THE COMBINATION OF NONCONTACT APOPTOSIS-INDUCING RADIOFREQUENCY AND EXTRACORPOREAL SHOCK WAVE THERAPY ACHIEVED SIGNIFICANT WAIST CIRCUMFERENTIAL REDUCTION: A PILOT STUDY

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This article has been submitted for publication to the journal *Laser Therapy* has been accepted, and is now pending

Abstract

Background and Aims: A paradigm shift towards noninvasive body contouring has occurred over the past few years. Radiofrequency (RF) is one popular treatment method. Noncontact-type RF systems with frequencies in the tens of megahertz represent a novel approach. The current pilot study investigated the efficacy of an interesting combination of extracorporeal shock wave therapy (ESWT) and an apoptosis-inducing RF (AiRF) system for circumferential reduction.

Subjects and Methods: Twenty-seven females, ages ranging from 13-69 years, (mean age 37.96 years) participated in the study. They were assigned to two treatment-based groups: Group A (n=19) and Group B (n=8). A voluntary dietary restriction plan (maximum intake: 500 kcal) was put in place for all subjects. A combination of two different devices was used; an extracorporeal shock wave therapy (ESWT) system and a 27.12 MHz AiRF system. Either 4 (n=28) or 6 sessions (n=19) were given, one week apart. In Group A, the ESWT was applied before the RF with the reverse order of application in Group B. Weight and waist circumference were noted at baseline, then one week after the 4th and the 6th treatment sessions at which points clinical photography was also obtained.

Results: All patients showed statistically significant waist circumferential loss in both the 4- and 6-week treated groups: Group A, 6.3 cm and 8.8 cm; Group B, 5.9 cm and 6.4 cm, respectively. Greater circumference loss tended to be seen in Group A in both groups, but without statistical significance. Significant weight loss was also noted in all patients, which may have been due to their dietary restriction regime. No patient complained of pain during or after the treatment sessions, and there were no adverse events.

Conclusions: This pilot study showed that the combination of ESWT and AiRF was safe and effective for significant waist circumferential reduction. The results tended to be better when ESWT was applied before AiRF, although the difference was not significant.

Key words: Waist circumference, body contouring, radiofrequency, apoptosis, shock wave therapy, lipolysis

Introduction

With awareness increasing in the general population regarding the importance of maintaining our health, the necessity to lose weight, to trim up the abdominal area and reduce waist circumference has attracted a great deal of attention. The aggressive and invasive methods of fat reduction, such as conventional mechanical liposuction and other forms, including laser-assisted liposuction, may offer good results, but are associated with a range of known side effects from mild through severe, to death.[1] In recent years, there has been a paradigm shift towards the patients' desire for noninvasive methods, which represents one of the fastest growing areas in aesthetic medicine.[2] These methods include cryolipolysis,[3] high-intensity focused ultrasound (HIFU) [4] and radiofrequency (RF).[5] Although RF is usually associated with the necessity for a delivery and a return electrode (or electrodes) in contact with the tissue, a more recently-developed system involves a delivery head positioned over the target tissue (*e.g.*, abdomen, flank, thighs) in noncontact mode, without the need for a return electrode attached to the body, known as field RF .[6]

In a recent meta-analysis on extracorporeal shock wave therapy (ESWT) for cellulite, in addition to suggesting the efficacy of ESWT, the authors proposed that ESWT could improve the results of other noninvasive modalities through its beneficial effects on blood supply and alterations in the permeability of the lipocyte membrane.[7] The author of the present study considered that these might aso be beneficial in abdominal fat removal adjunctive to the effects of RF, although abdominal fat does not have the same anatomical characteristics as cellulite. The present study was therefore designed to assess the safety and efficacy of the combination of a new apoptosis-inducing RF (AiRF) system and ESWT for abdominal fat and waist circumferential reduction.

Subjects and Methods

A total of 27 patients with intention to treat abdominal fat comprised the study subjects, ages ranging from 13-69 years, with a mean age of 37.96 years. (Table 1) All subjects gave written informed consent to participate in the study and for the use of their clinical photography. The study was conducted under the precepts of the World Medical Association Declaration of Helsinki (as amended 2013).

