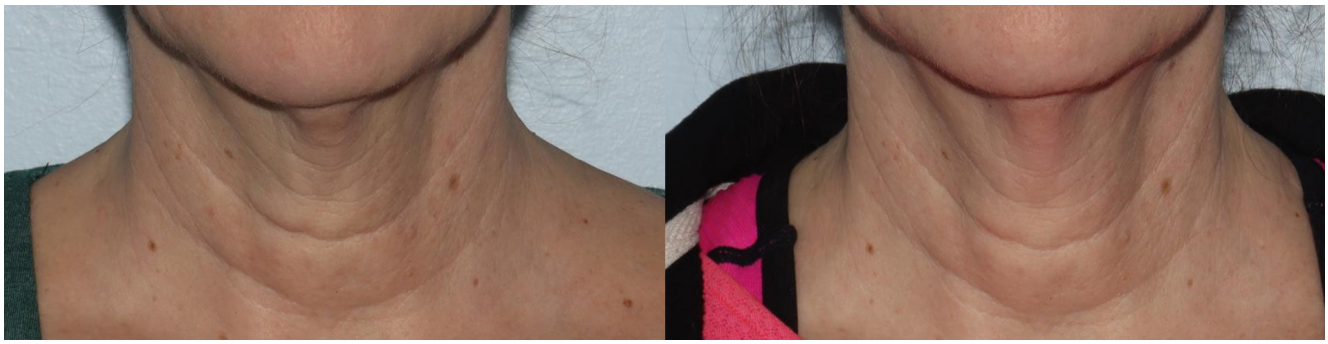

Figure 5. Softening of the crêpe-like texture of the upper neck observed 4 months after a single treatment using one syringe of hyperdilute CaHA (1:3 dilution). Note the persistence of horizontal "necklace" lines, which may require an additional treatment modality, such as HA, for further improvement; *photo courtesy of Vincent Richer, MD, FRCPC*.

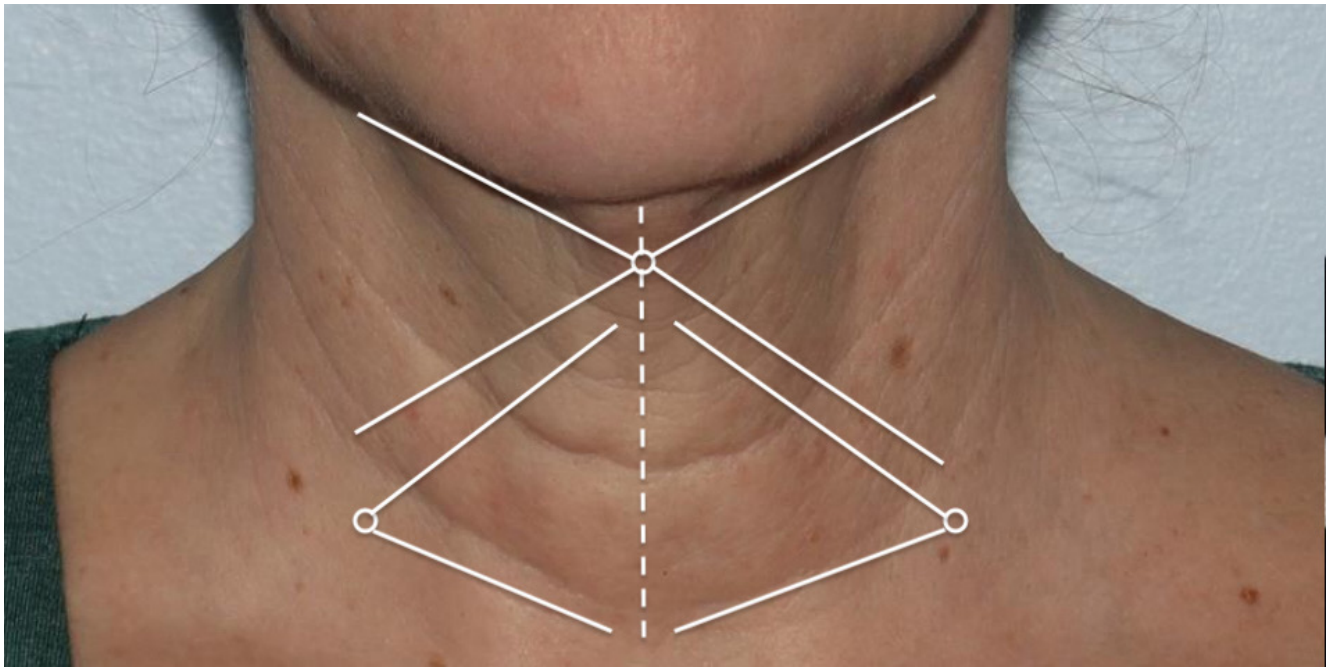

Figure 6. The author's preferred injection pattern for treating the neck with hyperdilute CaHA using a cannula, colloquially referred to as "the bowtie"; *photo courtesy of Vincent Richer, MD, FRCPC*.

The inferior treatment triangles can be accessed from the ipsilateral side, while the superior "bowtie" triangles are best approached from the contralateral side to optimize injector ergonomics. Carefully bending the cannula within its sterile cap can also aid navigation in this area. Similar to décolleté treatment, achieving clinically acceptable outcomes may require 2–3 sessions.

