

Short communication on “Prospective and randomized comparative study of calcium hydroxylapatite versus calcium hydroxylapatite plus HIFU in treatment of moderate to severe acne scars”.

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Accepted on January 25, 2021

Description

Acne scars are the most common sequela of the severe inflammatory process of acne. They affect almost 95 percent of patients with acne vulgaris, which is prevalent in more than 90 percent of adolescents [1,2]. A standard tool for assessing atrophic scars is the four-grade Goodman and Baron classification [3]. Managing acne scars is a challenge [4-6], and therapies are divided into nonsurgical [7-9] and surgical [10-12]. High intensity micro focused ultrasound (HIFU) is an energy-based technology that creates distinct thermal coagulation points in dermal and subcutaneous tissue. The heat generated causes collagen denaturation and contraction with subsequent de novo collagen synthesis and tissue remodeling [13-14] (Table 1).

Not satisfied	Questionnaire	Score
	I look worst then before	0
	I cannot see any difference before and after-My relatives do not notice any difference	1
	I can see minimal difference before and after-My relatives do not notice any difference	2
	I can see moderate difference before and after-My relatives notice minimal difference	4
Moderate satisfied	I can see moderate difference before and after-My relatives notice moderate difference	6
Satisfied	I can see good difference before and after-My relatives notice moderate difference	8
Very Satisfied	Beyond my expectation-All my relatives notice great improvement	10

Table 1. Patient Satisfaction Questionnaire (PSQ).

Synthetic Calcium Hydroxylapatite (CaHA) is a biocompatible material of small microspheres [15] that promote new tissue formation fibroblastic ingrowth and new collagen formation, without calcification [16,17], is safe [18] and effective in improving the quality of the extracellular matrix [19]. In the clinical trial we assessed the safety and effectiveness of CaHA monotherapy and its association with HIFU for treating moderate-to-severe atrophic acne scars. From October to

December 2019, twenty women (average age 38.8 ± 7.58 years, range 31-46 years) with grade 3-4 moderate-to-severe atrophic scars according to the Goodman classification (Figure 1) were enrolled in this study and were divided into two homogeneous groups (Table 2).

Grade	Level of disease	Characteristics	Examples of scars
1	Macular disease	Erythematous, hyper- or hypopigmented flat marks visible to patient or observer irrespective of distance.	Erythematous, hyper- or hypopigmented flat marks
2	Mild disease	Mild atrophy or hypertrophy that may not be obvious at social distances of 50 cm or greater and may be covered adequately by makeup or the normal shadow of shaved beard hair in males or normal body hair if extrafacial.	Mild rolling, small soft papular
3	Moderate disease	Moderate atrophic or hypertrophic scarring that is obvious at social distances of 50 cm or greater and is not covered easily by makeup or the normal shadow of shaved beard hair in males or body hair if extrafacial, but is still able to be flattened by manual stretching of the skin.	More significant rolling, shallow "box car," mild to moderate hypertrophic or papular scars
4	Severe disease	Severe atrophic or hypertrophic scarring that is obvious at social distances of 50 cm or greater and is not covered easily by makeup or the normal shadow of shaved beard hair in males or body hair (if extrafacial) and is not able to be flattened by manual stretching of the skin.	Punched out atrophic (deep "box car"), "ice pick," bridges and tunnels, gross atrophy, dystrophic scars, significant hypertrophy or keloid

Figure 1. Goodman classification.

		Group 1	Group 2	
Patient	20	10	10	
Age	38.8 ± 7.58	39.2 ± 4.19	38.3 ± 3.58	n.s.
BMI	23.9 ± 1.34	23.7 ± 1.34	24.1 ± 1.20	n.s.
Ethnicity (Caucasians)	20	10	10	n.s.
Fitzpatrick	3.35 ± 0.76	3.3 ± 0.82	3.4 ± 0.7	n.s.
Wrinkles	43.14 ± 1.49	42.1 ± 2.19		n.s.
Texture	39.3 ± 0.59	38.9 ± 1.6		n.s.
Hemoglobin	13.06 ± 1.17	12.35 ± 1.2		n.s.

Table 2. Patient data.

