

Microfocused ultrasound in combination with diluted calcium hydroxylapatite for improving skin laxity and the appearance of lines in the neck and décolletage

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Summary

Background: Skin laxity and wrinkling on the neck and décolletage reveal age as reliably as the face.

Objective: To evaluate the combined use of microfocused ultrasound with visualization (MFU-V; Ultherapy[®]) and diluted calcium hydroxylapatite (CaHA; Radiesse[®]) for treating the neck and décolletage.

Methods: Subjects with moderate-to-severe lines on the neck and/or décolletage were retrospectively enrolled. MFU-V was applied using 7 and 10 MHz transducers followed by subdermal injection of CaHA diluted 1:1 with lidocaine solution. Photographs at baseline and 90 days were assessed by two independent, blinded evaluators using three scales: Merz Aesthetics décolleté wrinkles, Fabi-Bolton chest wrinkle, and Allergan transverse neck lines scales.

Results: A total of 47 subjects were treated as follows: 29 (neck only), five (décolletage only), and 13 (both areas). Mean neckline score improved from 2.6 (moderate-to-severe lines) at baseline to 1.3 (mild lines) 90 days after treatment ($P < .001$). Mean décolletage scores improved from 2.6 and 3.3 (moderate-to-severe wrinkles) on the Merz Aesthetics and Fabi-Bolton scales, respectively, to 1.1 and 1.8 (mild wrinkles), respectively, after treatment (both $P < .001$). Both procedures were well tolerated with high subject satisfaction.

Conclusions: Combining MFU-V with 1:1 diluted CaHA is effective for improving the appearance of neck and décolletage lines and wrinkles.

KEYWORDS

calcium hydroxylapatite, décolletage, esthetic medicine, microfocused ultrasound, neck, skin laxity

1 | INTRODUCTION

With the availability of botulinum toxins and dermal fillers to smooth lines and wrinkles and restore volume to the face, imperfections in the neck and décolletage often stand out in stark contrast to reveal a person's age and are a significant esthetic concern for many people. These areas are also often neglected in terms of skincare and sun protection yet are just as prone to the effects of UV damage as

the skin on the face. The décolletage in particular receives considerable sun exposure, and its skin is thinner than the skin on the arms and the legs, making it extremely vulnerable to UV damage. In women, the décolletage is also subject to constant physical stresses from the weight and movement of the breasts, contributing to the worsening of the deep, vertical cleavage wrinkles that appear as the skin becomes older and thinner. As a result of hormonal changes relating to the menopause and estrogen deficiency, women in their

40s and 50s are more prone to aging in this area. These changes result in an accelerated breakdown of collagen and elastin, leading to skin thinning and laxity, and worsening lines and wrinkles.

Microfocused ultrasound with visualization (MFU-V) delivered by the Ulthera® System (Ultherapy®; Ulthera, Inc., Mesa, AZ, USA) is a proven technique for inducing neocollagenesis^{1,2} and subsequent skin tightening and is approved by the United States Food and Drug Administration and in Europe to noninvasively lift the eyebrow, submental and neck tissue, and improve lines and wrinkles of the décolletage. A number of studies have demonstrated its effectiveness for tightening the skin of the neck and décolletage with benefits including less skin sagging, fewer lines and wrinkles, and smoother skin texture.³⁻⁷

The collagen-stimulating properties of calcium hydroxylapatite (CaHA, Radiesse®; Merz North America, Inc., Raleigh, NC, USA) can also be harnessed to improve skin mechanical properties by diluting the product with either lidocaine or saline.^{8,9} The use of this technique alone in the skin of the neck and décolletage has recently been shown to stimulate the synthesis of collagen and elastin, and induce angiogenesis. Treatment was associated with a significant increase in dermal thickness and improved skin mechanical properties including elasticity and pliability.⁹

Both MFU-V and CaHA have individually demonstrated efficacy for skin tightening and improving skin properties in the neck and décolletage as well as other areas. The aim of this study was to evaluate the efficacy and safety of combining these two skin-tightening procedures for the treatment of moderate-to-severe lines of the neck and décolletage.

