Evidence-Based Medicine: Liposuction

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Learning Objectives: After reading this article, the participant should be able to: 1. Perform preoperative assessment and patient selection for liposuction surgeries. 2. Explain the differences among the various types of anesthesia and wetting solutions used in liposuction. 3. Identify the available literature about skin-tightening procedures. 4. Convey to patients the complication profile for various modalities of liposuction. 5. Recall important ASPS consensus guidelines when discussing liposuction.

Summary: The article was prepared to feature recent evidence-based publications pertaining to liposuction. The authors placed special emphasis on the most clinically relevant data. In addition, they highlighted current data regarding liposuction-related fields, including autologous fat transfer and minimally invasive skin tightening. (*Plast. Reconstr. Surg.* 132: 1697, 2013.)

The purpose of this evidence-based Maintenance of Certification article on liposuction is twofold: first, to briefly summarize the 2011 Maintenance of Certification article by Wells and Hurvitz on the same topic; and second, to highlight recent evidence-based publications that might not have been included in that article or were subsequently published. We will place special emphasis on the most clinically relevant data in the literature and endeavor to highlight the best evidence surrounding unresolved controversies of liposuction indications and treatment algorithms, and related topics such as autologous fat transfer and minimally invasive skin tightening.

REVIEW OF 2011 ARTICLE

The article by Wells and Hurvitz[1] began with the clinical vignette of an obese woman with significant medical comorbidities and on oral contraceptive pills who presented for liposuction. The authors performed an extensive literature search to obtain the best available evidence to develop a treatment plan for this clinical scenario. In doing so, they reviewed the preoperative assessment, anesthesia, surgical treatment plan, pain management, and postoperative outcomes associated with liposuction and summarized the general recommendations associated with this procedure. The current best clinical evidence supports the use of either power-assisted or water-assisted liposuction, performed under general anesthesia, with dilute epinephrine-based superwet technique, on an outpatient basis.[2–4] Wetting fluids can be warmed to room temperature and the patient should be maintained at normothermic temperatures to decrease postoperative complications associated with hypothermia such as infection and deep vein thrombosis.[5,6] Some authors suggest that lidocaine can be eliminated from the wetting solution when the operation is performed under general anesthesia.[7] However, the rationale for continuing to use lidocaine in all settings includes the potential for better postoperative pain control, earlier sensory return, bacteriostatic properties, and reduced systemic anesthesia requirements.[8] Ideally, operating room time should be minimized (<140 minutes), which is one factor felt to diminish the risk of pulmonary embolism.[9] Finally, Wells and Hurvitz noted that several authors use the American Society of Anesthesiologists rating 1 or 2 to qualify patients for liposuction; however, this practice is supported only by anecdotal practice patterns, not clinical evidence.[5,6,10]

UPDATES TO THE 2011 ARTICLE

We found relevant updates to the following topics since the 2011 liposuction Maintenance of Certification article: preoperative assessment and patient selection, anesthesia, surgical treatment plan and instrumentation, postoperative outcomes, lipolysis and skin-tightening technology, complications (with particular emphasis on venous

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thromboembolism), autologous fat transfer/stem cells, and future directions in adipocyte biology.

Preoperative Assessment and Patient Selection

When considering potential candidates for liposuction, we would concur with Rohrich et al. that patients who endeavor to improve their appearance through diet, exercise, and a healthy lifestyle are more likely to be satisfied with their long-term postoperative results.[11] Also, medical comorbidities such as obstructive sleep apnea should be evaluated as to the extent of impairment and can potentially require additional postoperative observation to prevent respiratory complications.[12] Particular attention should be paid to such medical conditions to avoid adverse events.

Since publication of the prior Maintenance of Certification article, a consensus statement on large-volume liposuction (defined as >5 liters of total aspirate), regardless of anesthetic method, has underscored the recommendation for operating in either an acute-care hospital or in an accredited or licensed facility when removing large volumes. Haeck et al. recommended that postoperative vital signs and urinary output should be monitored overnight in an appropriate setting by personnel familiar with the perioperative care of liposuction patients.[13] They advised that strict postoperative monitoring be in place for large-volume liposuction cases. Notably, they did not recommend a strict cutoff for aspirate volume removed, nor did they advocate admission to a facility (e.g., hospital) for this observation. The 2009 follow-up by Haeck et al.[13] to Iverson and Lynch's 2004 article,[14] both authored from the American Society of Plastic Surgeons Patient Safety Commission, are landmark articles both in their content and in their examples of Society consensus statements on safety.

