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Special Topic

Panfacial Approach to Rejuvenation Using Calcium Hydroxylapatite: A Case Series Illustrating Calcium Hydroxylapatite Versatility Through Dilution and a Multilayered Treatment Approach

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Abstract

Dermal fillers can be used in a wide range of applications. Although the versatility of hyaluronic acid fillers stems from the wide array of available products, for the biostimulatory filler calcium hydroxylapatite (CaHA), dilution can be used to control product volumizing capacity and flow properties, facilitating use for panfacial rejuvenation. Here, the authors share case studies illustrating how CaHA at various dilutions can be used to achieve global aesthetic improvement as part of a multilayered approach to rejuvenation. As part of a continuing medical education activity, the authors treated patients with 1 to 3 sessions of CaHA at various dilutions. Six months after the patients' initial treatments, the authors reconvened to share their experiences and discuss patient results. Select case studies are presented. Though each patient recieved a unique treatment tilored to their own needs, several themes emerged. Although undiluted product can be used to provide deeper volume and structural support in areas like the chin, jawline, and temples, more dilute product (1:1 and 1:2) can be used to provide some volume and/or smooth transitions in the face, whereas hyperdilute CaHA can be used over an even wider surface area in the face, neck, or décolletage to tighten skin and improve skin quality (1:3 and 1:4 dilutions). In the cases presented, patients achieved improvement in appearance through treatment with multiple dilutions of CaHA, providing several examples of how CaHA may be used as part of a multilayered approach to facial rejuvenation.

Level of Evidence: 5 (Therapeutic)

Dermal fillers represent a remarkable advancement in antiaging and rejuvenation. In 2022 alone, over 640,000 filler injections were performed in the United States.[1] Part of what makes fillers so successful is their versatility: They can be used for a range of purposes, from restoration of deeper volume or structural support to more superficial injections that can address skin quality. Fillers can be considered as 2 main classes: space-filling agents, such as hyaluronic acid (HA), and biostimulatory fillers, which provide volume by stimulating the body's own pathways for collagenesis. For HA fillers, diversity in applications stems from the array of products produced by manufacturers. By changing features like as crosslinking or manufacturing technology, products with different flow properties are produced.[2] In contrast,

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for biostimulatory fillers, versatility arises from the ability of the injector to control the flow properties and the volumizing capacity of the filler through dilution. With a single unaltered product, deeper structural support can be obtained,[3] or the product may be diluted and injected in the subdermal plane to tighten and improve the quality of the skin.[4,5]

For calcium hydroxylapatite (CaHA; Radiesse; Merz North America, Inc, Raleigh, NC), dilution results in a gradual decrease in volumizing capacity; however, even at higher dilutions, the CaHA microspheres retain their ability to promote neocollagenesis and elastogenesis, making hyperdilute CaHA well suited for improving skin quality over a larger treatment area.[6,7] The effect of dilution on both CaHA rheology and collagen-stimulating capacity is predictable. As CaHA is diluted, both viscosity and G' (stiffness) steadily decrease[8] and because collagen stimulation is contingent upon direct contact between individual microspheres and fibroblasts, dilution also decreases biostimulatory activity (and therefore volumizing capacity).[9-13] Together, these impacts of dilution mean that a single product can be used for volume repletion and deeper structural support, intermediate dilutions can be used for purposes where softer, more viscous filler is needed with some volume, and dilute/hyperdilute microspheres can be used to induce improvements in skin quality. Although there are multiple guidelines published on injection techniques for both undiluted and diluted CaHA,[3,4] there is a need for further discussion of how multiple dilutions can be applied together by injectors to achieve global improvement. Here, the authors present several case studies using CaHA at multiple dilutions as part of a treatment approach to facial rejuvenation.