2 | METHODS

2.1 | Inclusion criteria

This was a retrospective study of patients who had undergone MFU-V and CaHA treatment for skin laxity and lines on the neck or décolletage. The study included male and female subjects aged 35-65 years with moderate-to-severe lines on the neck and/or décolletage. Signed informed consent forms were obtained from each subject prior to study initiation in accordance with the principles of the Declaration of Helsinki. Individuals who were not compatible with the prescribing criteria for the products were excluded, as were those who had received any other treatment for lines in the neck and décolletage area in the previous 12 months, had undergone prior surgery in this area or any treatment for skin laxity in the previous 90 days. Individuals receiving anticoagulant or immunosuppressor treatment, those with autoimmune diseases, and pregnant or breastfeeding women were also excluded.

2.2 | Assessment scales

Each subject made two visits to the center. At the first visit and before the treatment, subjects underwent a pretreatment evaluation by the investigator. Three scales were used to assess skin laxity and

wrinkling in the neck and décolletage area at baseline: the Merz Aesthetics Décolleté wrinkles at rest scale,¹⁰ the Fabi-Bolton chest wrinkle scale,¹¹ and the Allergan transverse neck lines scale.¹² The Merz and Fabi-Bolton scales are both validated five-point scales for the décolletage area. The Fabi-Bolton scale considers wrinkles at rest only and uses grades from 1 to 5,¹¹ whereas the Merz scale considers both dynamic and at rest wrinkles as well as pigmentation changes and uses grades from 0 to 4.¹⁰ The Allergan scale is validated to assess horizontal necklines with grading ranging from 0 to 4.¹²

2.3 | Treatment procedure

Prior to the procedure, the areas to be treated were marked with a pen and a thin layer of ultrasound gel applied in addition to a topical anesthetic (7% lidocaine, 7% prilocaine cream). For both the neck and décolletage, subjects were treated at two depths using the 7-MHz transducer at a focal depth of 3.0 mm and the 10 MHz transducer at a depth of 1.5 mm, applying 150 lines per site (Figures 1 and 2).

Immediately after MFU-V, subjects received treatment with CaHA 1.5 mL diluted 1:1 with 1.5 mL of 2% lidocaine solution.

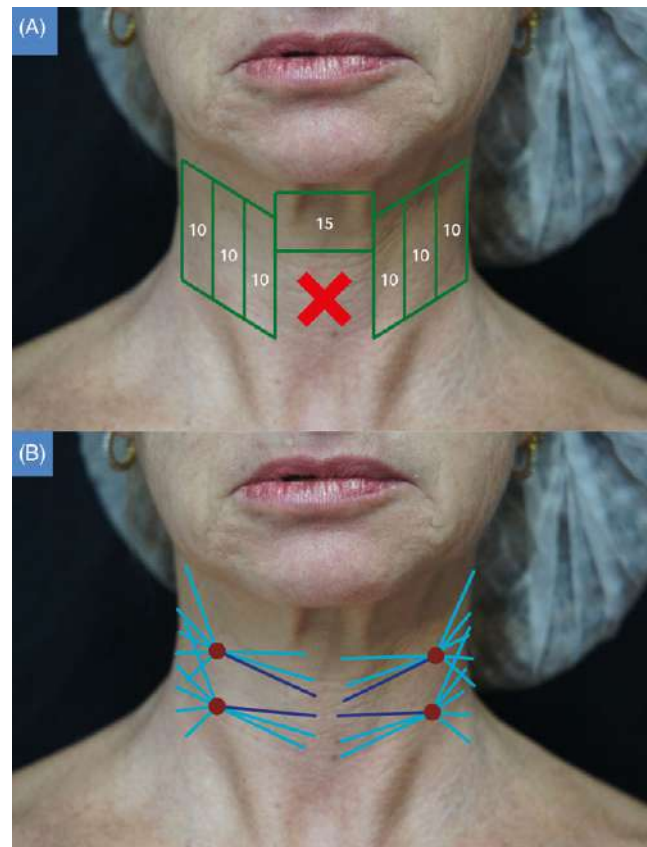


FIGURE 1 Treatment plan for the neck illustrating A, location and number of lines for microfocused ultrasound with visualization and B, entry points of calcium hydroxylapatite injection and direction of lines used in fanning technique

