

SDC3. Summary of findings of the included studies.

Author, year	Injected area	Results
Facial		
Pavicic, 2022 ⁵	NLFs, marionette lines, and/or cheeks	<p>Investigators Nasolabial Folds improvement: Post-CaHA: Above the pre-defined 60% rate (p<0.0001).</p> <p>Investigators Marionette Lines improvement: Post-CaHA: Above the pre-defined 60% rate (p<0.0001).</p> <p>Investigators Upper Cheek Fullness improvement: Post-CaHA: Above the pre-defined 60% rate (p<0.0001).</p> <p>Investigators Global Aesthetic Improvement: 96.5% of subjects were improved</p> <p>Patients Global Aesthetic Improvement: 93.5% of patients reported the improvement.</p> <p>Patients satisfaction:</p> <ul style="list-style-type: none"> • <i>Pre-CaHA (Mean Rasch-Transformed Score per FACE-Q Module):</i> <ul style="list-style-type: none"> • Satisfaction with facial appearance: 37.8 • Satisfaction with cheeks: 40.6 • Appraisal of marionette lines: 37.8 • Appraisal of NLF: 68.7 • <i>Post-CaHA (Mean Rasch-Transformed Score per FACE-Q Module)::</i> <ul style="list-style-type: none"> • Satisfaction with facial appearance: 56.1 • Satisfaction with cheeks: 66.3 • Appraisal of marionette lines: 67 • Appraisal of NLF: 68.7
Tzikas, 2004 ⁵⁰	NLFs, Upper/lower lip, Glabella region, Prejowl area, Marionette lines.	Patients satisfaction: 47% of patients reported as excellent satisfaction, 41% good, 6% fair, 2% poor, 3% NA.
Barbarino, 2021 ³⁵	Temple area	<p>Investigators Global Aesthetic Improvement: 80% of patients very much improved and 20% much improved.</p> <p>Patients satisfaction: 6 subjects were extremely satisfied, 3 were very satisfied, and 1 was satisfied.</p> <p>Temple Hollowing Scale:</p> <ul style="list-style-type: none"> • <i>Pre-CaHA:</i> 3 subjects were rated as grade 2, 5 as grade 3, and 2 as grade 4. • <i>Post-CaHA:</i> 9 were rated as grade 1 indicating a flat temple with no depression, and one subject who was rated grade 4 before treatment had improved to grade 2.
Juhász, 2018 ¹²	Temporal fossae at the level of the deep fascial plane	<p>Investigators Temple volume improvement:</p> <ul style="list-style-type: none"> • <i>Pre-CaHA (Mean):</i> 2.7 • <i>Post-CaHA (Mean):</i> 1.5.