METHODS

As part of a continuing medical education (CME) series on panfacial rejuvenation (xMedica, Alpharetta, GA), which took place between June 2023 and March 2024, each of the authors was provided with CaHA, incobotulinum toxin A (INCO; Xeomin; Merz North America, Inc, Raleigh, NC), and cohesive polydensified matrix HA gel (CPM-HA; Belotero Balance; Merz North America, Inc, Raleigh, NC) and asked to select 2 or 3 case study patients for treatment. Once patients were identified and initial treatments were administered, the authors participated in a roundtable to discuss their patients' presenting concerns and their respective treatment approaches. Six months later, the authors reconvened to discuss the treatments administered and share their experiences and patient results. Selected case studies are presented below. Cases were selected based on photograph quality, and the need to prevent a diverse array of patients with a range of baseline conditions and complaints, as well as the full range of treatment approaches. Case patients were treated as part of normal clinical practice, and institutional review board approval was not obtained for this study. All patients provided consent for the use of their photographs and were treated in agreement with the principles outlined in the Declaration of Helsinki. This CME activity was sponsored by Merz Aesthetics (Raleigh, NC).

RESULTS

Six case studies selected by the authors for presentation in the final roundtable are presented here. Overall, injection techniques for varying CaHA dilutions adhered to published guidelines (Figure 1).[4,14] In general, for undiluted product, the primary goal of treatment is volumization and/or support, and placement is supraperiosteal or subdermal. Dilute product (diluted 1:1) can provide some support and volume, albeit to a lesser degree, while also improving skin quality.[14] For hyperdilute CaHA, the goal of treatment is skin tightening, and placement is in the subcutaneous plane. In this series, undiluted product was most often used to provide structural support along the mandible[15] and in the posterior temple[16,17]; CaHA diluted 1:1 was more often used in the midface, chin, and marionette area; 1:2 dilutions were used across facial areas; and 1:3 dilutions were used to treat the neck and body, where the skin was thinner. For reference, dilution volumes are shown in Figure 2. Each of the authors voiced that it is helpful to keep this type of diagram posted in the clinic to avoid confusion when discussing dilutions. In terms of diluent, the authors most often dilute CaHA(+) (CaHA with 0.3% integral lidocaine) with normal saline. When treating larger areas with higher volumes, it is rare but possible to reach lidocaine toxicity thresholds using diluent with 2% lidocaine as the diluent. In the authors' clinical experience, the lidocaine in CaHA(+) is generally sufficient to avoid any discomfort, even if the product is diluted. None of the authors reported adverse events, but they did note that patients must be informed that swelling following injection is expected and will resolve without the need for intervention. The authors have not noticed a difference in the amount of swelling that occurs for different dilutions of CaHA. Thus, all patients are informed of the potential for swelling.

Case Studies

Case 1

A 61-year-old female patient presented for rejuvenation with concerns around skin texture and quality and voiced a desire to improve her overall appearance, in particular, the contour of her jawline. In order to improve contour and facial shape, as well as to improve skin quality, the patient was treated with a combination of neuromodulators and CaHA at various dilutions. The patient is shown at baseline in Figure 3A-E.

The first treatment consisted of undiluted CaHA(+) (2.2 cc to the lateral bilateral zygoma, 0.3 cc in the chin, and 0.2 cc in the perioral area) to improve overall contour, 6.0 cc of CaHA(+) diluted 1:4 to the bilateral cheeks (30 cc total), and 4.5 cc of CaHA diluted 1:3 (18 cc total) to the perioral area. All diluted CaHA(+) was delivered with a 22 G cannula in the subcutaneous plane, and undiluted CaHA(+) was delivered with a 27 G, 1.25 inch needle to the supraperiosteal plane. A 1:4 dilution was used in the midface because the patient had thin skin and did not need further projection in this area. In addition, a total of 100 U of INCO was administered to the lateral canthal lines, and glabella (40 U), the jawline (above and below the mandible; 30 U), and the platysmal bands (30 U).

At the second treatment 6 weeks later, undiluted CaHA(+) was administered to the temples (0.8 cc) and the posterior jawline (1.2 cc), and a total of 6 cc of CaHA diluted 1:4 (30 cc total) was administered to the lateral cheeks.

