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REVIEW ARTICLE

Non-invasive subcutaneous fat reduction: a review

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Abstract

The risks, financial costs and lengthy downtime associated with surgical procedures for fat reduction have led to the development of a number of non-invasive techniques. Non-invasive body contouring now represents the fastest growing area of aesthetic medicine. There are currently four leading non-invasive techniques for reducing localized subcutaneous adipose tissue: low-level laser therapy (LLLT), cryolipolysis, radio frequency (RF) and high-intensity focused ultrasound (HIFU). To review and compare leading techniques and clinical outcomes of non-invasive subcutaneous fat reduction. The terms 'non-invasive', 'low-level laser', 'cryolipolysis', 'ultrasound' and 'radio frequency' were combined with 'lipolysis', 'fat reduction' or 'body contour' during separate searches in the PubMed database. We identified 31 studies (27 prospective clinical studies and four retrospective chart reviews) with a total of 2937 patients that had been treated with LLLT (n = 1114), cryolipolysis (n = 706), HIFU (n = 843) or RF (n = 116) or other techniques (n = 158) for fat reduction or body contouring. A majority of these patients experienced significant and satisfying results without any serious adverse effects. The studies investigating these devices have all varied in treatment regimen, body locations, follow-up times or outcome operationalization. Each technique differs in offered advantages and severity of adverse effects. However, multiple non-invasive devices are safe and effective for circumferential reduction in local fat tissue by 2 cm or more across the abdomen, hips and thighs. Results are consistent and reproducible for each device and none are associated with any serious or permanent adverse effects.

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Conflicts of interest

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Background

Public awareness is quickly spreading of the health consequences of obesity, including increased risk of metabolic, cardiovascular, orthopaedic and neoplastic diseases, among many others. This increasingly common knowledge, mounted on highly pressured cultural ideals of beauty and attractiveness, have instilled a strong desire amongst the population to obtain slimmer and healthier appearing bodies. The growing demand for methods of fat reduction is perhaps driven by the fact that over 69.0% of American adults age 20 years and older are now overweight or obese (BMI $\geq$ 25 kg/m^2), up from 54% in 1988.[1] In 2013, over 11 million cosmetic procedures were performed in the United States, a 279% increase since 1997.[2] Liposuction is the most common cosmetic surgery in the United States with 363 912 procedures in 2013, a 16% increase from 2012.[2] More specifically, liposuction is the most common cosmetic surgery overall in men, in all adults age 35–50, and second overall in women, behind breast augmentation.[2]

Although liposuction is extremely effective at removing large amounts of excess fat, it is accompanied by significant risk of complications and severe adverse effects. These may include postprocedural pain, infection, prolonged recovery, scarring, haematoma, ecchymosis or oedema.[3] Long-term and potentially fatal complications may include deep vein thrombosis and pulmonary embolism in addition to anaesthesia-related complications.[4,5] Another significant complication, though non-fatal, is contour irregularity which may require surgical revision in 2–10% of cases.[3]

Given the significant risks, substantial financial costs and extended recovery time associated with surgery, developments in non-invasive cosmetic techniques have been thoroughly pursued. These procedures have grown 521% since 1997 and now account for 83.5% of total cosmetic procedures and 42% of $12 billion in total expenditures.[2] In addition, non-invasive devices for body contouring have become the fastest growing area of aesthetic medicine.[6,7] Such methods are ideal for non-obese patients

seeking safer, more affordable methods of modest reductions of localized fat deposits and improved skin laxity and appearance without the serious adverse effects or significant downtime associated with surgery. Likewise, these technologies are attractive to physicians because they allow for profitable procedures with satisfying, reliable and reproducible results and little disposable costs.[8] There are currently four leading non-invasive techniques of reducing localized subcutaneous adipose tissue: low-level laser therapy (LLLT), cryolipolysis, radio frequency (RF) and high-intensity focused ultrasound (HIFU). All are believed to cause the efflux of triglycerides from fat cells and result in either reduced size, necrosis or apoptosis of targeted adipocytes.