		Patients Global Aesthetic Improvement: Patients reported that their global aesthetic improved moderately with injection into the temporal fossae.
Aletaha, 2017 ⁵⁷	Orbit	Sulcus deformity: The grading of deep superior sulcus deformity showed an improvement of 0.83 (range, 0-2 grades) (p= 0.004) from preoperative to postoperative status.
Alghoul, 2020 ³⁴	Lateral periorbital region	Investigators Global Aesthetic Improvement: <ul style="list-style-type: none"> • <i>Post-CaHA</i>: 4 ± 0.63 corresponding to much improved. Patients satisfaction: 6 of 20 were satisfied and 14 were very satisfied.
Corduff, 2019 ⁵⁴	Periorbital	Skin thickness: Improvements in hyperpigmentation and skin tone, thickness, and color were visible in the treated areas at 14–16 weeks. Aesthetic Improvement: GAIS and modified TTRS scores showed that all patients experienced satisfactory post treatment improvements.
Juhász, 2018 ⁵⁶	Jawline	Jawline volume loss: <ul style="list-style-type: none"> • <i>Pre-CaHA (Mean)</i>: 2.2 (moderate volume loss). • <i>Post-CaHA (Mean)</i>: 0.7 point improvement with a reported mean assessment of 1.3. • <i>Post vs Pre</i>: p=0.001 Patients Global Aesthetic Improvement: 7 patients reported much improved, 3 moderately improved, 4 minimally, 5 not improved, 1 minimally worse.
Rokhsar, 2008 ⁴³	Dorsal nasal surface	Patients satisfaction: 13 out of 14 (~92%) reported extreme satisfaction.
Stupak, 2007 ⁴⁸	Dorsal nasal surface	Patients satisfaction: 62% of patients reported the satisfaction as excellent, 15% good, 8% fair and 8% poor. Efficacy assessment by physician: 88% of the injection sites demonstrated improvement (kappa statistics = 0.62).
Becker, 2008 ³⁶	Nasal bridge, lateral nose, columella, nasal tip.	Patients satisfaction: <i>Post-CaHA</i> : 50% of the patients rated their satisfaction as 10; approximately 78% as 8 or better; approximately 90% as 6 or higher. The mean degrees of satisfaction with the treatment results was 7.9.
Tanaka, 2014 ⁴⁹	Anterior nasal spine	Patients satisfaction: <i>Post-CaHA</i> : 90% of the patients were either satisfied or very satisfied. The mean degrees of satisfaction with the treatment results a 5-point scale from 0 to 4 were 3.38 ± 0.81.
Silvers, 2006 ⁴⁶	Cheek area (usually the sub malar region)	Patients Global Aesthetic Improvement: 91% of patients reported as improved (defined as GAIS at least 3) at month 18. Patient satisfaction: at month 12, 100% reported the treatment beneficial to them. Skin thickness: <i>Pre-CaHA (Mean)</i> : 4.7mm <i>Post-CaHA (Mean, at month 12)</i> : 7.10mm <i>Mean change</i> : 2.33 <i>Post vs Pre</i> : p<0.05
Carruthers, 2008 ⁵³	Sub malar region (extended to malar eminence and zygoma)	Patients Global Aesthetic Improvement: 2 (6.9%) patients reported as very much improved, 13 (44.8%) much improved and 14 (48.3%) improved. Skin thickness: <i>Pre-CaHA (Mean±SD)</i> : 5.3±0.8mm <i>Post-CaHA (Mean±SD)</i> : 8.8±1.5 mm <i>Mean change</i> : 3.5±1.3 <i>Post vs Pre</i> : p<0.01