Liposuction to treat cellulite is unpredictable, has never been formally endorsed, and, in contrast to liposuction permanently improving lipodystrophy, has never been shown to have a permanent effect (probably because cellulite, even it could be effectively eradicated, continues to appear throughout a person's lifetime). Despite a large number of products claiming to be effective, no large-scale study to date has demonstrated any reliable method of permanent cellulite treatment.[15] However, a number of new technologies have yielded intriguing, albeit variable results, that are reviewed later in this article.

Anesthesia

Anesthesia techniques for liposuction remains varied based on a number of factors, including patient comorbidities, anatomical areas being treated, type of liposuction being performed, length and extent of procedure, volume of liposuction planned, and physician and patient preference. Although no evidence supports the use of any single technique, the American Society of Plastic Surgeons Practice Advisory recommends avoiding neuraxial anesthesia (i.e., spinal, epidural) in office-based settings because of potential hypotension and volume overload issues.[14]

Much attention was paid to wetting solutions in the 1990s, particularly maximum and safe doses of lidocaine and appropriate replacement fluid volumes achieved by intravenous and oral administration and by means of hypodermoclysis. Recently, little has changed with regard to the best evidence for lidocaine and epinephrine concentrations in wetting solutions. Lidocaine use continues to vary between surgeons; however, some studies have demonstrated that the lidocaine component of wetting solutions can be eliminated without increased postoperative pain.[7,10] Other studies recommend the use of bupivacaine,[16] or assess lidocaine and bupivacaine concentrations in superwet fluids and serially measure their levels postoperatively, and firmly advocate for their necessity in pain control.[17] For the majority who do use lidocaine, published reports demonstrate lidocaine use up to 55 mg/kg without complications,[18] although most surgeons seem to prefer far lower doses that still achieve satisfactory analgesia alone or with systemic anesthesia. The maximum safe dose of epinephrine is considered to be 0.7 mg/kg.[8,19] Moreover, the debate regarding wetting solutions alone referred to as "pure" local anesthesia (tumescent) versus wetting solutions (superwet anesthesia) with some form of systemic anesthesia administered by the surgeon or anesthesiologists has receded in discussion, and preference is frequently based on specialty background, where the procedure is performed, or surgeon or patient preference.[19] Finally, and surprisingly, there is no consensus of enhanced liposuction safety according to board certification or office operating room accreditation.[20]

Surgical Treatment Plan/Instrumentation

One of the most significant changes to surgical treatment plans since publication of the 2011 Maintenance of Certification article has been the modality (e.g., power-assisted, water-assisted, laser-assisted liposuction) chosen to perform the liposuction. New devices continue to emerge for use in this procedure, most of them with little evidence to support their claims of superiority. It is a formidable task for surgeons to stay abreast of all the latest techniques, technologies and, more importantly, evidence surrounding their uses. In 2011, 1713 American Society for Aesthetic Plastic Surgery members received a liposuction practice survey, and 28.7 percent (n = 492) responded. Most (56 percent) reported performing between 50 and 100 procedures annually. Fifty-one percent reported using conventional suction-assisted liposuction, 20.9 percent used ultrasound-assisted liposuction, and 23 percent used power-assisted liposuction. Complications were most commonly reported with ultrasound-assisted liposuction, laser-assisted liposuction, and conventional suction-assisted liposuction.[21] Varied levels of evidence exist in the literature to support the broad spectrum of invasive and noninvasive techniques. These are listed in Figures 1 and 2 alongside PubMed and Google search results for each technique to compare and contrast popularity in the scientific versus the mainstream literature. For "Liposuction" in general there were 3,280,000 results in Google and 3227 in PubMed. We review the impact of surgical treatment plan/instrumentation based on postoperative outcomes and skin-tightening technology.