Additional techniques that do not fall into these categories have also been investigated for efficacy. Among the earliest was LPG Endermologie®, a mechanical message-suction device which is believed to cause cell membrane disruption and emptying of fat from adipocytes. Other techniques include extracorpeal shockwave therapy (ECST), acoustic wave therapy and topical creams. There are also a variety of injectable treatments, referred to as mesotherapy, which have been used in attempts to reduce subcutaneous fat deposits. However, the safety and efficacy of these chemicals have not been established. Although new studies are currently underway, mesotherapy treatments are not currently approved by the FDA for this purpose.

Objectives

Several clinical studies have confirmed the safety and efficacy of various non-invasive devices for fat reduction, specifically observing clinically relevant factors such as patient satisfaction, recovery time, time to peak results and longevity of effects. The objective of this article was to systematically review and compare leading techniques and clinical outcomes of non-invasive of fat reduction devices.

Methods

The terms 'non-invasive', 'low level laser', 'cryolipolysis', 'radio frequency' and 'ultrasound' were combined with 'lipolysis', 'fat reduction' or 'body contour' during separate searches in the PubMed database. The articles retrieved as well as their references, were reviewed and determined to be relevant if the study included measures of clinical efficacy (quantified circumferential or fat thickness reduction) in human subjects and if a full-length English text was available. Non-randomized and/or non-controlled clinical studies, as well as retrospective chart reviews, were included if they met criteria.

Results

We identified 31 studies (27 prospective clinical studies and four retrospective chart reviews) with a total of 2937 patients that had been treated with LLLT (n = 1114), cryolipolysis (n = 706), HIFU (n = 843) or RF (n = 116) or other techniques (n = 158) for subcutaneous fat reduction or body contouring. All studies are summarized by type of device in Tables 1–4.[4,9–38] All results reported were statistically significant mean changes from baseline measurements unless otherwise noted. If measurements were taken at multiple locations for the same treatment area, only their means were reported. Nearly all studies were performed on non-obese subjects (BMI < 30 kg/m^2), encompassing a wide range of ages (15–84 years), multiple races and both sexes. With the exception of two studies,[4,24] no significant weight change was observed over the study period and thus, fat reductions were attributed to the treatment. In addition, there were no significant differences in results between men and women and baseline BMI positively correlated with fat reduction.[12] Circumferential increases were generally seen in subjects with significant weight gain over the study period.[4,24]

Trends in efficacy

Fat reduction in the waist All studies which performed treatments on the abdomen (with or without flanks) or waist, except for two,[25,27] reported circumferential reductions greater than 2 cm. The only study of cryolipolysis to measure abdomen circumference showed a 6.86 cm reduction.[21] One study of LLLT reported a 6.83 cm reduction in the abdomen and flanks.[13] All other LLLT studies reported reductions of 2.15–2.9 cm in the abdomen.[11,12,15,17] RF studies showed reductions of 4.93 cm,[23] 3.58 cm,[26] 2.7 cm[24] and 1.4 cm.[25] Three HIFU studies showed reductions of 4.1–4.7 cm[9,31,33] and four showed reductions of 2.1–2.5 cm.[28–30,32] The only study to use both HIFU and RF therapies showed a 3.91 cm reduction.[27] One study of LPG Endermologie reported 1.34 cm and 2.05 cm reductions from the waist after 7 and 14 treatments respectively.[36] Lastly, one study investigating topical aminophylline (a phosphodiesterase inhibitor and adenosine receptor antagonist), reported 11 cm after 3 months of daily use combined with an supplemental treatment protocol.[37]

Fat reduction in the hips Of the four leading energy techniques, LLLT studies were the only to perform treatment on the hips and reported mean circumferential reductions of 1.95–2.67 cm.[12,13,15,17] The only other study to measure efficacy in the hips was with LPG Endermologie, which reported 1.85 cm and 3.19 cm reduction after 7 and 14 treatments respectively.[36]