Muti, 2019 ¹³	1-3 areas (cheeks, marionette lines, prejowl sulcus, jawline)	Doctors Aesthetic improvement: <i>Post-CaHA (Mean):</i> 1.1 Patients Aesthetic improvement: <i>Post-CaHA (Mean):</i> 2.2 (range 1.0 - 3.0).
Jacovella, 2005 ⁴⁰	Glabella wrinkles, NLFs, lips, nose, infraorbital areal	Patient satisfaction: 87% of patients reported as very good rating.
Beer, 2008 ³⁷	Malar area	Patient satisfaction: 5 (31%) of patients reported very satisfied, 7 (44%) satisfied, 3 (19%) no opinion, and 0 dissatisfied. Investigators aesthetic rating: Investigators reported 3 (19%) of patients as very much improved, 12 (75%) improved, 1 (<1%) unchanged, 0 worse. Patients Global Aesthetic Improvement: 3 (19%) of patients reported as very much improved, 4 (25%) as much improved, 7 (44%) as improved, 2 (13%) as no change, 0 worse. Investigators Global Aesthetic Improvement: Investigators reported 2 (13%) of patients as very much improved, 7 (44%) as much improved, 6 (38%) as improved, 1 (<1%) as no change, 0 worse.
Dayan, 2008 ⁵⁵	lower one third of face (NLFs, prejowl sulcus, oral commissure grooves, marionette lines)	Physicians severity of wrinkles: <i>Pre-CaHA (Mean):</i> ~ 4.2 <i>Post-CaHA (Mean):</i> ~ 3.1 Wrinkle severity scores demonstrated marked improvement at 2 weeks after optimal treatment and remained improved throughout the 1 year of follow-up. Patients Global Aesthetic Improvement: 77% of patients reported at least improved. Investigators Global Aesthetic Improvement: Investigators reported 48% of patients at least improved.
Rauso, 2013 ⁴²	NM	Patient satisfaction: High patients satisfaction was achieved in all cases.
Baspeyras, 2017 ⁵¹	Mandibular angle, prejowl sulcus, posterior cheek vector, cheek bone	Investigators Aesthetic improvement score for jawline contour: <i>Pre-CaHA (Mean):</i> 2.42 <i>Post-CaHA (Mean):</i> 1.45 <i>Post vs Pre:</i> p= 0.0015 Investigators Aesthetic improvement score for marionette lines: <i>Pre-CaHA:</i> 2.33 <i>Post-CaHA:</i> 1.50 Patients Aesthetic Improvement: Over 89% of the subjects rated the esthetic effect as improved to very much improved at every follow-up visit. Investigators Aesthetic Improvement: The esthetic effect was rated as improved to very much improved in 81% (among 26 patients) subjects.
Roy, 2006 ⁴⁴	Melolabial folds and lips	Patients satisfaction: <i>Post-CaHA (Mean):</i> 4.6 Investigator satisfaction: <i>Post-CaHA (Mean):</i> 4.5
Sadick, 2007 ⁴⁵	NLFs, lips, perioral lines, Cheeks, tear trough depression, pre jowl sulcus	Patient satisfaction: <i>Post-CaHA (Mean):</i> 4.8 Investigator satisfaction: <i>Post-CaHA (Mean):</i> 4.5
Fakhre, 2009 ³⁸	NLFs	Patients satisfaction: Overall patient satisfaction with Radiesse was 3.7 (range: 1–5) or moderately to very satisfied.
Sklar, 2004 ⁴⁷	NLFs, tear trough, lips, infraoral, cheeks, mental crease, above upper lip, buccal region.	Patient and Investigator satisfaction: Patient and physician satisfaction were high.
Vagefi, 2011 ⁴	Orbital	Relative enophthalmos measurement: 2.4 mm reduction per syringe of filler.

		Patients clinical and aesthetic improvement: 87% of patients demonstrated clinical and aesthetic improvement that was observed to continue up to 1.5 years.
Bernardini, 2014 ⁵²	Tear trough area	Patient and Investigator aesthetic improvement: 92% of patients reported improvement. Investigators reported improvement among 92.5% of patients.
Hevia, 2009 ³⁹	Under the eyes (malar crease, the nasojugal folds, and the tear trough, which constitute the infraorbital groove)	Patients satisfaction: Anecdotal comments from the 301 patients were overwhelmingly favorable (Patients expressed satisfaction with the improvements in their infraorbital areas). Investigator improvement assessment: As is the case with other areas of the face, improvement in appearance of the infraorbital region tended to be proportional to the severity of the defect.
Wollina, 2020 ¹¹	Cheeks, tear troughs, jawline, Marionette lines	Investigators Global Aesthetic Improvement: <i>Post-CaHA:</i> 2.5 ± 0.7 (2 corresponds to minute improvement). Patients Global Aesthetic Improvement: <i>Post-CaHA:</i> 2.4 ± 0.8 (2 corresponds to minute improvement).
Kim, 2018 ⁸	Forehead	Effectiveness on Forehead: In all cases, physician analysis of results indicated that tissue indentations were relieved, forehead projections increased, forehead curves were evened out, profiles were balanced, and skin surfaces smoothened. Patient satisfaction: Satisfaction rate was 100%.
Jansen, 2006 ⁴¹	NLF, lips, Radial lip lines, Corner of mouth, Marionette lines, Glabellar lines, Cheek/chin lines, Acne scars, Scar deformities, Facial depression (HIV lipoatrophy), Cheek augmentation, Nasal depressions, Tear troughs	Patients satisfaction: 77 (69%) of patients were satisfied, 27 (24%) dissatisfied and 8 (7%) undecided.
Rovatti, 2020 ⁷	Mid and lower face (upper cheek fullness, NLFs, marionette lines, oral commissures, jawline)	Investigator Severity Scores for Mid and Lower Face Scales (Mean ± SD): <i>Pre-CaHA (Mean±SD):</i> Upper cheek fullness: 2.7 ± 0.6 Nasolabial fold at rest: 2.8 ± 0.6 Oral commissure at rest: 2.4 ± 0.7 Marionette lines at rest: 2.4 ± 0.8 Jawline at rest: 2.1 ± 0.7 <i>Post-CaHA(Mean±SD):</i> Upper cheek fullness:0.97 ± 0.4 Nasolabial fold at rest: 0.95 ± 0.4 Oral commissure at rest: 0.8 ± 0.5 Marionette lines at rest:0.7 ± 0.6 Jawline at rest:0.8 ± 0.5 <i>Post vs Pre (Mean±SD):</i> Upper cheek fullness:1.7 ± 0.5 Nasolabial fold at rest: 1.9 ± 0.4 Oral commissure at rest: 1.5 ± 0.6 Marionette lines at rest:1.6 ± 0.5 Jawline at rest:1.3 ± 0.5 <i>Post vs Pre:</i> p<0.0001
Di Maria, 2024 ⁵⁸	Orbital area	Patient satisfaction: 87.5% of patients were very satisfied and the other 12.5% were satisfied. Orbital volume: <i>Pre-CaHA:</i> 14.16 ± 2.15 mm <i>Post-CaHA(Mean reduction):</i> 3.35 ± 0.91 (month 6) 2.97 ± 1.35 (year 3) <i>Post vs Pre:</i> p<0.001