Table 1: Patient demographics for groups A and B, showing weight in kg at baseline (WB), 1 week after 4 treatment sessions (WE) and the actual weight loss (WL) from baseline values; waist circumference (cm) at baseline (CB), 1 week after 4 sessions (CE) and circumference decrease (CL) from baseline values. The final row for each group shows the mean values (± standard error of means [SEM])

			Group A			
Pat No/ age	WB (kg)	WE* (kg)	**WL (kg)**	CB (cm)	CE* (cm)	**CL (cm)**
1 F/48	75	72.1	2.9	99	92.2	6.8
2 F/49	67.1	65.5	1.6	86.5	83	3.5
3 F/69	68.2	62.8	5.4	99	95	4
4 F/31	61.5	57.9	3.6	89.5	82	7.5
5 F/37	113.4	106.2	7.2	132.3	124	8.3
6 F/44	60.9	57.4	3.5	87	82.5	4.5
7 F/47	64.2	60.8	3.4	89	82.5	6.5
8 F/30	80.9	75.3	5.6	93	85	8
9 F/45	63.1	59.2	3.9	87.3	76	11.3
10 F/47	51	47.9	3.1	84	72.5	11.5

11 F/42	70.7	67.4	3.3	93	86.5	6.5
12 F/56	63.3	60	3.3	86	85	1
13 F/27	71.2	65.3	5.9	93	86.5	6.5
14 F/23	57.8	52.6	5.2	87	75	12
15 F/35	62	59.3	2.7	90.5	85.5	5
16 F/20	72.3	69.7	2.6	90	84.5	5.5
17 F/13	66.3	64.8	1.5	89.2	87	2.2
18 F/43	52.4	52	0.4	89	87.5	1.5
19 F/20	58.5	57	1.5	84.5	79	5.5
	67.4 (3.07)	63.8 (2.8)	**3.6 (0.39)**	92.0 (2.43)	85.8 (2.48)	**6.3** (0.76)**

***p=0.0001**

Group B

Pat No/ age	WB (kg)	WE** (kg)	**WL (kg)**	CB (cm)	CE** (cm)	**CL (cm)**
20 F/45	77.1	74	3.1	99	94	5
21 F/23	102.8	96.4	6.4	104.5	96	8.5
22 F/29	100.6	92.8	7.8	118	111	7
23 F/38	76.7	72.8	3.9	89.3	84.5	4.8
24 F/26	69	64.8	4.2	96	86.5	9.5
25 F/43	63.3	60	3.3	86	85	1
26 F/47	76.2	71.9	4.3	99.5	93	6.5
27 F/48	56.1	54.5	1.6	84	79	5
	77.7 (5.83)	73.4 (5.21)	**4.3 (0.69)**	97.0 (3.91)	91.1 (3.49)	**5.9 (0.93)**

****p=0.0004 (by paired 2-tailed Student's *t*-test)**

In the first 19 subjects, the ESWT was delivered before the RF treatment, but in the final 8 subjects the order of treatment was reversed as the author decided to check which order was more effective. Six treatment sessions were given at weekly intervals. Body weight (in kg, digital scale) and waist circumference (in cm) were measured and tabulated at baseline, with digital clinical photography. All 27 patients received 4 sessions at weekly intervals, and 19 patients went on to receive a further 2 sessions, also at weekly intervals. Body weight and waist circumference were measured again at 1 week after the 4th and 6th treatments. Standardised digital photography was taken at the same time. Alongside the AiRF and ESWT treatment, all patients voluntarily took part in a dietary restriction regimen recommended by a qualified nutritionist with a maximum daily intake target of 500 kcal to assist in weight loss.

The apoptosis-inducing RF (AiRF) system used was the enCurve™ (Lutronic Corporation, Goyang, South Korea), delivering RF energy at the frequency of 27.12 MHz from an adjustable noncontact applicator placed over the abdomen and flanks. Each session was 30 min, with a power setting of 200 W. The system offers the ability for cool air to be blown over the abdomen to eliminate perspiration and increase comfort. The ESWT system was the Z-Wave™ (Zimmer Aesthetics, New-Ulm, Germany), delivering electromagnetic induced radial shock waves from a contact probe. The abdomen and flanks were covered in around 2000 shots, 120 mJ pulse energy setting.