Fat reduction in the thighs Cryolipolysis and shockwave combined showed a 5.78 cm circumferential reduction in both thighs combined.[21] LLLT studies reported reductions of 2.97–3.81 cm.[12,13,15,17] Of the two LLLT studies which only treated one thigh to maintain the other as an internal control, one achieved only a 0.64 cm mean reduction[16] and the other found no significant reduction.[18] One HIFU study showed a 1.6 cm reduction[33] and one RF study reported a 1.2 cm reduction in the thighs.[25] Reductions of 1.95 cm were shown after

Table 1 Summary of LLLT studies

Study	Study design	Device	Treatment regimen	Treatment location	Mean reduction from baseline	Posttreatment follow-up	Adverse effects	Result satisfaction
McRae and Boris (2013) *n* = 86	RCR	Erchonia® Zerona (635 nm LLLT)	1 session/week for 6 weeks or 2/week for 4 weeks (6 or 8 total, <30 min each)	Waist, hips and thighs	Circumference: −2 cm (waist), −1.95 cm (hips), −2.97 cm (thighs), −7.59 cm (all sites combined)	1 week	NR	NM
Savoia *et al.* (2013) *n* = 33	PCS	Vibro Light™ (635 nm LLLT + Vibration)	3/week for 2 weeks (6 total, 40 mins each)	Abdomen, flanks, thighs or buttocks	Circumference: −6.83 cm (abdomen and flanks), −3.42 cm (thighs), −6.16 cm (buttocks)	4 weeks	NR	NM
Nestor, Zarraga and Park (2012) *n* = 40	PCS	635 nm LLLT device	3/week for 2 weeks (6 total, 20 mins each)	Arms	Circumference: −3.7 cm (both arms combined)	Final treatment	NR	80%
Jackson *et al.* (2012) *n* = 689	RCR	Zerona (635 nm LLLT)	3/week for 2 weeks (6 total, 40 mins each)	Waist, hips and thighs	Circumference: −2.90 cm (waist), −2.41 cm (hip), −3.00 cm (thighs), −8.31 cm (sites combined) −0.66 cm (neck), −1.88 cm (chest) and −0.81 cm (each arm)	1 week	NR	NM
Gold *et al.* (2011) *n* = 85	PCS	SmoothShapes (650 + 915 nm LLLT) and Photomology (vacuum-message)	2/week for 4 weeks (8 total, 30 mins each)	One thigh	Circumference, 4 weeks: −0.64 cm (active group) vs. −0.2 cm (control) 12 weeks: -.32 cm (active) vs. -.02 cm (control)	4 weeks (*n* = 85) and 12 weeks (*n* = 72)	Erythema, swelling and increased urination	NM
Caruso-Davis *et al.* (2011) *n* = 40	PCS	LAPEX 2000 \(635–680 nm LLLT)	2/week for 4 weeks (8 total, 30 mins each)	Waistline	Circumference: −2.15 cm (active group) vs. −0.78 cm (control)	Final treatment	NR	NM
Jackson *et al.* (2009)*n* = 67	PCS	Erchonia® Lipolaser (635 nm LLLT)	3/week for 2 weeks (6 total, 20 mins each)	Waist, hips and thighs	Circumference: −2.49 cm (waist), −2.67 cm (hip), −3.81 cm (thighs), −8.97 cm (all sites combined)	Final treatment	NR	NM
Lach (2008) *n* = 74	PCS	SmoothShapes (650 + 915 nm LLLT)	3/week for 4–6 weeks (14.3 total, 40 mins each)	One thigh	Circumference (*n* = 71): Not significant Fat layer thickness (*n* = 65): −1.19 cm^2 (active) vs. +3.82 cm^2 (control)	Final treatment	Erythema (38%), pain or tingling (32%)	31.90%

NM, not measured; NR, none reported; PCS, prospective clinical study; RCR, retrospective chart review.