In a double blinded manner, ten patients (CaHA group) were treated with 3.0 ml of CaHA (Radiesse®-Merz North America, Inc., Raleigh, NC, USA), and ten patients (control group) were treated with 3.0 ml of normal saline. After 3 weeks, all patients received 400 lines of HIFU (Hifu Finesse®-Biotec, Dueville, Vicenza, Italy). Patients were assessed by digital macrophotographs, by Antera 3D® [20-22] and by a Patient Satisfaction Questionnaire (PSQ). Results at 1, 3, and 6 months were compared to baseline, and results at 3 and 6 months were compared to results at 1 month. No minor or major side effects were reported during the study, and all of the patients completed the follow-up after 6 months. We obtained results in CaHA group (Table 3 and Figures 2-4),

Group 1	Before	1 Months	3 Months	6 Months
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Wrinkle s	43.14 ± 1.49	35.74 ± 1.33	p<0.05	31.64 ± 1.31	p<0.05	30.64 ± 1.31	p<0.05
Texture	39.3 ± 0.59	30.79 ± 0.94	p<0.05	26.79 ± 0.94	p<0.05	25.1 ± 2	p<0.05
Hemogl obin	13.06 ± 1.17	15.26 ± 1.42	N.S.	17.76 ± 1.63	p<0.05	18.06 ± 1.4	p<0.05
PSQ		6.86 ± 0.48	p<0.05	8.62 ± 0.72	p<0.05	7.6 ± 0.49	p<0.05

Table 3. Result in group 1.

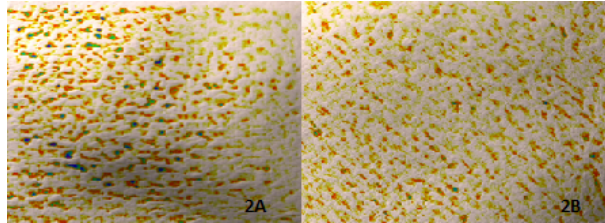


Figure 2. Antera 3D_wrinkles_ female_43_y.o_pre Treatment and 6 months post Treatment with CaHA.

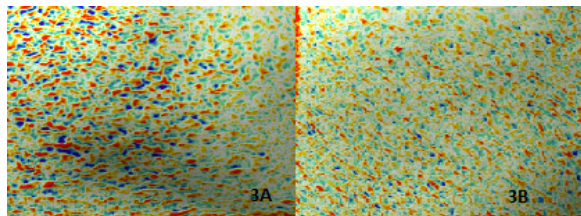


Figure 3. Antera 3D_texture_ female_43_y.o_pre Treatment and 6 months post Treatment with CaHA.

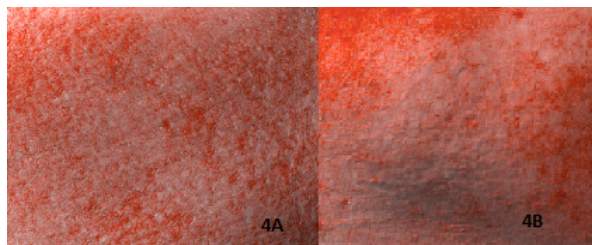


Figure 4. Antera 3D_hemoglobin_ female_43_y.o_ pre Treatment and 6 months post Treatment with CaHA.

In control group (Table 4 and Figures 5-8) and among groups (Table 5). Previous studies reported the effectiveness of HIFU in monotherapy for atrophic acne scar [23] and the combination of microfocused ultrasound with calcium hydroxylapatite [24] but, no controlled study had yet investigated the efficacy and safety of CaHA or its combination with HIFU for atrophic acne scars.

Group 2	Before	1 Months		3 Months		6 Months	
Wrinkle s	42.1 ± 2.19	40.7 ± 2.2	N.S.	29.8 ± 2.0	p<0.05	30.1 ± 2.17	NS
Texture	38.9 ± 1.6	37.63 ± 1.57	N.S.	26.3 ± 1.98	p<0.05	27.53 ± 1.9	NS
Hemogl obin	12.35 ± 1.2	12.95 ± 1.25	N.S.	17.0 ± 1.2	p<0.05	17.35 ± 1.16	NS

PSQ		1.1 ± 0.28	N.S.	6.82 ± 0.36	p<0.05	6.1 ± 0.56	p<0.05
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Table 4. Result group 2.