Subjects were asked to report any discomfort during or after the treatment sessions including late onset pain, and the appearance of any other side effects such as erythema and edema. Standardized clinical photography was taken at baseline and at the assessment points one week after the 4th and 6th treatment sessions. The weight and waist circumference data from the baseline, 4-week and 6-week assessments were tabulated and examined with a Student's two-tailed paired t-test. Values $P<0.05$ were considered significant.

Results

All 27 subjects completed the treatment and the 4-week treatment protocol. Nineteen subjects went on to complete the 6-week treatment program. No erythema or edema was seen in any patient at any time during the study period, and there were no instances of delayed late-onset pain. Subjects reported gentle warmth during the 30-min AiRF treatment with no discomfort either during or after the treatment. Subjects could physically feel the impact of each shot during the ESWT session, but did not find it uncomfortable.

At the first assessment, 1 week after the 4th treatment session, all subjects had some weight loss: this was probably attributable at least in part to the subjects' dietary regimen. All 27 subjects had achieved significant reduction in their waist circumference. Table 1 shows the separate data for Groups A (ESWT followed by RF) and B (RF followed by ESWT). In Group A, the average weight loss at 4 weeks was 3.6±0.39 kg (mean ± SEM, range 0.4 – 7.2 kg), and average circumference loss was 6.3 cm (range 1 – 11.5 cm, $P<0.0001$ for both). In Group B (Table 1) the average weight loss was 4.3 kg (range 1.6 – 7.8 kg) and circumference loss was 5.9 cm (range 1 – 9 cm, $P=0.0004$ for both). Table 2 gives the data for the 2nd assessment point, one week after the 6th treatment session in 19 subjects. In Group A, the average weight loss at 6 weeks was 4.6 ± 0.55 kg (range 1.7 – 6.9 kg), and average circumference loss was 8.8 ± 1.09 cm (range 5 – 14.8 cm, $P<0001$ for both), compared with the baseline values. In Group B the average weight loss was 5.2 ±1.17 kg (range 2.6 – 10.5 kg, $P=0.007$) and circumference loss was 6.4 ± 0.98 cm (range 2.5 – 9.5 cm, $P=0.0013$). Both weight and circumference loss were still highly statistically significant in the 2nd assessment compared with the baseline values in both groups, however there was not a statistically significant difference between the groups ($P=0.2839$ and $P=0.0589$, respectively, for weight and circumference). A trend towards better results was seen in Group A, particularly for the circumference loss which just failed to reach statistical significance.

Table 2: The 19 subjects in Groups A and B who went on to complete 6 treatment sessions compared 1 week after the final session: see Table 1 for patient ages. Weight in kg at baseline (WB), 1 week after the final session (WE) and weight loss (WL) from baseline values; waist circumference (cm) at baseline

(CB), 1 week after the final session (CE) and circumference decrease (CL) from baseline values. The final row for each group shows the mean values (± standard error of means [SEM])

Group A

Pat No	WB (kg)	WE (kg)	WL* (kg)	CB (cm)	CE (cm)	CL* (cm)
1	75	72.5	2.5	99	93	6
3	68.2	62.4	5.8	99	94	5
4	61.5	57.9	3.6	89.5	79	9.5
5	113.4	105.4	8	132.3	124	8.3
6	60.9	59.2	1.7	87	82	5
7	64.2	60.5	3.7	89	83	6
8	80.9	74.3	6.6	93	85	8
9	63.1	58.2	4.9	87.3	72.5	14.8
10	51	47.9	3.1	84	69.5	14.5
11	70.7	68.6	2.1	93	88	5
12	66.8	62.1	4.7	87	80	7
13	71.2	64.3	6.9	93	85	8
14	57.8	51.8	6	87	71	16
	69.6 (4.22)	65.0 (3.94)	**4.6 (0.55)**	93.9 (3.45)	85 (3.87)	**8.8 (1.09)**