Table 2 Summary of cryolipolysis studies

Study	Study design	Device	Treatment regimen	Treatment location	Mean reduction from baseline	Posttreatment follow-up	Adverse effects	Result satisfaction
Garibyan *et al.* (2014) *n* = 11	PCS	Zeltiq System (Cryolipolysis)	Single treatment (60 mins)	One flank	Fat thickness (caliper): −14.9% (treated) vs. −0.7% (control) Volumetric fat loss (3D photography): −56.2 ± 25.6 cc (treated) and −16.6 ± 17.6 cc (control)	8 weeks	Erythema, oedema and decreased sensation (100%) and pain (55%)	82%
Sasaki, Abelev and Tevez-Ortiz (2014) *n* = 85	PCS	Zeltiq System (Cryolipolysis)	Single treatment (60 mins)	Multiple sites	Fat thickness (caliper): −10 mm/−27% (abdomen), −10 mm/−25% (hip) Fat thickness (ultrasound): −19.6%	24 weeks	Erythema (100%), bruising (>50%) and dysaethesia (<50%)	NM
Dierickx *et al.* (2013) *n* = 518	RCR	Zeltiq System (Cryolipolysis)	Single treatment (86.5%)	Multiple sites	Fat thickness (*n* = 49, caliper): −23%	12 weeks	Erythema (100%), discomfort (96%), bruising (9.8%), severe pain (4%)	73%
Shek, Chan, and Chan (2012) *n* = 33	PCS	Zeltiq System (Cryolipolysis)	A: Single treatment (60 min) B: 2 treatments, 3 months apart	Abdomen and/or flanks	Fat thickness (caliper) Group A: −14.67% Group B, 1st treatment: −14% (abdomen), −13.4% (side flanks) Group B, 2nd treatment: −7.2% (abdomen), −3.4% (side flanks)	Group A: 8 weeks Group B: 12 weeks after 1st treatment and 8 weeks after 2nd	Transient pain and numbness (100%), numbness for >3 weeks (28.6%), erythema (23.8%) and bruising (9.5%)	80%
Ferraro *et al.* (2012) *n* = 50	PCS	Proshockice (Cryolipolysis + shockwave)	3.73 sessions over 8 weeks (<60 min each)	Multiple sites	Circumference: −6.86 cm (abdomen), −5.78 cm (thighs), −2.75 cm (arms), −5 cm (buttocks), −2.25 cm (ankles) Fat thickness (caliper): −4.5 cm (abdomen), −3.6 cm (thighs), −2.1 cm(arms), −4 cm (buttocks), −1 cm (ankles)	4 weeks	Erythema	100%
Coleman *et al.* (2009)*n* = 9	PCS	Zeltiq System (Cryolipolysis)	Single treatment (60 min)	One flank	Fat thickness (ultrasound), 8 weeks: −20.4%; 24 weeks: −25.5%	8 and 24 weeks	Erythema (100%) and numbness (96%)	NM

NM, not measured; PCS, prospective clinical study; RCR, retrospective chart review.