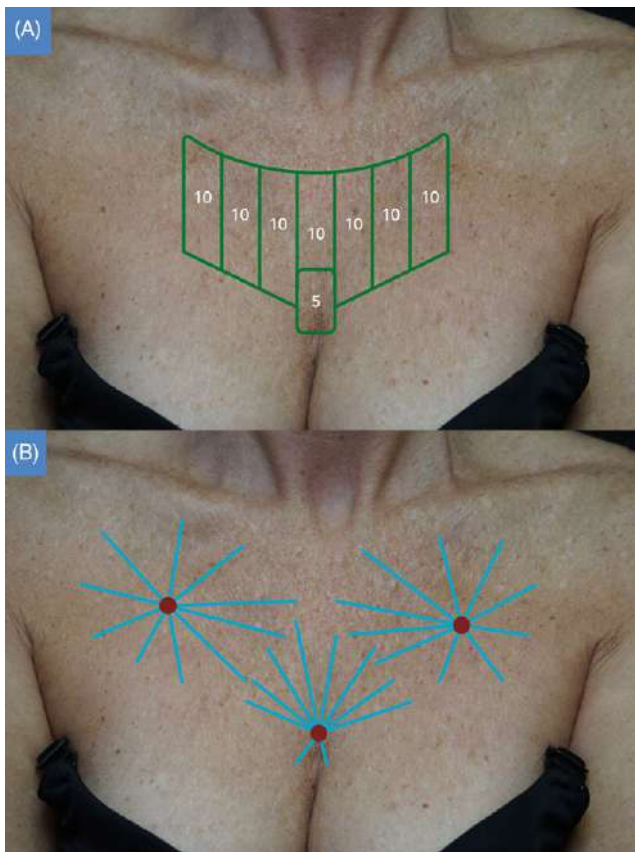


FIGURE 2 Treatment plan for the décolletage illustrating A, location and number of lines for microfocused ultrasound with visualization and B, entry points of calcium hydroxylapatite injection and direction of lines used in fanning technique

Cannula entry points were injected with 0.05 mL 2% lidocaine with 2% epinephrine. For the neck, CaHA was injected subdermally in microdroplets using a fanning technique with a 50 mm-long 25G cannula from four points of entrance starting on top of the lines and extending in a fan shape around the lines to cover the same area as the MFU-V (one-half of a syringe per side). The same technique was used for the décolletage, but with three points of entry as illustrated in Figure 2. Injections were followed by vigorous massage to ensure that the product was evenly dispersed. Subjects were instructed to refrain from exercising the treatment area for 24 hours. Photographs were obtained at baseline and 90 days using standardized patient positioning and lighting.

2.4 | Efficacy evaluation

Efficacy was determined by two independent evaluators using the Merz Aesthetics, Fabi-Bolton, and Allergan neck line scales to conduct a blinded comparison of baseline and 90-day photographic images. A patient satisfaction questionnaire was also undertaken at the 90-day visit during which patients compared their baseline and 90-day photographs. Subjects were required to respond using a five-point scale from 1 = very unsatisfied to 5 = very satisfied. Pain was assessed and adverse events were documented.

2.5 | Statistical methodology

Statistical analyses were primarily descriptive. Quantitative variables were described using the mean, standard deviation, and range. Rating scale scores at 90 days were statistically compared with baseline scores using the Wilcoxon test for related samples. Changes from baseline were considered significant at the $P < .05$ level. Analyses were conducted using SAS System for Windows (Statistical Analysis System), version 9.2 (SAS Institute Inc, 2002-2008, Cary, NC, USA).