*** P=0.0001**

Group B

Pat No/ age	WB (kg)	WE (kg)	WC*** (kg)	BC (cm)	BE (cm)	BC**** (cm)
21	102.8	97	5.8	104.5	98	6.5
22	100.6	90.1	10.5	118	110.2	7.8
23	76.7	73.3	3.4	89.3	82.5	6.8
25	63.3	60.7	2.6	86	83.5	2.5
26	76.2	71	5.2	99.5	94.5	5
27	56.1	52.6	3.5	84	74.5	9.5
	79.3 (7.78)	74.1 (6.91)	**5.2 (1.17)**	96.9 (5.33)	90.5 (5.26)	**6.4 (0.98)**

***** P=0.007 **** P=0.0013**

Table 3 summarizes the average and total weight and circumference losses at one week after the 4th and 6th treatment sessions. Table 4 compares the difference between the baseline values and the 1st and 2nd assessment values for both the weight loss (expressed as W) and circumference loss (expressed as C) for the 4-treatment and 6-treatment groups. From the table it can be seen that there was some additional weight and circumference loss in the 2 weeks between the 1st and 2nd assessment points, in some cases quite considerable in the case of circumference loss (Patients 12, 14 and 27 with an additional loss of 6.0. 4.0 and 4.5 cm, respectively) compared with weight loss. On the other hand, 7 and 5 of the 19 subjects respectively regained some weight and girth, although the final result was still lower than the baseline values.

Table 3: Summary of the average (avge.), minimum (min.) and maximum (max.) values for weight reduction (weight) in kg and circumference reduction (circ.) in cm at 1 week after the 4th and 6th treatment sessions in groups A and B.

Item	4 weeks Tx	6 week Tx
Avge. weight	3.95 kg	4.9 kg
Min. weight loss	0.4 kg	1.7 kg
Max. weight loss	7.8 kg	6.9 kg
Avge. circ.	6.1 cm	7.6 cm
Min. circ. loss	1.0 cm	2.5 cm
Max. circ. loss	12 cm	14.8 cm

Table 4: Differences between weight loss (∆**W** in kg) and circumferential loss (∆**C** in cm) from the baseline values as seen in Tables 1 and 2 between the 2 assessment points for all patients (Patients: Nos 1-19, Group A; Nos 20 -27, Group B: see Table 1 for patient ages). "--" denotes subjects who completed only 4 sessions. Whereas the majority of those 19 subjects who completed 6 treatment sessions showed increased weight and circumference loss at the 2nd assessment, 7/19 and 5/19 subjects regained some slight weight and circumference, respectively.

Pats (No)	WL-4	WL-6	∆W	CL-4	CL-6	∆C
1	2.9	2.5	+0.4	6.8	6	+0.8
2	1.6	--	--	3.5	--	--
3	5.4	5.8	0.4	4.0	5.0	1.0
4	3.9	3.6	+0.3	8.5	10.5	2.0
5	7.2	8.0	0.8	8.3	8.3	0.0
6	3.5	1.7	+1.8	4.5	5	0.5
7	3.4	3.7	0.3	6.5	6	+0.5
8	5.6	6.6	1.0	8	8	0.0
9	3.9	4.9	1.0	11.3	14.8	3.5
10	3.0	3.1	0.1	11.5	14.5	3.0
11	3.3	2.1	+1.0	6.5	5	+0.5
12	3.3	4.7	1.4	1	7	6.0
13	5.9	6.9	1.0	6.5	8	1.5
14	5.2	6.0	0.8	12	16	4.0
15	2.7	--	--	5	--	--
16	2.6	--	--	5.5	--	--
17	1.5	--	--	2.2	--	--
18	0.4	--	--	1.5	--	--
19	1.5	--	--	5.5	--	--
20	3.1	--	--	5.0	--	--
21	6.4	5.8	+0.6	8.5	6.5	+2.0
22	7.8	10.5	2.7	7.0	7.8	0.8
23	3.9	3.4	+0.5	4.8	6.8	2.0
24	4.2	--	-	9.5	--	--
25	3.3	2.6	+0.7	1.0	2.5	1.5
26	4.3	5.2	0.9	6.5	5.0	+1.5

Pats (No)	WL-4	WL-6	ΔW	CL-4	CL-6	ΔC
27	1.6	3.5	1.9	5.0	9.5	4.5

Representative Cases

Case 1: Figure 1a, c and d show the baseline front, right profile and back findings in a 31-year-old female from Group A (Patient No 4), who weighed 61.5 kg at baseline, with a waist circumference of 89.5 cm. Figure 1b, d and e illustrate the good results at 1 week after the 6 weekly sessions with a total circumference loss of 9.5 cm. She received the ESWT intervention first, followed immediately by the AiRF. There is clear flattening of the abdomen around the waist area, and reduction in the size of the flanks. This patient lost an additional 2 cm from her waistline between the 1st and 2nd assessments. She was extremely satisfied with the result.