Table 3 Summary of RF and HIFU studies

Study	Study design	Device	Treatment regimen	Treatment location	Mean reduction from baseline	Posttreatment follow-up	Adverse effects	Result satisfaction
Fajkošová *et al.* (2014) *n* = 35	PCS	Vanquish™ (RF)	1/week for 4 weeks (30 min each)	Abdomen	Circumference: −4.93 cm	Final treatment	Transiet erythema and some pain (9.5%)	71%
Boisnic *et al.* (2014) *n* = 21	PCS	BodyFX (RF + suction)	1/week for 6 weeks	Abdomen	Circumference: Final treatment: −1.9 cm 1 month: −2.4 cm 3 months: −2.7 cm Fat thickness (ultrasound): 1 month: −2 mm	Final treatment, 1 and 3 months	Slight discomfort, transient and mild bruising	NM
Adatto, Adatto-Neilson and Morren (2014) *n* = 35	PCS	VelaShape II (RF, IR and mechanical)	1/week for 6 weeks	Multiple sites	Circumference: −1.4 cm (abdomen/flanks), −1.2 cm (thighs), −0.5 cm (buttocks) Fat thickness (*n* = 12): −29% (across all sites)	12 week	Erythema, oedema, strong heating sensation	97%
Mulholland and Kreindel (2012) *n* = 25	PCS	TiteFx (RF)	1/week for 6 weeks	Abdomen and flanks	Circumference: −3.58 cm (range: −1.5 to −4.4)	12 weeks	Erythema and strong heating sensation	NM
Chang *et al.* (2013) *n* = 32	PCS	UltraShape Contour I (HIFU) and RFVac™ (RF)	1/2 weeks for 6 weeks (3 total)	Abdomen	Circumference: −3.91 cm Fat thickness (MRI, *n* = 2): −21.4% (upper abdomen), −25% (lower abdomen)	4 weeks	Mild discomfort (<9.5%), transient mild erythema (*n* = 1), swelling erythema (*n* = 1)	71.90%
Shek *et al.* (2014) *n* = 12	PCS	Liposonix (HIFU)	Single treatment (46.3 min)	Abdomen	Circumference, max point: −1 cm (range: −2.9 to +1.7) Circumference, iliac crest: −2.1 cm (range: −4.45 to +0.3)	12 weeks	Pain, bruising	58.30%
Jewell *et al.* (2011) *n* = 180	PCS	Liposonix (HIFU)	Single treatment (<50 min)	Abdomen and flanks	Circumference: 177 J active group: −2.52 cm 141J active group: −2.1 cm Sham group: −1.21 cm	12 weeks	Procedural pain (90.2%), postprocedural pain (56.6%), ecchymosis (66.4%) and oedema (9%)	47.50%
Solish *et al.* (2011) *n* = 45	PCS	Liposonix (HIFU)	Single treatment	Abdomen	Circumference: −2.5 cm	12 weeks	Mild pain, mild bruising or erythema	69–85%
Fatemi and Kane (2010) *n* = 282	PCS	Liposonix (HIFU)	Single treatment (45–60 min)	Abdomen and flanks	Circumference: −4.7 cm	12 weeks	Ecchymosis (9.9%), prolonged tenderness (3.5%), oedema (2.1%), significant pain (1.8%), and hard lumps (1.1%)	>70%
Fatemi (2009) *n* = 85	RCR	Liposonix (HIFU)	Single treatment (60–90 min)	Abdomen and flanks	Circumference: −4.4 cm (range: −9 to +4)	8–12 weeks	Ecchymosis (3.5%), prolonged tenderness (3.5%), hard lumps (2.4%), oedema (1.2%), severe pain (1.2%)	>70%
Hotta (2010) *n* = 70	PCS	UltraShape Contour I (HIFU)	At least 1 treatment	Abdomen and flanks and/or lateral thighs	Circumference: −2.5 cm	Not reported	Burning sensation, severe pain (*n* = 1)	NM

Table 3 *Continued*

Study	Study design	Device	Treatment regimen	Treatment location	Mean reduction from baseline	Posttreatment follow-up	Adverse effects	Result satisfaction
Teitelbaum *et al.* (2007) *n* = 137	PCS	UltraShape Contour I (HIFU)	Single treatment (60–120 min)	Abdomen, flanks, and/or thighs	Circumference: −2.3 cm (abdomen), −1.8 cm (flanks), −1.6 cm (thighs) Fat thickness (ultrasound): −2.6 mm (day 14), −2.9 mm (day 28)	12 weeks	Some discomfort (8%), mild erythema (2.2%), small blisters (*n* = 2), purpitic lesion (*n* = 1)	>50%

NM, not measured; PCS, prospective clinical study; RCR, retrospective chart review.

seven treatments with LPG Endermologie,[36] 1.8 cm with acoustic wave therapy,[35] 0.3 cm with topical glycyrrhetinic acid[38] and no significant reduction was achieved with shockwave therapy alone.[34]