Keys to Success When Using CaHA as a Biostimulator

1. **Managing expectations and timelines:** Clinical results develop gradually over several weeks to a few months. For patients requiring more advanced correction, 2–3 treatments may be needed.

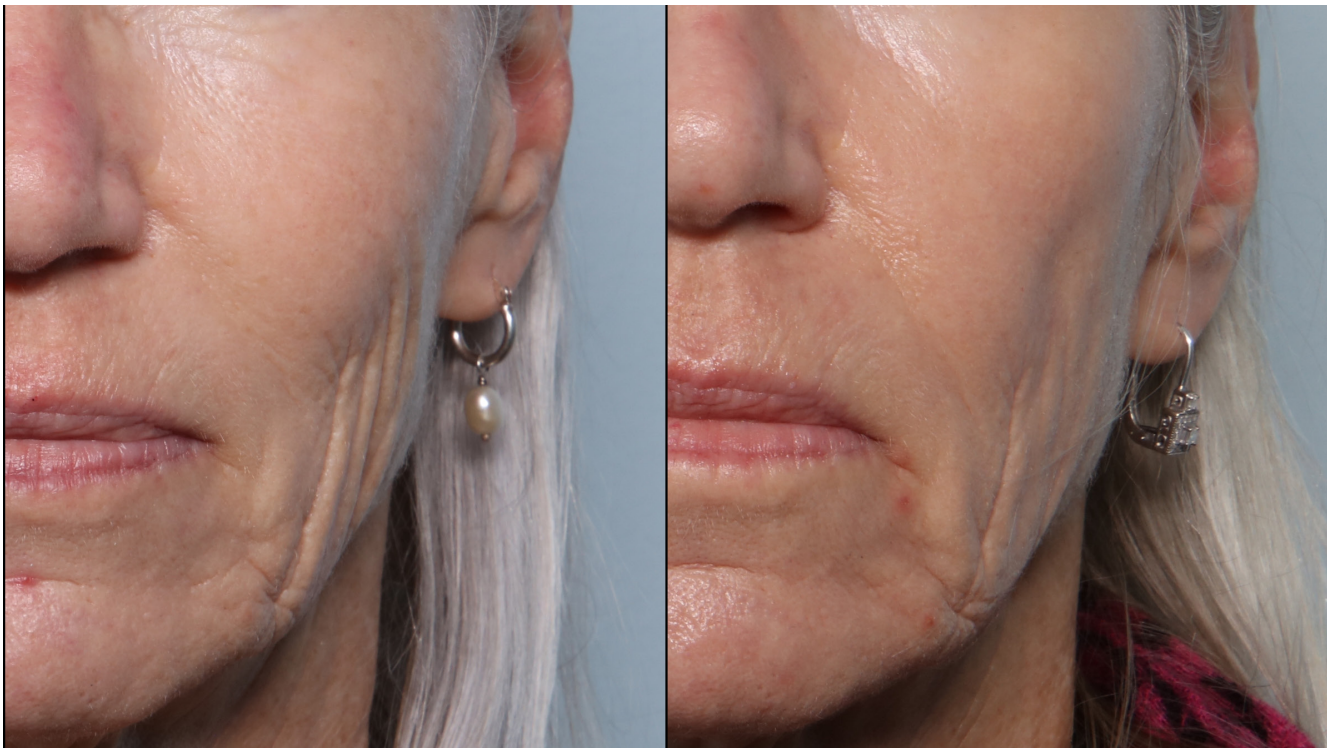

Figure 7. Combination treatment using high-density fractional thulium 1927 nm laser resurfacing with dilute CaHA (1:1) injected via cannula to the lower cheek rhytides; *photo courtesy of Vincent Richer, MD, FRCPC.*

2. **Treatment guideline—One 1.5 mL syringe per 10 × 10 cm² area:** This recommendation, frequently mentioned in position papers and trials on CaHA biostimulation, is often a footnote that may be overlooked. A practical rule of thumb is to use one syringe of CaHA per 100 cm² area, with larger surface areas requiring require more than one syringe per treatment session.
3. **Injection technique:** This treatment lends itself well to cannula injection. The cannula outline should remain visible under the skin, ideally positioned in the subdermal layer to maximize CaHA's biostimulatory effect. This also avoids overly superficial needle injections. Massage for a few minutes after the procedure is recommended to help ensure even product distribution.
4. **Combination treatments:** Same-day device-based treatments for skin quality or further skin tightening can improve outcomes with fewer sessions (**Figure 7**). In general, device treatments are delivered prior to injection of CaHA.

Blending CaHA with HA Dermal Fillers and Beyond

For several years, physicians worldwide have been modifying the rheological properties of CaHA by combining it with agents beyond lidocaine or normal saline. Some approaches have used platelet-rich plasma, platelet-rich fibrin, or other biologically-derived products to potentially boost the regenerative potential of CaHA. When CaHA is mixed with HA fillers and diluent, the formulation has been termed a "blend" or "hybrid". The objective is to provide greater short- to medium-term revolumization than the CMC carrier gel alone, while still benefiting from the biostimulatory effects of CaHA. This technique has been studied clinically for applications such as cheek revolumization, jawline enhancement, hand rejuvenation, and various other indications.[11]

Health Canada is expected to approve a fixed-dose hybrid product containing HA and CaHA (HarmonyCa®, Allergan Aesthetics) in the near future. The product is already available in

Brazil and in several countries across Europe and the Middle East.[12] Its introduction will further expand the CaHA-based therapeutic options that we can offer our patients.

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