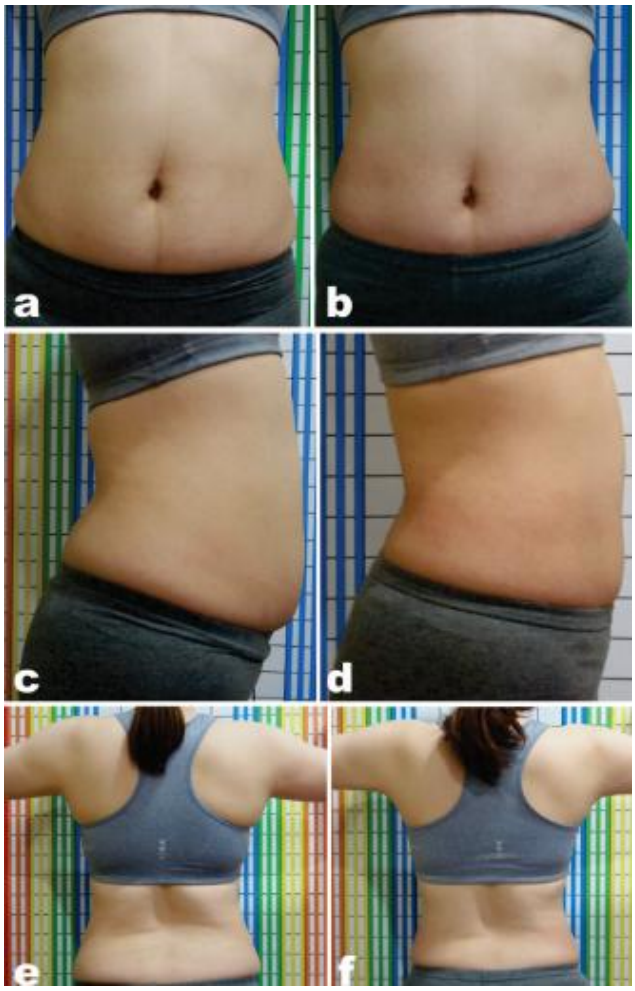

Figure 1. A 31-year-old female (Patient 4, Group A) is seen at baseline from the front (1a), right profile (1c) and back (1e). The very good results seen at 1 week after the 6th weekly treatment session with ESWT followed by apoptosis-inducing RF (AiRF) are seen in 1b, d, and f (9.5 cm circumferential reduction). Please see the text for details.

Case 2: A 48-year-old female from Group B (Patient No 27) is seen at baseline in Figure 2a, c and e. Her baseline weight and waist circumference were 56.1 kg and 84 cm, respectively. She was also treated over 6 weekly sessions, in her case AiRF was followed by ESWT. At the 2nd assessment she had lost an additional 4.5 cm from her waist measurement by 1 week after the additional 2 treatments, losing a total of 9.5 cm after the 6 weekly sessions.