Fat reduction in other areas Only one study of LLLT treated both arms and reported a mean combined circumferential reduction of 3.7 cm.[14] In addition, significant circumferential reductions were measured in non-treated areas with LLLT, including the neck, chest and arms.[15] The only other study to treat the arms used Proshockice (cryolipolysis and shockwave combination), and reported a mean reduction of 2.75 cm.[21] The same study reported 2.25 cm reduction in the ankles and was the only study that treated this area. The greatest reduction reported in the buttocks was 6.16 cm with LLLT,[13] followed by 5 cm with Proshockice,[21] 0.5 cm with VelaShape (RF, IR and mechanical combination)[25] and no significant reduction with shockwave therapy alone.[34]

Trends in adverse effects

Because all the techniques described are non-invasive by nature, nearly all studies observed only mild and transient adverse effects, which resolved spontaneously. Adverse effects for all devices were generally limited to mild discomfort, erythema and oedema. Any serious adverse effects or complications were rare and isolated. Most studies suggested no downtime and the majority of subjects, who did not experience bruising, were able to wear swimwear or summer clothing immediately.

Complications of LLLT treatments were generally the fewest and most mild of all devices, with several studies reporting no adverse effects at all.[11–15,17] Other studies reported swelling or erythema on the treatment area (38%), pain or tingling during treatment (32%) and increased urination; all of which were temporary and resolved spontaneously.[16,18] One study specifically reported the absence of adverse events; no parathesisas, haematomas, ecchymoses or oedema.[13] Despite the excess lipids being cleared through the lymphatic system, LLLT has not been shown to increase serum lipids but rather, has been shown to reduce serum cholesterol and leptin levels.[39–41]

RF studies reported transient erythema and some pain in 9.5% of subjects; both of which resolved within 60 min of treatment.[23,27] However, 89% of subjects treated with Vanquish RF found it to be comfortable or very comfortable.[23] Other studies reported adverse effects limited to erythema, oedema and strong heating sensation in most subjects, bruising in two subjects, and a burn in one subject.[25,26]

High-intensity focused ultrasound studies reported procedural pain (90.2%), postprocedural pain (56.6%), ecchymosis (66.4%), oedema (9–72%), dysaesthesia (59%) and erythema on treatment sites (45%).[29,30,42] Most of these adverse events resolved spontaneously within 4 weeks, and all by 12 weeks

Table 4 Summary of other device studies

Study	Study design	Device	Treatment regimen	Treatment location	Mean reduction from baseline	Posttreatment follow-up	Adverse effects	Result satisfaction
Knobloch *et al.* (2013) *n* = 25	PCS	CelluShock-2009 (Shockwave)	1 ESWT/1–2 weeks (6 total) & daily gluteal thigh exercise	Thighs and buttocks	Circumference: Not significant	12 weeks	NM	NM
Adatto *et al.* (2011), *n* = 14	PCS	CELLACTOR® SC1 (Acoustic wave)	8 treatments over 4 weeks	Lateral thighs	Circumference: −1.2 cm (week 1), −1.5 cm (week 4), −1.8 cm (week 12) Fat thickness (ultrasound): −1.6 mm, −17.7% (week 1), −2.1 mm, −23.3% (Week 4), −2.0 mm, −22.2% (week 12)	1, 4, and 12 weeks	Minor pain, slight erythema	100%
Chang *et al.* (1998) *n* = 85	PCS	LPG Emermologie (Message/suction)	Group A: 1–2/1–2 weeks, 7 total (45 mins each) Group B: 14 total	Multiple sites	Circumference Group A: −1.34 cm (waist), −1.85 cm (hips), −1.95 cm (thighs), −0.97 cm (knees), −0.59 cm(calf) Group B: −2.05 cm (waist), −3.19 cm (hips), −1.93 cm (thighs), −1.28 cm (knees), −0.71 cm (calf)	Final treatment	NM	NM
Caruso *et al.* (2007) *n* = 25	PCS	0.5% Aminophylline cream (topical)	2 applications/day for 3 months	Waist	Circumference: −11 cm	Final treatment	NR	NM
Armanini *et al.* (2005) *n* = 9	PCS	2.5% Glycyrrhetinic acid cream (topical)	1 application/day for 1 month	One thigh	Circumference: −0.3 cm Fat thickness (ultrasond): −2.1 mm	Final treatment	NR	NM