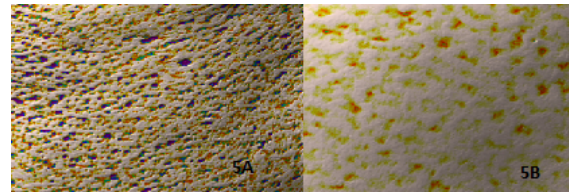


Figure 5. Antera 3D_wrinkles_ female_38_y.o._Pre Treatment and 6 months post Treatment with HIFU.

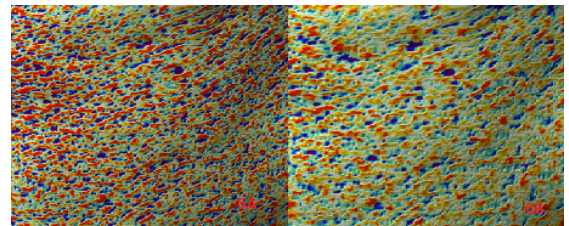


Figure 6. Antera 3D_texture_ female_38_y.o_ Pre Treatment and 6 months post_treatment_ HIFU.

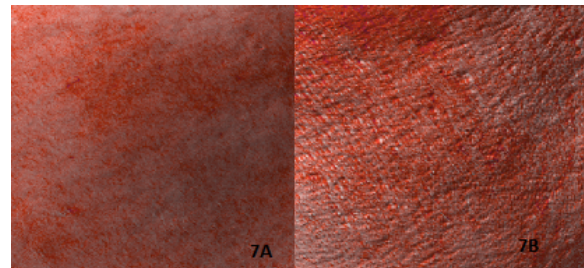


Figure 7. Antera 3D_hemoglobin_ female_38_y.o_ Pre Treatment and Post Treatment_HIFU.



Figure 8. Female-32 y.o. Pre Treatment and 6 months post_treatment_CaHa plus HIFU.

In our clinical study we compared the CaHA group with a homogeneous control group at 1 month and compared CaHA plus HIFU versus HIFU alone at 3 and 6 months. Our study proved that CaHA monotherapy significantly improved wrinkles and skin texture and reduced clinical evidence of atrophic acne scars when compared with placebo at 1 month. Furthermore, HIFU, used with a 10 MHz (0.25 J) transducer at 1.5 mm focal depth as the sole treatment, significantly improved wrinkles, skin texture, and hemoglobin both at 3 and 6 months suggesting that HIFU was able to regenerate collagen and increase the vascularity of the targeted tissue (Table 5).

Wrinkles	Group 1	Group 2	
Before	43.14 ± 1.49	42.1 ± 2.19	N.S.
1 Month	35.74 ± 1.33	40.7 ± 2.2	p<0.05
3 Months	31.64 ± 1.31	29.8 ± 2.0	N.S.
6 Months	30.64 ± 1.31	30.1 ± 2.17	N.S.
Texture	Group 1	Group 2	
Before	39.3 ± 0.59	38.9 ± 1.6	N.S.
1 Month	30.79 ± 0.94	37.63 ± 1.57	p<0.05
3 Months	26.79 ± 0.94	26.3 ± 1.98	N.S.
6 Months	25.1 ± 2	27.53 ± 1.9	N.S.
Hemoglobin	Group 1	Group 2	
Before	13.06 ± 1.17	12.35 ± 1.2	N.S.
1 Month	15.26 ± 1.42	12.95 ± 1.25	N.S.
3 Months	17.76 ± 1.63	17.0 ± 1.2	N.S.
6 Months	18.06 ± 1.4	17.35 ± 1.16	N.S.

Table 5. Comparative result among groups.

Discussion and Conclusion

However, even though CaHA monotherapy significantly improved wrinkles and skin texture when compared with the control, its combination with HIFU failed to show any difference with HIFU alone. This was explained by the fact that HIFU was already so effective in monotherapy in regenerating dermal tissue that the adjunct of the CaHA was not clinically relevant. In addition, the small cohort of patients enrolled on the study was not enough to reach statistical significance. Finally, the PSQ reflected the clinical results. In fact, at 1-month post-treatment, only patients in group 1 treated with CaHA were moderately satisfied compared to the placebo group. Meanwhile, at 3 and 6 months, their satisfaction raised from moderately satisfied to satisfied, and this can be explained by the added use of HIFU. No complications were recorded after the treatments; this indicated that both CaHA and HIFU in monotherapy and their combined use are safe.

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