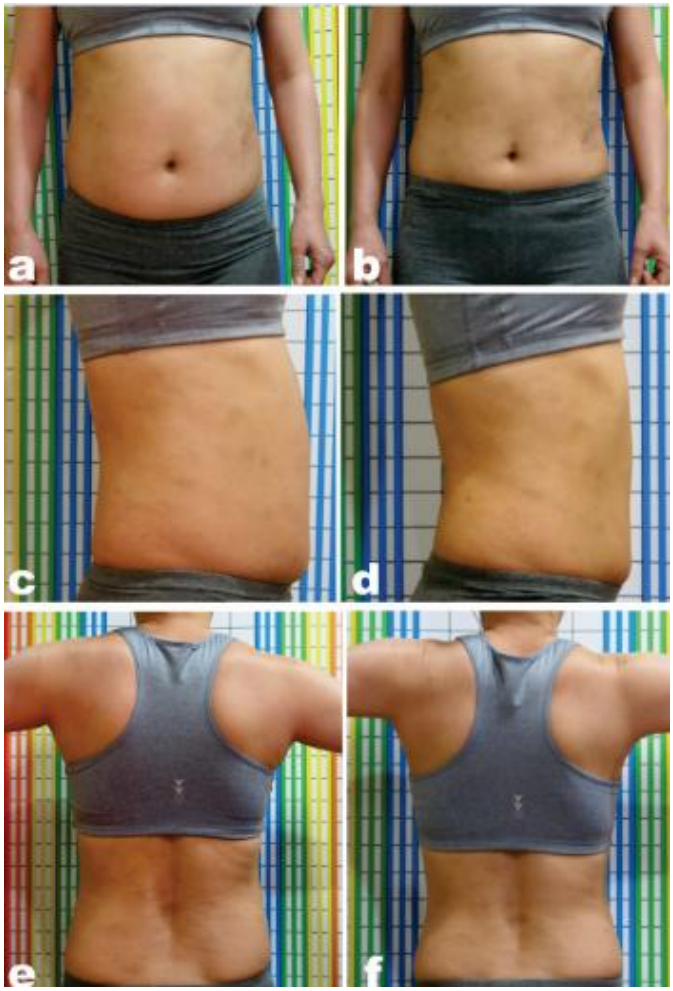

Figure 2. Figure 2a, c and e show aspects of a 48-year-old female (Patient 27, Group B) at baseline. Figure 1b, d, and f show the very good results seen at 1 week after the 6th weekly treatment session with AiRF followed by ESWT (9.5 cm circumferential reduction). Please see the text for details.

Discussion

The present study has two limitations. First, although the order of treatment was compared in the study protocol, (ESWT + AiRF vs AiRF + ESWT), there was no comparison between the effect of each modality on its own to see if the ESWT did in fact add something to the effect of the apoptosis-inducing RF. This should be addressed in a future study, with a controlled arm to further verify the results. Second, a longer follow-up than just 1 week should be used in any future study: this was a pilot study, however, and the author wanted to review the

results reasonably quickly to assess efficacy of the combined treatment approach.

That having been said, the results were reasonably solid and clear. The combination of the ESWT and AiRF delivered weight and circumference reduction at 1 week after the 4th treatment session, which was mostly maintained or improved at the 2nd assessment in the 19 subjects who went on to compete a total of 6 sessions. All reduced values were statistically significant at both assessments compared with the baseline values. There was no pain or discomfort, and no immediate or delayed side effects, making this noninvasive approach ideal for patients wishing to resume their normal activities of daily living immediately after treatment. This would make a "lunchtime body contour" possible. Although significant weight reduction was achieved in the study, this may have been attributable to the dietary regimen in which the subjects were voluntarily participating. Unfortunately there is no record of how assiduously the subjects followed the program, so it is difficult to assign any value to weight loss possibly induced by the AiRF/ESWT treatment. It should be noted from Tables 1-3 that some subjects with similar weight loss values had much greater circumference loss. For example, patients 3, 8, 13 and 14 lost 5.5-7 kg, but with a significantly different loss in waist circumference. This could point to the efficacy of AiRF/ESWT specifically for waist circumference reduction.

Apoptosis-inducing RF relies on oscillating an electric current at very high frequencies in the treatment head: in the case of the system used in the present study the frequency is 27.12 MHz. This frequency has been used in diathermy for the selective treatment of tumors,[9] and has been shown to have a specific affinity for lipocytes, rather than blood vessels or other organs. At this frequency, the epidermis and dermis are left undisturbed, whereas the incident energy is absorbed in the lipocyte membranes, inducing brisk vibrational and rotational changes in the membrane molecule electrons. This generates a great deal of heat through friction between the vibrating components, and the membranes are partially denatured at a temperature at or over 40°C, sending the target lipocytes into apoptosis, programmed cell death. As the membranes disintegrate, the lipid droplets contained within the cells are allowed to escape. The target lipocytes have also had their structures slightly modified by the gentle heating, so they become a good target for the macrophages recruited into the target area as a result of the response to the "wounding" of the fatty tissues. Both lipid droplets and cellular debris are therefore mopped up by the macrophages, and excreted from the body.