NM, not measured; NR, none reported; PCS, prospective clinical study; RCR, retrospective chart review.

posttreatment. Similar effects, as well as hard lumps, prolonged tenderness, discomfort, burning sensation, mild blisters and one case of purpuric lesions were also reported in other studies.[9,31–33] Allergic reactions to cream ($n = 2$)[42] and to adhesive tape used in the procedure ($n = 1$)[27,32] were observed, but were not a direct result of the device itself. 24 week follow-up safety data from physical examination revealed no dimpling, indurations, burns, scars or changes in skin laxity and ultrasound imaging showed no abnormalities in the treatment areas.[43] HIFU has been shown to have no effect on serum lipids, markers of inflammation, coagulation, liver or kidney function, haematological assessments or blood chemistry.[9,29,42]

Nearly 100% of patients who received cryolipolysis developed erythema, oedema and dysaesthesia in the treatment sites.[4,10,19–22] Discomfort (96%), pain (55%) and bruising (9.5–50%) were commonly observed.[4,10,20] Increased or decreased sensitivity, as well as nodular or diffuse infiltration was reported in rare cases, though there was no blistering, necrosis, dyschromia, cold burns, ulcerations, scarring or infections in treated areas.[10] Pain subsided in all patients within 1 week, erythema in all by 2 weeks, and oedema in all by 3 weeks. Dysaesthesia persisted in 73% at 3 weeks and 18% of at 2 months.[19] Histological studies revealed no long-term change in nerve fibre structure or other permanent sensory changes or skin damage.[22] One recent case study described an incident of paradoxical adipose hyperplasia in the treatment area of a male patient 3 months after cryolipolysis, as well as the existence of 32 other cases, although the prevalence is estimated to be only 0.0051%.[44] Lastly, Ferraro *et al.* (2012) found no clinically significant increases in lipid panels or changes in hepatic function.

Trends in patient satisfaction

Self-reported subject satisfaction with results was recorded in several studies by varying measures. One study of LLLT on the arms reported 80% satisfaction[14] whereas another, which only treated one thigh, reported that 31.9% of subjects were definitely pleased with results.[18] No other LLLT studies measured patient satisfaction. Studies of cryolipolysis have reported result satisfaction rates of 73–100%[4,19–21] and similarly, RF studies have reported rates of 71%[23] and 97%.[25] HIFU studies have reported satisfaction rates ranging from 47.5–85%[9,28–33] and one study of RF and HIFU combined reported 71.9%.[27] One study of acoustic wave reported satisfaction in 100% of patients.[35]

Discussion

Available evidence indicates that multiple non-invasive techniques for reducing subcutaneous fat tissue have proven to be safe and effective. The studies investigating these devices have all varied in treatment protocol, body locations, follow-up times and outcome measurements, making it difficult to accurately compare their results directly. One such limitation present in some studies was that additional stipulations were added to the treatment regimen to supplement the effects of the device. In these cases, subjects were asked to adhere to a calorie or fat restricted diet,[36,37] a specific exercise routine,[34,36] increased water intake[36] or nutritional supplements.[12] Another important note is that the study by Caruso *et al.* (2007) was the only to be performed on obese subjects. Based on the studies included in this review, it is reasonable to conclude that the four common energy devices (LLLT, cryolipolysis, RF and HIFU) consistently provide greater circumferential reduction and more favourable clinical results with fewer treatment sessions compared to other techniques including: mechanical message, shockwave therapy, acoustic wave therapy and topical creams. Overall, it should be noted that Zeltiq and Liposonix were the only devices of any energy that accomplished significant reductions with only a single treatment session.