Improvement: Most patients demonstrated clinical and cosmetic improvement, which was observed to continue for up to 10 years

Hands

Kim, 2021 ²¹	Hand	Hand grading: <i>Pre-CaHA (Mean±SD): 3±1</i> <i>Post-CaHA (Mean±SD): 2.5±0.6</i>
Sadick, 2011 ²²	Hand	Investigators wrinkle severity: <ul style="list-style-type: none">• <i>Pre-CaHA:</i>• Right hand wrinkles: 20 percent as deep, 50 percent as moderately deep and 30 percent as some wrinkles.• Left hand wrinkle: 20 percent of left hand wrinkles as deep, 40 percent as moderately deep and 40 percent as some wrinkles.• <i>Post-CaHA:</i> 20 percent of right and left hand wrinkles as moderately deep, 40 percent as some wrinkles and 30 percent as barely perceptible wrinkles. Patients wrinkle severity: <ul style="list-style-type: none">• <i>Pre-CaHA:</i> 20 percent of right and left hand wrinkle severity as deep, 60 percent as moderately deep and 20 percent as some wrinkles.• <i>Post-CaHA:</i>• Right hand wrinkles: 10 percent as deep, 10 percent as moderately deep, 50 percent as some wrinkles and 20 percent as barely perceptible wrinkles.• Left hand wrinkles: 10 percent as deep, 20 percent as moderately deep, 40 percent as some wrinkles and 20 percent as barely perceptible wrinkles. Patients satisfaction: 60% of the patients rated their results as satisfactory or better.
Haq, 2010 ¹⁹	Thinning tissue of aging hand	Investigators Global Aesthetic Improvement: Physicians evaluated 98% of the patients as improved or better on the GAIS. Investigator satisfaction: 93% of physicians reported satisfied or better Patients satisfaction: 86% of patients reported satisfied or better.
Adel, 2023 ⁵⁹	Hand	Patient satisfaction: <i>Post-CaHA (Mean±SD): 4.79 ± 0.17</i> <i>Post vs 14 days after treatment (Mean±SD): 0.18 ± 0.03 (p=0.537)</i>
<u>Abdomen/Upper arm</u>		
Lapatina, 2017 ⁶¹	Abdomen	Dermal thickness: Results demonstrated a statistically significant increase in dermal thickness after injection of diluted CaHA at both the center and sides of the abdomen (p≤0.05 for both areas). The improvement was greatest in the area of the umbilicus, where an increase in thickness of 0.7 mm vs 0.4 mm at the sides of the abdomen was noted. Combining measurements from the two abdominal ultrasound scan areas to give a mean dermal thickness, the results showed that treatment with a 1:4 dilution of CaHA resulted in a statistically significant increase in dermal thickness of 26.7% (p≤0.05) Patients Global Aesthetic improvement: 70% of patients reported very much improved, 20% much improved, 10% improved.
Lapatina, 2017 ⁶¹	Upper arm	Skin elasticity: <i>Pre-CaHA (Mean): 72 U</i> <i>Post-CaHA (Mean): 82 U</i> <i>Post vs Pre: p<0.05</i> Patients Global Aesthetic improvement: 90% of patients rated themselves as having good to very good improvement and the remaining 10% rated as improved.