3 | RESULTS

A total of 47 patients (44 women and three men) were treated with combined MFU-V and 1:1 diluted CaHA: 29 for horizontal necklines only, five for décolletage only, and 13 for both the neck and décolletage. All patients completed the 90-day visit. The mean age of subjects enrolled was 49.3 ± 9.9 years.

The neckline scores for subjects at baseline are shown in Table 1. Overall, approximately 20% of subjects had very severe horizontal necklines, 25% had severe, and about 55% had moderate lines. Following treatment with MFU-V and CaHA, both evaluators reported significant improvements in necklines at 90 days (Table 1). In over two-thirds of subjects, lines were then classed as mild, and around 30% had moderate lines. Only one subject was rated as having severe horizontal necklines, and no subjects had very severe lines. The combined mean neckline score from both evaluators improved from 2.6 (moderate-to-severe lines) at baseline to 1.3 (mild lines) 90 days after treatment ($P < .001$). Images illustrating the improvement in neck line wrinkles 90 days after treatment compared with baseline are shown in Figure 3.

Evaluator-rated décolletage scores also improved significantly following treatment whether evaluated using the Merz Aesthetics or Fabi-Bolton scale (Table 1). Evaluator scores improved from a mean of 2.6 on the Merz Aesthetics and 3.3 on the Fabi-Bolton scales at baseline (both indicating moderate lines due to the one-point score difference between the scales), to 1.1 and 1.8, respectively, 90 days after treatment (both $P < .001$). Images illustrating the improvement in skin of the décolletage 90 days after treatment compared with baseline are shown in Figure 4.

Patients' satisfaction score ratings and their percentage at baseline and 90 days after treatment for the neck and décolletage are illustrated in Figures 5 and 6, respectively. Mean patient satisfaction scores at baseline were 3.2 ± 0.6 for the neck and 3.1 ± 0.6 for the décolletage, indicating patients were neither satisfied nor dissatisfied (Figure 5). After treatment, the mean satisfaction scores had improved to 4.5 ± 0.6 and 4.4 ± 0.6 , respectively, indicating patients were satisfied to very satisfied with the appearance of their neck and décolletage. When the satisfaction scores for the neck and décolletage were combined, a statistically significant improvement was observed from 3.2 ± 0.6 at baseline to 4.5 ± 0.6 after treatment ($P < .001$). Of the 60 procedures performed, over half of the

Treatment area/grading scale	Grade	Number of subjects with grading scale score			
		Baseline		90 days	
		Evaluator 1	Evaluator 2	Evaluator 1	Evaluator 2
Neck/Allergan	0	–	–	–	–
	1	–	–	30	27
	2	24	23	11	14
	3	10	11	1	1
	4	8	8	–	–
Décolletage/Merz Aesthetics	0	–	–	4	5
	1	1	2	7	7
	2	8	8	7	6
	3	6	4	–	–
	4	3	4	–	–
Décolletage/Fabi-Bolton	1	–	–	3	5
	2	2	4	15	13
	3	8	6	–	–
	4	8	8	–	–
	5	–	–	–	–

TABLE 1 Number of subjects with neck and décolletage grading scale scores at baseline and 90 days according to independent evaluators

Allergan transverse neck line scale and Merz Aesthetics décolleté wrinkles grading: (0) no wrinkles; (1) mild wrinkles; (2) moderate wrinkles; (3) severe wrinkles; (4) very severe wrinkles. The grading on the Fabi-Bolton scale ranges from: (1) no wrinkles to (5) very severe wrinkles.

subjects ($n = 31$) were very satisfied with the treatment results, 25 were satisfied, and only four were neither satisfied nor dissatisfied.

Mild pain was experienced by 90% of subjects during the procedure; 10% reported no discomfort at all. All subjects experienced bruising, which resolved in 3-7 days. No other adverse events were reported.