Comparing device efficacy

Because of the inconsistency of experimental parameters in LLLT studies, most of these devices cannot be compared for superiority. However, it is worthy to note that one study with Vibro Light™ (PromoItalia Group S.p.A, Naples, Italy), yielded 2–3 times the reduction on the waist of multiple other studies with Zerona lipolaser (Erchonia Medical, McKinney, TX, USA) or LAPEX 2000 (Meridian Co., Korea), see Table 1. For RF devices, TiteFx (Invasix, Inc., Yokneam, Israel) yielded similar results to Vanquish™ (BLT Industries Inc., Boston, MA, USA) and both were superior to BodyFX (InMode, Inc., Yokneam, Israel) and Velashape (Syneron, Inc., Irvine, CA, USA), see Table 3. Results from HIFU studies with different devices did not appear to differ greatly, Table 3. All cryolipolysis studies used similar Zeltiq systems (Zeltiq Aesthetics, Pleasanton, CA, USA) except for one which used Proshockice (PromoItalia Group S.p.A, Naples, Italy). The latter was the only cryolipolysis study to measure circumference and unlike the others, reported fat thickness reduction in centimetres, not percentage. Therefore, the results of these devices appear similar, but are difficult to compare directly, Table 2.

The greatest reductions across the abdomen (6.86 cm) and thighs (5.78 cm) as well as the second greatest reduction in the buttocks (5.00 cm) were reported by Ferraro *et al.* (2012) using Proshockice, which combines cryolipolysis and shockwave therapy. The greatest reduction in the buttocks (6.16 cm) and the second greatest reductions in the abdomen (6.83 cm) and thighs (3.42 cm) were reported by Savoia *et al.* (2012) using Vibro Light™, which combines 635 nm LLLT and vibration therapy. This data suggest that the synergistic effects of shockwave with cryolipolysis or vibration with LLLT provide greater clinical efficacy than any of the available energy modalities alone. Though these devices were each only used in one study each, they yielded greater circumferential reductions than all other devices.

One notable difference between the mechanisms of different energies and their resulting clinical outcomes is the time

required to observe peak results. Because LLLT causes nearly immediate emptying of targeted adipocytes, results are noticeable as soon as the treatment is completed. However, because LLLT does not cause necrosis or apoptosis of the adipocytes, it is believed that recurrence of fat deposition is greater than that of other devices like HIFU or cryolipolysis, which do cause the death or destruction of the adipocyte. This finding was best demonstrated in a LLLT study by Gold *et al.* (2011), who reported that circumferential reduction at 12 weeks (0.32 cm) was half of what it was at 4 weeks (0.64 cm). These findings suggest both advantages and disadvantages of LLLT, in that maximum results are seen immediately, though they are believed to diminish over the following months. Whereas maximum results for cryolipolysis, HIFU and RF are generally seen within 4–12 weeks, though they progressively increase over this time and tend to remain longer. This is best evidenced by 2 and 5 year follow-up case reports of cryolipolysis treatments in two men who maintained significant fat reduction, despite one who gained 10 pounds since his treatment.[45]

Generally, cryolipolysis result satisfaction was similar to that for RF (about 70–100%), and were both overall superior to that of HIFU, which had multiple reports of satisfaction below 60%. Because no LLLT studies which measured satisfaction performed treatment on the abdomen, the rates cannot be accurately compared to other devices. However, because LLLT treatments have been reported to be comfortable, virtually absent of adverse effects and to yield relatively fast results, short-term satisfaction could be expected to be very high.

Conclusion

Multiple non-invasive devices have consistently proven to be effective for circumferential reduction of local fat tissue by 2 cm or more, without any serious or permanent adverse effects. Supplementary improvements in skin laxity and appearance have also been noted with these devices. Additional clinical trials investigating the long-term safety, efficacy and satisfaction of these devices and recurrent treatments are necessary, especially for LLLT devices where the longest follow-up time was 12 weeks in only one study. Future studies should use standardized experimental parameters so that their results may be more accurately compared to existing devices and techniques. We suggest that future investigators quantify fat reduction using as many measures as possible, including circumference and fat thickness with a caliper, ultrasound, MRI and/or 3D photography. All outcomes should be measured using standardized instruments, techniques, anatomical locations and posttreatment intervals. Measurements should also be reported in SI units, including percentage change for fat layer thickness. Subjective ratings of improvements and satisfaction by patients or physicians are also helpful in measuring and comparing clinical outcomes.

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