At the third treatment 6 weeks later, a total of 100 U of INCO was administered to the glabellar area and lateral brow (35 U), the jawline (30 U), and the platysmal bands (35 U). The patient is shown in Figure 3F-J, 12 weeks following the final treatment (18 weeks after the final treatment with CaHA). The patient's skin quality was

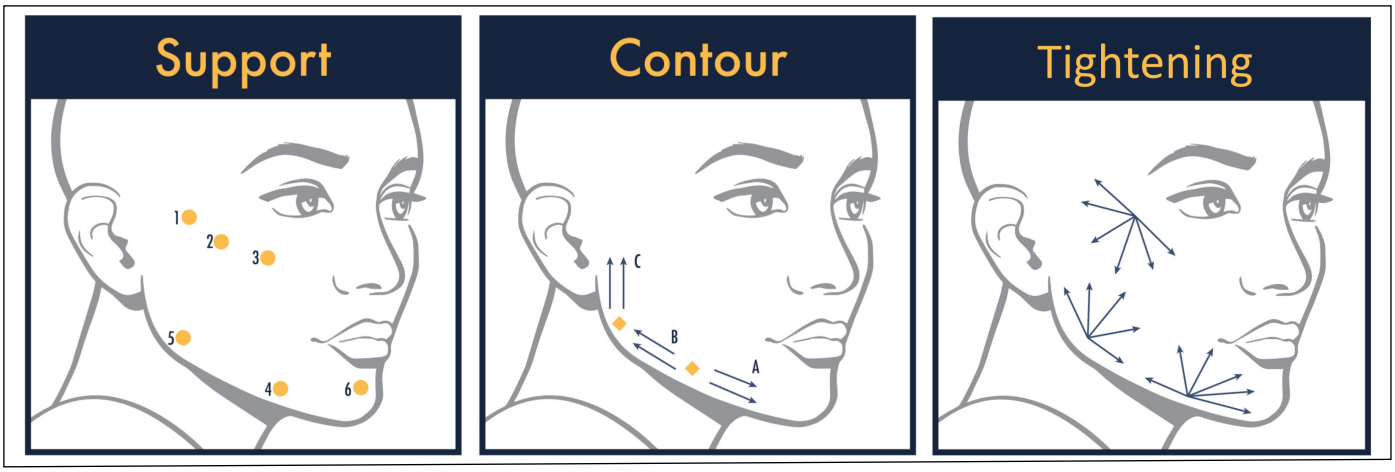


Figure 1. Injection patterns for undiluted and hyperdilute calcium hydroxylapatite. Illustration created by James Silvera, reproduced with permission from xMedica, LLC (Alpharetta, GA). (Image is modified from Lorenc et al,[14] with permission).

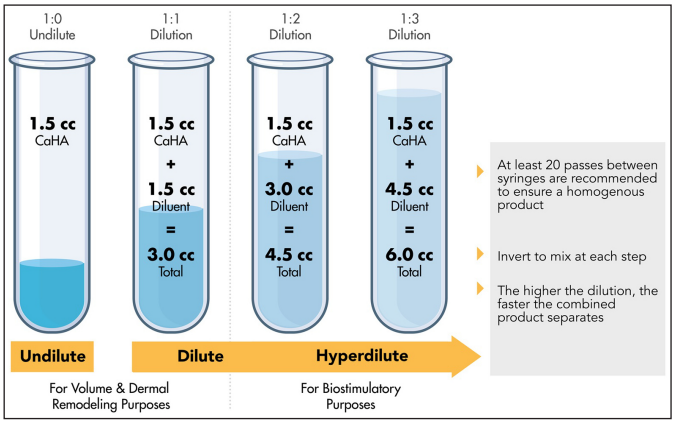


Figure 2. Schematic showing dilution volumes for diluting calcium hydroxylapatite 1:1, 1:2, and 1:3. Illustration created by James Silvera, reproduced with permission from xMedica, LLC (Alpharetta, GA).

substantially improved, and her overall facial shape was improved and more aesthetically balanced.