4 | DISCUSSION

The results of this retrospective study confirm that combination treatment with MFU-V followed by 1:1 diluted CaHA is effective for improving skin laxity and the appearance of lines on the neck and the décolletage. Mean neck and décolletage wrinkle severity scores improved by at least one grade compared with baseline after only one treatment session regardless of which grading scale was used. Although both treatments have previously demonstrated efficacy for neck^{3,4,7,9,13,14} and décolletage^{5,6,9} indications individually, to the authors' knowledge, this is the first study to evaluate combined use of MFU-V and diluted CaHA for skin tightening in the neck and décolletage.

Combining MFU-V and CaHA procedures is intuitive, given that both stimulate neocollagenesis in the treatment area. MFU-V delivers microfocused ultrasound energy at preselected depths, while simultaneously providing high-resolution ultrasound imaging of the skin layers to ensure the precision and consistency of energy delivery. Absorption of the ultrasound energy causes intermolecular vibration and heat production to temperatures of around 65°C,

causing collagen denaturation and initiating neocollagenesis without injuring the skin's surface. Real-time visualization allows physicians to avoid anatomic structures such as blood vessels, nerves, and bones.

Following injection of CaHA, the microspheres act as a scaffold for new tissue formation, activating fibroblasts with subsequent collagen and elastin production.^{8,15,16} These collagen-stimulating properties of CaHA can be used for skin-tightening procedures by diluting the product with either lidocaine or saline. The rationale for combining MFU-V and CaHA in the same treatment area is for an enhanced level of neocollagenesis above that which can be achieved with either procedure alone, with greater skin tightening and/or a longer duration of effect. Current consensus is that MFU-V should be performed first, but can be followed immediately by CaHA injection as in the current study.¹⁷ A previous histological analysis conducted by the author of the present study showed similar immunologic patterns in skin biopsies treated with CaHA alone compared with samples treated with CaHA followed by MFU-V, indicating that the combination of both procedures is safe.¹⁸ Furthermore, the study revealed increased numbers of collagen fibers in areas treated with the combination approach vs areas treated with the single agents CaHA, MFU-V, or a hyaluronic acid filler.¹⁸ In a recent study, significant improvements in skin laxity and cellulite severity were noted in female subjects who were treated with MFU-V followed by injection of 1:1 diluted CaHA.¹⁹ Both procedures were well tolerated and patient satisfaction was high.

In this study, subjects were treated with MFU-V at two focal depths (3.0 mm and 1.5 mm) to stimulate neocollagenesis in more

than one tissue level. Recent research has shown slightly greater esthetic improvements when patients are treated in this manner in the neck area.⁴ Results were very consistent between the

independent evaluators and observed with three different validated grading scales (one for necklines¹² and two for the décolletage^{10,11}), illustrating the robustness of the treatment results. The Merz Aesthetics scale offers a further advantage relative to other scales by providing a dynamic assessment (ie while contracting the breast area by pulling the arms together toward the medial line) in addition to a static assessment. This component is helpful in classifying intermediate grades, thus improving the sensitivity of the scale.

Patient-reported outcome data are particularly relevant for esthetic procedures because patients' perception of treatment results is subjective. Overall, 93% of subjects were very satisfied or satisfied with the improvement in their neckline appearance and 94% of subjects in the appearance of their décolletage. This rate of patient satisfaction compares very favorably with 90-day results from studies in which MFU-V or CaHA were used to treat the neck



FIGURE 3 Photographs A, before and B, 3 months after treatment of horizontal necklines with combined microfocused ultrasound with visualization and diluted calcium hydroxylapatite



FIGURE 5 Percentages of subjects with patient satisfaction scores at baseline and 90 days after treatment of the neck (N = 42). Patient satisfaction grading: (1) very unsatisfied; (2) unsatisfied; (3) neither satisfied nor dissatisfied; (4) satisfied; (5) very satisfied