Postoperative Outcomes

Little has been published comparing outcomes of newer liposuction techniques with those of suction-assisted liposuction (the criterion standard), therefore limiting our ability to draw indisputable claims of safety or superiority. In one comparative study, Prado et al. conducted a randomized, double-blind, controlled study examining laser-assisted liposuction and suction-assisted liposuction that showed no clinical difference in aesthetic outcomes between these techniques (**Level of Evidence: Therapeutic, II**).[22] In an industry-funded study, Nagy and Vanek compared VASER (Sound Surgical Technologies, Louisville, Col.)-assisted lipoplasty and suction-assisted liposuction. They evaluated two objective endpoints: skin retraction, in which VASER showed a 6 percent increase; and blood loss, which also showed a minimal benefit of 3 cc per 100 cc of aspirate. In many of their secondary subjective data points measured, VASER was worse than suction-assisted liposuction, and in terms of satisfaction, patients (blinded) preferred suction-assisted liposuction and surgeons (unblinded) were equally satisfied with VASER and suction-assisted liposuction. Both groups were unable to tell the difference between sides treated with either system.[23,24]

Technique	# of Google Results	# of Pubmed Results	Highest level of evidence
Suction Assisted Liposuction (SAL)	81,900	221	II
Tumescent	738,000	294	II
Ultrasound Assisted Liposuction (UAL)	132,000	157	III
Laser Assisted Liposuction (LAL)	629,000	55	II
Power Assisted Liposuction (PAL)	346,000	38	IV
Water Assisted Liposuction (WAL)	490,000	12	II
Radio Frequency Assisted Liposuction (RFAL)	35,900	11	IV

Fig. 1. Search results and highest levels of evidence: invasive technique. SAL, suction-assisted liposuction; UAL, ultrasound-assisted liposuction; LAL, laser-assisted liposuction; PAL, power-assisted liposuction; WAL, water-assisted liposuction; RFAL, radiofrequency-assisted liposuction.

Technique	# of Google Results	# of Pubmed Results	Highest level of evidence
Lipodissolve	646,000	9	IV
Injectable phosphadylcholine	107,000	28	III
Injectable deoxycholate	117,000	10	III
LipoLaser	234,000		
Zerona	775,000	0	N/A
LipoLite	75,600	0	N/A
I-Lipo	39,700,000	0	N/A
Thermage	2,040,000	22	IV
LipoSonix	112,000	4	IV
VASER	112,000	4	II
Ultrashape	361,000	6	IV
Zeltiq	144,000	1	V
Cryolipolysis	273,000	8	II
MedSculpt	6,530	1	V
TriActive	228,000	1	IV
VelaSmooth	301,000	3	IV
VelaShape	796,000	3	IV
Endermologie	1,420,000	15	III

Fig. 2. Search results and highest levels of evidence: noninvasive technique. PC, phosphatidylcholine; DC, deoxycholate.

Patients frequently ask about the quantity of fat that will be removed by liposuction, whether it will come back elsewhere, and how long it will take for the effect of surgery to be noticeable. Most practitioners rely on their own anecdotal experience to answer these questions. For example, the senior author (A.M.) translates the number of grams (cubic centimeters) of fat aspirated into pounds, which patients can comprehend easier, and then states that for each pound removed the patient would have had to burn 3500 calories. In a randomized trial of 32 patients, Hernandez et al. demonstrated that body fat is restored and redistributed from the thighs to the abdomen after suction lipectomy of the abdomen, thighs, and flanks.[25] Swanson recently addressed the issue of postoperative edema in a presentation at the 2011 American Society of Plastic Surgeons Annual Meeting in Denver, Colorado.[26] He performed magnetic resonance imaging studies on three women who underwent ultrasonic liposuction of the lower body (i.e., abdomen, flanks, buttocks, thighs, and knees) using a superwet technique. He demonstrated that 66 percent of the swelling associated with the procedure resolved after 1 month and 87 percent of the swelling resolved after 3.3 months. At 9.3 months, all swelling had resolved. Based on these magnetic resonance imaging data, we may be able to reassure our patients that their residual edema 1 month following liposuction, which represents one-third of the total edema immediately following surgery, will resolve. Further studies with a larger patient population are required to corroborate these data.