Case 2

A 46-year-old female patient presented seeking global rejuvenation and skin quality improvement, noting some heaviness along the brow. She voiced some apprehension around treatment and a fear of an unnatural-looking outcome. The patient had tried HA fillers in the past, but felt that the texture was “lumpy” and the results unnatural looking. The patient was also very active and had thin facial skin (Figure 4A-F). Initially, she was treated with CaHA(+) in the temples (4.5 cc, diluted 1:2; 13.5 cc total), midface (4.5 cc, diluted 1:2; 13.5 cc total), jawline (3 cc, diluted 1:1; 6 cc total), and neck (6 cc, diluted 1:3; 24 cc total). Higher dilution in the neck area permitted an even distribution of the product and avoided visibility under the skin. Dilute CaHA was delivered in the superficial subdermal plane with a 22 G cannula using a retrograde linear threading technique, consistent with published recommendations.[3,4]

Eight weeks later, at her second visit, the patient voiced satisfaction with the softening of the transitions in her face and elevation of her brow, as well as an improvement in skin quality. At this time, she was treated with CaHA(+) in the temples (3 cc, diluted 1:2; 9 cc total), midface (3 cc, diluted 1:1; 6.0 cc total), along the angle of the jawline (3 cc, diluted 1:1; 6 cc total), neck (6 cc, diluted 1:3; 24 cc total), and décolletage (6 cc, diluted 1:3; 24 cc total).

At her third visit, 4 weeks later, the patient was treated with CaHA(+) in the décolletage (6 cc, diluted 1:3) and 104.5 U of INCO in the face and neck. The patient is shown 6 weeks after the last treatment (18 weeks following her first treatment) in Figure 4G-L.

Case 3

A 61-year-old patient presented for rejuvenation, complaining of general aging and poor skin quality, descent of facial features, and skin laxity. The patient is shown at baseline in Figure 5A-E. The patient’s first treatment consisted of a total of 12 cc of CaHA administered first as an undiluted product in deeper layers with undiluted CaHA, followed by a more dilute product. The product was also placed laterally before more medial areas were injected. First, the patient received 1.5 cc of undiluted product to each posterior temple using a needle to place filler in the supraperiosteal plane. Next, 1.5 cc of CaHA diluted 1:1 (total volume. 3.0 cc) was injected into the temples in the subdermal plane with a 22 G cannula. The midcheeks were then treated with 0.75 cc CaHA diluted 1:3 per side (6.0 cc total) and 3.0 cc of CaHA diluted 1:3 in the lateral face, midcheek, and lateral cheeks (12 cc, total). Undiluted product, 0.75 cc per side, was then injected along the jawline. A total of 1.5 cc, diluted 1:1 (3.0 cc total), was injected into the chin and lower marionette area. She was also treated with 64 U of INCO in the glabella, lateral canthal lines, and frontalis.

The second treatment 8 weeks later consisted of 7.5 cc of CaHA: 2.0 cc of undiluted product injected with a needle in the temples (0.3 cc per side in the superior temple and 0.7 cc per side in the inferior temple), 0.5 cc per side in the pyriform, and then 1.0 cc in the chin and prejowl sulcus area. A total of 3.5 cc diluted 1:3 (13.6 cc) was placed in the marionette, lower cheek, preauricular area, and cheeks. The patient is shown 7 months after the second treatment in Figure 5F-J.



Figure 3. Case study Patient 1. A 61-year-old female patient at baseline (A-E) and 18 weeks after the second of 2 treatments with calcium hydroxylapatite (F-J). Treatment areas included the perioral area (1:3); bilateral zygoma and cheeks, posterior jawline, and temples (1:4); and the chin and jawline (undiluted). The patient also received incobotulinum toxin A in the crow's feet, glabella, jawline, and platysma bands.



Figure 4. Case study Patient 2. A 46-year-old female patient at baseline (A-F) and 6 weeks after the third of 3 treatments with calcium hydroxylapatite[+] (diluted 1:1, 1:2, and 1:3) to the temples, midface, jawline, neck, and décolletage (G-L).



Figure 5. Case study Patient 3. A 61-year-old female patient at baseline (A-E) and 7 months after the second of 2 treatments with calcium hydroxylapatite (undiluted and diluted 1:1 and 3:1; F-J). The patient was treated in the lateral face, midcheeks, lower cheek/preauricular area, jawline, marionette, temple area, piriform, and chin.