FIGURE 4 Photographs of the décolletage of two patients (A1, A2) before and (B1, B2) 3 months after treatment with combined microfocused ultrasound with visualization and diluted calcium hydroxylapatite

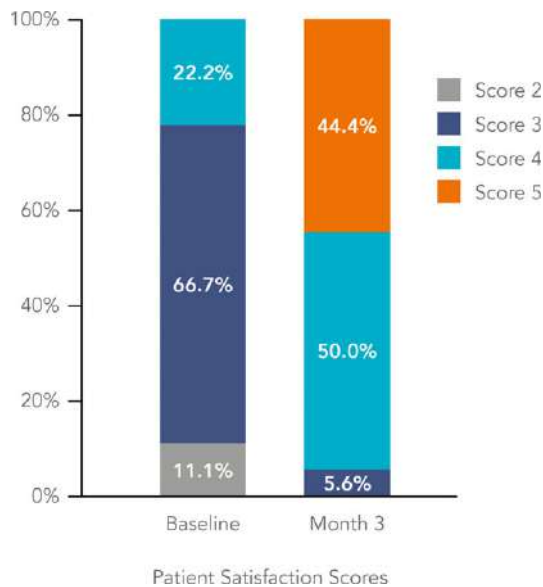


FIGURE 6 Percentages of subjects with patient satisfaction scores at baseline and 90 days after treatment of the décolletage (N = 18). Patient satisfaction grading: (1) very unsatisfied; (2) unsatisfied; (3) neither satisfied nor dissatisfied; (4) satisfied; (5) very satisfied

or the décolletage individually,^{3-7,9,13} albeit with different patient questionnaires and different study inclusion criteria. Careful selection of patients is important as the aging neck and décolletage can be characterized by many different changes including skin dyspigmentation, laxity, rhytides, loss of the mandibular contour, accumulation of submental fat, volume loss, and prominence of the platysmal bands; not all of these concerns are appropriate for treatment with MFU-V and CaHA. For example, in a prospective study of 93 patients who underwent MFU-V for improving skin laxity and tightening in the lower face, the relationship between treatment outcomes and body mass index was also examined.¹³ Overall improvement in skin laxity was noted in 64% of evaluated patients, but no change was detected in 55% of patients whose BMI exceeded 30 kg/m² compared with 12% of patients whose BMI was ≤30 kg/m². Injection of diluted CaHA may specifically address skin laxity in subjects with considerable volume loss accompanied by decreased dermal thickness.^{9,19} The filler acts by supplementing the dermis with a scaffold which provides cells of the extracellular matrix with additional support for mechanical stretching of fibroblasts and induction of de novo collagen synthesis.²⁰ Hyperdilution of the product allows the CaHA microspheres to be distributed in larger areas, which is an important step for treating large surfaces such as the neck and décolletage.

The combination of MFU-V and CaHA was well tolerated. Adverse events were limited to mild pain and transient bruising, similar to adverse events observed in skin-tightening studies in which the two procedures have been used individually. Both treatments have previously been shown to be safe in all Fitzpatrick skin types^{21,22} and in combination with other esthetic procedures.²³⁻²⁵

The results of this retrospective skin-tightening study with MFU-V and CaHA are very encouraging. Individually, MFU-V and CaHA have both demonstrated a duration of effect of at least 1 year.^{7,26} It is unknown if combining the treatments will extend this further. A prospective study with longer follow-up may help to clarify this question.

5 | CONCLUSIONS

Combination treatment with MFU-V followed by injection of 1:1 diluted CaHA is effective for improving skin laxity and the appearance of moderate-to-severe lines in the neck and décolletage. The procedures were well tolerated and subject satisfaction was very high.

ACKNOWLEDGMENTS

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CONFLICTS OF INTERESTS

G. Casabona is a speaker for Merz and Allergan but has no conflicts of interests to disclose related to this study. D. Nogueira Teixeira was an employee of Merz Pharmaceuticals and was involved in the design of the study, analysis of the data, and preparation of the manuscript.

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