Extracorporeal shock wave therapy (ESWT) is now well established and is used more than 90% worldwide as the principal method for treating kidney and urethral stones. Its use for fat-related conditions is more recent. In the previously cited meta-analysis on ESWT for the treatment of cellulite by Knobloch and Kraemer,[7] the authors postulated applications for ESWT beyond cellulite, and suggested interest in exploring the combination of ESWT with other noninvasive body contouring modalities. It has been suggested that ESWT acts on cellulite tissues through the delivery of an extracorporeally-administered, electromagnetically induced radial shock wave. There is no electromagnetic energy delivered, simply a series of very short pulses of osmotic energy. This is suggested to temporarily alter the permeability of the lipocyte membranes, enhance the blood supply, and accelerate clearance of debris by macrophages.[8]

The author felt that these aspects would add value to the use of AiRF for body contouring, and so for the first 19 patients in the study, ESWT was applied immediately before the AiRF, with the aim of affecting lipocyte membrane permeability and blood supply to the area to prepare the way for the AiRF. However, the author was interested to see what would happen if the order of treatment was reversed, and so the final 8 patients were treated with AiRF first followed by ESWT. The author's idea was that mopping up of debris by the endogenous macrophage response would be accelerated by this order of treatment: the blood supply and lipocyte membranes would have already been altered by the RF and would no longer be the primary target for the ESWT. As can be seen from Tables 1-3, the order of application using the ESWT first followed by the AiRF gave better results in waist circumferential loss than AiRF followed by ESWT, although the difference was not statistically different between Groups A and B. Having said that, Group A almost showed significance in waist circumference reduction after the 6th treatment session, where the P value was 0.0589, just short of the $P<0.05$ criterion for significance.

Conclusion

The noninvasive combination of ESWT with noncontact apoptosis-inducing RF proved safe and effective for circumferential reduction in all patients enrolled in the study at 1 week after the 4th treatment in all 27 subjects, which mostly improved in the 19 subjects who went on for a further 2 treatment sessions. The treatment was well-tolerated by all patients and was pain- and side effect-free. Both ESWT followed by AiRF and AiRF followed by ESWT gave significant girth reductions, with the first of these combinations showing slightly better (though not statistically significant) results, especially in circumferential reduction. Further controlled trials with larger populations and longer follow-ups are warranted to confirm the optimistic results presented by the present study.

References

1: Tierney EP, Kouba DJ, Hanke CW: Safety of tumescent and laser-assisted liposuction: review of the literature. J Drugs Dermatol, 2011; 10: 1363-1369.

2: Kennedy J, Verne S, Griffith R, Falto-Aizpurua L, Nouri K: Non-invasive subcutaneous fat reduction: a review. J Eur Acad Dermatol Venereol, 2015; 29: 1679-1688.

3: Derrick CD, Shridharani SM, Broyles JM: The safety and efficacy of cryolipolysis: a systematic review of available literature. Aesthet Surg J. 2015; 35: 830-836 Epub 2015 Feb 9.

4: Robinson DM, Kaminer MS, Baumann L, Burns AJ, Brauer JA: High-intensity focused ultrasound for the reduction of subcutaneous adipose tissue using multiple treatment techniques. Dermatol Surg, 2014; 40: 641-651.

5: McKnight B, Tobin R, Kabir Y, Moy R: Improving Upper Arm Skin Laxity Using a Tripolar Radiofrequency Device. J Drugs Dermatol, 2015;14: 1463-1466.

6: Moradi A, Palm M: Selective non-contact field radiofrequency extended treatment protocol: evaluation of safety and efficacy. J Drugs Dermatol, 2015; 14: 982-985.

7: Knobloch K, Kraemer R: Extracorporeal shock wave therapy (ESWT) for the treatment of cellulite--A current metaanalysis. Int J Surg, 2015; 24(Pt B): 210-217.

8: Angehrn F, Kuhn C, Voss A: Can cellulite be treated with low-energy extracorporeal shock wave therapy? Clin Interv Aging. 2007; 2: 623-630.