Case 4

A 61-year-old patient presented with complaints of aging and skin quality concerns (Figures 6A-E and 7A-C). The patient was treated with 1.5 cc of CaHA (diluted 1:1) in the upper face (3.0 cc total), including the cheeks, temples, and lateral midface from the jawline to the temple and periorbital area. She was also treated with 1.5 cc of CaHA diluted 1:1 in the lower face (3.0 cc total), including the perioral area and the subdermal plane. All products were injected with a 22 G cannula. The patient was also injected with 35 U of INCO (30 U in the glabella and forehead and 5 U in the perioral lines, above and below the lip) and 0.5 cc of CPM-HA gel (Belotero Balance) in the corners of her mouth and 0.5 cc to her lips.

Six weeks later, the patient was treated with 4.5 cc of CaHA. Most areas of her face were treated with a 1:1 dilution, including the lateral cheeks, periorbital area, temples, nasolabial folds, and chin (9.0 cc total). The patient was also treated with 3.0 cc in the neck (diluted 1:2, 9 cc total volume).

Six weeks later, 1.5 cc of CaHA diluted 1:4 (7.5 cc total) was used to treat the left side of the neck and wrinkles around the eyes and around the mouth, and 1.5 cc diluted 1:6 was used to treat the right side of the neck (10.5 cc, total). The patient is shown 12 weeks after the final treatment in Figures 6F-J and 7D-F.

Case 5

A 60-year-old female patient who presented for rejuvenation, voicing concerns about looking tired (Figure 8A-E). Before this treatment, the patient's aesthetic interventions had been limited to topical creams: she had no history of injectables or facial surgery. Initial treatment included 1.5 cc of CaHA diluted 1:2 for the bilateral temples (4.5 cc total), 1.5 cc diluted 1:2 for the midface (4.5 cc total), and 1.5 cc diluted 1:3 (6.0 cc total) for blending in the submalar area and lateral posterior cheeks. She also received 0.5 cc of undiluted CaHA in the prejowl sulcus and in the anterior and posterior mandible and 1.0 cc of CaHA diluted 1:3 (4.0 cc, total) to the neck. Diluted forms of CaHA were injected subcutaneously using a 25 G cannula, and undiluted forms were injected supraperiosteally using a 27 G, 1.25 inch needle. The patient also received 94 U of INCO to the forehead, glabella, lateral canthal lines, masseters, and platysmal bands and CPM-HA gel (Belotero Balance) to manage fine lines around the mouth and bilateral oral commissures (0.6 cc) and in the glabella (0.4 cc).

Six weeks later, the patient received 4.5 cc of CaHA: 1.5 cc diluted 1:3 (6.0 cc total) in the lower face, neck, and arms; 1.5 cc diluted 1:2 in the midface (4.5 cc total); and 1.0 cc undiluted to the jawline.

Six weeks later the patient was treated with 46 U of INCO in the forehead, lateral canthal lines, and CPM-HA (Belotero Balance) in the left oral commissure (0.1 cc) and left marionette (0.1 cc). The patient is shown 5 weeks after the third treatment in Figure 8F-J). At this time, the patient was offered additional injections for further refinement, which she declined because of satisfaction with the current outcome, instead choosing to start annual maintenance treatments.

Case 6

A 60-year-old female patient presented with concerns of skin texture in the decolletage. The patient was treated with 1.5 cc of CaHA at a 1:2 dilution (4.5 cc total volume per treatment), injected with a 22 G



Figure 6. Case study Patient 4. A 61-year-old female patient at baseline (A-E) and 12 weeks after 3 treatments with calcium hydroxylapatite (diluted 1:1, 1:2, 1:4, and 1:6; F-J).