		Investigators Global Aesthetic improvement: Investigators rated 80% of patients as much improve, 10% very much, 10% improved.
Wasylkowski, 2015 ⁶²	Thigh, hemiabdomen or brachial zone	<p>Skin flaccidity: Across all treatment zones, Cutometer data showed improvements in skin flaccidity vs baseline in 78% of cases at 5 weeks after treatment, most commonly in the thighs (82% of cases). The mean reduction in flaccidity from baseline to 5 weeks after treatment was also calculated, and was 0.0924 mm, 0.0117 mm, and 0.0814 mm for the brachial zone, thighs, and abdomen, respectively. The overall mean reduction in flaccidity from baseline to 5 weeks after treatment was 0.093 mm.</p> <p>Skin flaccidity (Subjects rated): <i>Pre-CaHA:</i> Mean subject-assessed flaccidity scores for the thighs, abdomen, and brachial zones were 3.6, 3.7, and 3.8, respectively. <i>Post-CaHA:</i> Following treatment, subject-assessed flaccidity scores showed an improvement versus baseline in 27 of the 36 treated zones (75%): The mean self-assessed flaccidity score following treatment was 2.6 for the thighs, 2.7 for the abdomen, and 3.0 for the brachial zones.</p> <p>Skin density: Improvements in skin density relative to baseline were recorded in the majority of measurements across all treatment zones. The abdomen showed the best treatment response, with improvements versus baseline in 88% of cases.</p> <p>Skin thickness: Skin thickness showed improvement versus baseline in the majority of cases, but most frequently in the thighs (88% of cases).</p>
Amselem, 2016 ⁶⁰	Upper arm	<p>Investigator satisfaction: <i>Post-CaHA (Mean):</i> 4.6</p> <p>Patient satisfaction: <i>Post-CaHA (Mean):</i> 4.53</p> <p>Skin flaccidity (Subjects rated): <i>Pre-CaHA (Mean):</i> 2.8 <i>Post-CaHA (Mean):</i> 7.63</p> <p>Skin flaccidity (Investigator rated): <i>Pre-CaHA (Mean):</i> 3.5 <i>Post-CaHA (Mean):</i> 7.53</p> <p>Volume (Investigator rated): <i>Pre-CaHA (Mean):</i> 3.6 <i>Post-CaHA (Mean):</i> 7.5</p>
		<u>Neck/ Chest/ Décolletage</u>
Guida, 2021 ⁶⁴	Neck	<p>Neck skin laxity severity:</p> <ul style="list-style-type: none"> • <i>Pre-CaHA (Mean±SD):</i> 2.3±0.8 • <i>Post-CaHA (Mean±SD):</i> 1.2±0.5 <p>Patients satisfaction: After treatment, 65% of patients were very satisfied and 30% were satisfied, 5% neither satisfied nor dissatisfied.</p>
Fabi, 2021 ⁶³	Chest wrinkle/ Décolletage	<p>Chest wrinkle appearance (Dynamic and at rest): significant improvement in both dynamic and at rest scores at the end of study compared to baseline (p<0.01).</p> <p>Patients satisfaction: a non-significant increase from 3.25±2.0 at day 180 to 3.59±2.1 at day 360. (No comparison with baseline was reported)</p>
Yutskovskaya, 2017 ⁶⁵	Neck and Décolletage	<p>Skin elasticity: <i>Pre-CaHA (Mean):</i> 0.57 <i>Post-CaHA (Mean):</i> 0.73 <i>Post vs Pre:</i> p<0.00001.</p> <p>Skin viscoelasticity: <i>Pre-CaHA (Mean):</i> 0.66 <i>Post-CaHA (Mean):</i> 0.5 <i>Post vs Pre:</i> p<0.05.</p> <p>Dermal Thickness:</p>