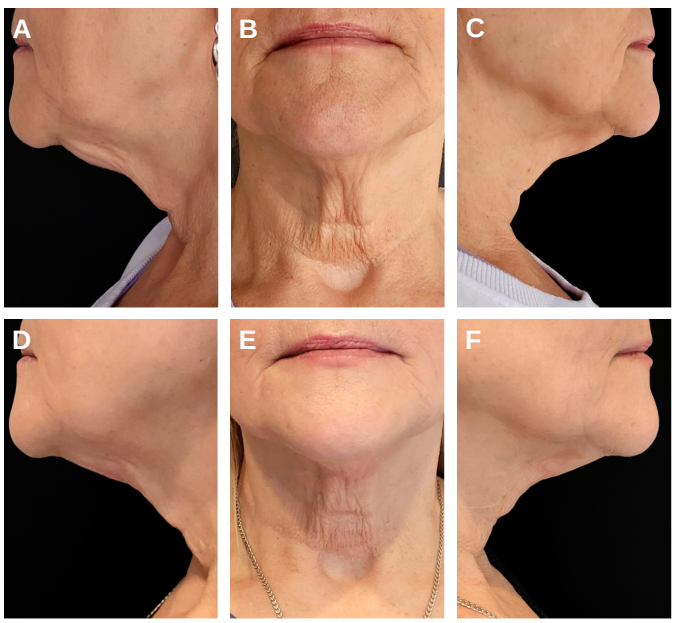


Figure 7. Case study Patient 4. A 61-year-old female patient at baseline (A-C) and 12 weeks after 2 treatments with calcium hydroxylapatite (D-F); the first treatment was calcium hydroxylapatite diluted 1:2, and the second was calcium hydroxylapatite diluted 1:4 (left side of the neck) and 1:6 (right side of the neck).

cannula in a fanning pattern in the subcutaneous plane, with strands perpendicular to the vertical chest lines. This patient was treated for 3 sessions, ~6 weeks apart. The patient was satisfied with the results both in terms of the volume effect and the improvement in her skin quality (Figure 9).

DISCUSSION

The case studies presented here illustrate the clinical versatility of CaHA when used at various dilutions for panfacial, neck, and décolleté rejuvenation. When CaHA is diluted, multiple depths and injection techniques may be used to treat a single patient to achieve a combination of volumetric and structural improvements, as well as improvements in skin quality. The behavior of CaHA when diluted is predictable, and results are natural looking, a central concern for many patients. Because treatments can be performed as a series, the patient is repeatedly assessed over time, and the product can be used judiciously. The injector is also able to combine the techniques that have been established for undiluted and diluted CaHA in order to suit the patient's needs. Although skin quality changes are especially difficult to capture with clinical photography, the impact of treatment on the patients' skin texture, and skin tone can be appreciated in the presented cases.[18]

The patients presented here had varying levels of experience with aesthetic interventions. For example, the patient in Figure 8 had never been injected before, whereas the patient in Figure 4 had previous, albeit negative, experience with fillers. For each of these patients, the experience of injection with CaHA was accessible and resulted in global improvement that the patient found satisfying. In each instance, CaHA treatment was tailored with both product dilution and placement to ensure the best outcome.



Figure 8. Case study Patient 5. A 60-year-old female patient at baseline (A-E) and 5 weeks after 3 treatments with various dilutions of calcium hydroxylapatite to the jawline (undiluted), neck and submalar area (1:3), midface and cheeks (1:2) alongside 90 U of INCO to the forehead, glabella, lateral canthal lines, brow, masseters, and platysmal bands (F-J). The patient also received CPM-HA to manage fine lines around the mouth and fine lines in the glabella.

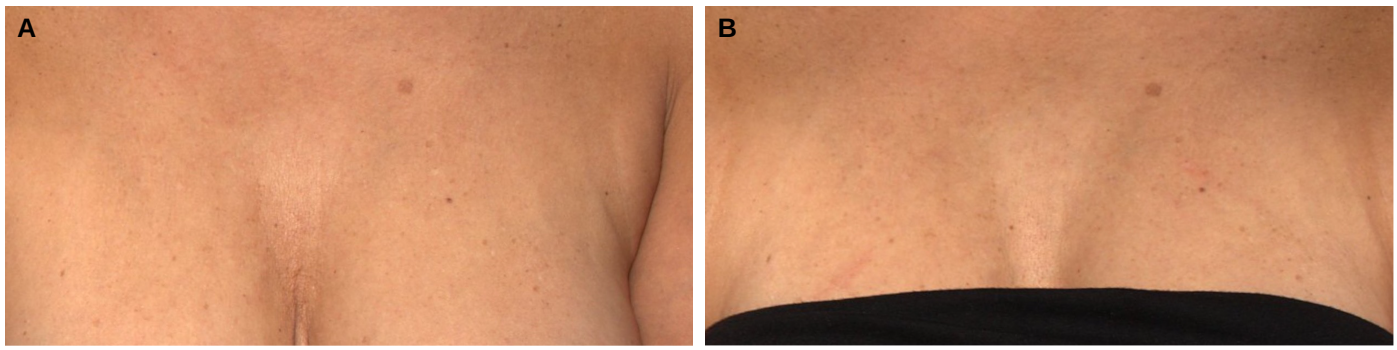


Figure 9. Case study Patient 6. A 60-year-old female patient at baseline (A) and 5 weeks after (B) 3 treatments with calcium hydroxylapatite diluted 1:2 to the décolletage.

In addition, the nature of the key outcomes is diverse. For example, the patients in Figures 3 and 5 have a more balanced facial shape, whereas the patients shown in Figures 4 and 6 each have smoother facial transitions and improved skin quality, as well as some lifting of facial features. Of note, in Figure 6, the patient was treated primarily with a 1:1 dilution. In this treating author's experience, injection of 1:1 CaHA throughout the entire face, including temporal, periorbital areas achieves predictable results. In her experience, hyperdilution of product, past 1:3 (ie, 1:4 and 1:6) has resulted in variable or inconclusive results. Additionally, she often injects the area above the lip (superior to the vermillion border and laterally relative to the philtrum up to the nasolabial folds) which is particularly prone to volume loss with age, with a 1:1 dilution.

Dilution allows for control of CaHA filler rheology while maintaining biostimulatory activity, and thus personalized treatment with a single product can be achieved. Importantly, many of the patients presented here would be candidates for facelift surgery or other surgical interventions; however, improvement is achieved with biostimulatory fillers. It is important that patients are educated about both the benefits and limits of nonsurgical interventions so that they are able to make the treatment choice that best suits their objectives. Biostimulatory fillers are able to support and tighten tissues; however, they are not able to achieve the lift possible with excisional surgery. Helping patients to understand the nature of the results that can be achieved is critical for ensuring satisfaction. During the roundtable, the authors agreed that it is best to stop

treatments with CaHA a minimum of 6 months before facelift surgery to avoid any unnecessary difficulty with dissection. Importantly, improving skin mechanical properties, including thickness and elasticity[7] with CaHA before surgery, may permit a better outcome. Although thin skin can be pulled tight, it is still thin unless measures are taken to improve thickness and mechanical properties. It would be interesting to collect data or document outcomes for patients treated with biostimulatory fillers before surgery so that any benefit can be determined.

In the authors' experience, the safety profile of using multiple dilutions in a single treatment session is good; use of multiple dilutions does not pose any added risk. Patients should be informed of and prepared for the minor swelling typical of CaHA injection. Aside from swelling, the most commonly encountered adverse event is bruising, which occurs in roughly 3% of patients at cannula insertion sites, and is more common with body injections than facial injections. When undiluted product is placed in the supraperiosteal plane, away from concentric muscle groups, and is injected properly, the risk of lumps or nodules is low, especially with postinjection massage.[19] To date, none of the authors have experienced delayed inflammatory nodule formation in their patients when using diluted CaHA; however, a retrospective assessment of a larger, multicenter, real-world study population would be of benefit for identifying any risk factors for nodules. Irrespective of dilution, it is critical that biostimulatory fillers not be injected intradermally or in the infraorbital hollows.[20] There are several publications detailing injection techniques that can be used for reference.[3,14,15,21-23]

The limitations of this case series are inherent—in order to build a complete picture of safety profile and to quantify improvement and duration, a clinical study would need to be conducted. It is impossible to draw conclusions about efficacy and duration from a case series; however, these cases provide examples of how CaHA, which has an established clinical activity at multiple individual dilutions, can be used to help patients reach their aesthetic goals. In addition, the cases were selected to showcase a variety of techniques in a range of patients—cases were not selected randomly.

CONCLUSIONS

Biostimulatory fillers represent a versatile class of fillers that can be diluted to achieve multiple different aesthetic effects. CaHA is a potentially valuable tool, when used in undiluted and diluted forms as part of an approach to panfacial rejuvenation.

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Disclosures

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