		<p><i>Pre-CaHA (Mean):</i> 1462.3 mm <i>Post-CaHA (Mean):</i> 1865.9 <i>Post vs Pre:</i> p<0.0001.</p> <p>Investigators Global Aesthetic Improvement: <i>Post-CaHA (Mean):</i> 2.15 ± 0.37 <i>Post vs Pre:</i> indicating much improved compared to baseline.</p> <p>Patients Global Aesthetic improvement: <i>Post-CaHA (Mean±SD):</i> 2.55 ± 0.51 <i>Post vs Pre:</i> indicating much improved compared to baseline.</p>
De Almeida, 2023 ⁶⁶	Neck	<p>Horizontal necklines: 86.4% (95% CI: 68.3 - 99.9%) decrease by at least 1 point. Neck Laxity: 81.8% (95% CI: 72.7 - 90.1%) decrease by at least 1 point. Dermal Thickness: There was an overall time-dependent improvement in dermal thickness (p<0.01). The total dermal thickness increased by 14.9% (95% CI: 8.5–21.3%). Patients Global Aesthetic Improvement: 90.9% (95% CI: 77.3–99.9%) reported improvement compared to baseline. Patient satisfaction: 82% of patients were very stratified, 9% satisfied, 4% neutral, and 5% reported worsened results.</p>
<u>Knee/ Foot/ Buttocks</u>		
Guida, 2020 ⁶⁷	Area above the knee	<p>Knee cellulite severity score: <i>Pre-CaHA (Mean±SD):</i> 4.9±1.4 (range 2-9) <i>Post-CaHA (Mean±SD):</i> 1.8±1.5 (range 0-6) <i>Post vs Pre:</i> p<0.05</p> <p>Patients satisfaction: 66.7% of cases were very satisfied and 33.3% satisfied.</p>
Custozzo, 2020 ⁶⁸	Dorsum of foot	<p>Patients Global Aesthetic Improvement: Graded by the patients as 4, connoting good improvement (range 3 to 5). Thickness of the layers of the dorsum: <i>Post-CaHA (Mean±SD):</i> Dorsal superficial fatty layer: 0.72±0.12 mm. Dorsal intermediate fatty layer: 0.60±0.08 mm. Dorsal deep fatty layer: 2.13 ± 0.28 mm</p>
Durariaj, 2024 ⁶⁹	Buttocks	<p>Cellulite severity: <i>Pre-CaHA (Mean±SD):</i> 9.77 ± 2.71 (severe) <i>Post-CaHA (Mean±SD):</i> 5.48 ± 2.55 (Mild to moderate) <i>Post vs pre:</i> mean of 4.29 (3.58 – 5.05) decreases, p < 0.0001</p> <p>Investigators Global Aesthetic Improvement: 20.8% of patients were scored as very much improved, 6.5% as much improved, and 12.5% as improved. Patients Global Aesthetic Improvement: 20.8% of patients reported very much improvement, 54.2% much improvement, and 16% improvement.</p> <p>Number of visible dimples and dimple depth- Investigators: Visible dimples: <i>Pre-CaHA (Mean±SD):</i> 5.56 ± 0.98 <i>Post-CaHA (Mean±SD):</i> 2.56 ± 1.36 <i>Post vs pre:</i> mean of 3 (2.56 - 1.36) decreases, p < 0.0001 Dimple depth: 0.015 mm (50.9%) reduction.</p>

NLFs: Nasolabial folds; GAIS: Global Aesthetic Improvement Scale; TTRS: Tear Trough Rating Scale.