In addition, Swanson published a prospective outcomes survey of 360 patients treated with liposuction, abdominoplasty, or lipoabdominoplasty.[27] He reported that liposuction patients saw improvement in pain significantly more quickly than lipoabdominoplasty patients (pain ratings, 6.1 of 10 and 7.5 of 10, respectively; $p < 0.001$). The patient satisfaction ratings for lipoabdominoplasty (9.0 of 10) and abdominoplasty (8.7 of 10) were higher than for liposuction alone (7.8 of 10; $p < 0.001$)[28] (**Level of Evidence: Therapeutic, II**).

Of note, Swanson demonstrated an ancillary metabolic benefit to liposuction; a statistically significant reduction in triglyceride levels was seen in patients with elevated preoperative levels. A decrease in leukocyte counts was also observed.[27] Clinical significance of either of these reductions in laboratory values remains to be demonstrated. Moreover, in another report of 76 patients, he confirmed the safety of bupivacaine, lidocaine, and epinephrine (using its active metabolite monoethylglycinexylidide) at the higher levels found in liposuction wetting solution. He also reported that blood loss is underrepresented when looking at the lipoaspirate and included a plethora of additional laboratory and perioperative data about liposuction patients (**Level of Evidence: Therapeutic, IV**).[29,30]

Lipolysis and Skin-Tightening Technology

Procedures such as ultrasound-assisted, laser-assisted, and water-assisted liposuction, in addition to noninvasive methods (lipolysis), can be evaluated according to postoperative outcomes, instrumentation, or skin tightening. Lipolysis is a term used to describe various noninvasive or minimally invasive procedures for reducing subcutaneous fat volume in areas usually treated with traditional liposuction techniques. Medications (i.e., phosphatidylcholine or deoxycholate) that impact the content and integrity of adipocytes are injected subcutaneously,[31] or shock waves (usually used in procedures such as lithotripsy), lasers, and radiofrequency are applied to skin with the aim of simultaneously reducing fat (lipodystrophy) and remodeling collagen, thereby improving the appearance of cellulite and tightening skin.[32,33]

Cryolipolysis is another noninvasive procedure intended to cause the localized destruction of subcutaneous adipocytes. In a study by Ferraro et al., 50 patients were treated with a cryolipolysis protocol using the Proshockice apparatus (PromoItalia Group, S.p.A, Naples, Italy). They reported a mean reduction in fat thickness of 3.02 cm and a mean reduction in circumference of 4.45 cm after treatment.[34] Recently, Zeltiq (Zeltiq Aesthetics, Inc., Pleasanton, Calif.) and Zerona (Erchonia Corp., McKinney, Texas) have received U.S. Food and Drug Administration approval for noninvasive body contouring and fat reduction.

The holy grail of liposuction is a procedure that removes fat and tightens skin without large excisional procedures,[35] whether by surgical or noninvasive techniques. Recently, Kim et al. revisited the concept of superficial liposuction which, as in earlier reports, was designed to stimulate skin retraction at the time of liposuction (**Level of Evidence: Therapeutic, IV**).[36]

Laser-assisted liposuction is a surgical procedure designed to achieve traditional adipocyte removal along with skin tightening from the thermal effect of the laser in the dermis. In laser lipolysis, there is selective photothermolysis of the targets (known as chromophores) that are fat and water. Lasers within the near- and mid-infrared spectrum of 900- to 2800-nm optical wavelengths have been studied. Three major lasers have been tested, each with its own advantages. The 1064-nm neodymium:yttrium-aluminum-garnet (longest history of safety and reliability), 980-nm diode (continuous wave emission and high-power setting therefore best for large volumes), and the 1064-nm/1320-nm neodymium:yttrium-aluminum-garnet lasers (selective for collagen, neocollagenesis, and therefore possibly skin tightening and hemostasis). In the 1064-nm/1320-nm neodymium:yttrium-aluminum-garnet lasers, fat is targeted by the 1064-nm wavelength, and water bound in collagen is targeted by the 1320-nm wavelength.[37] Using a proprietary laser (1064-nm and 1320-nm wavelengths) device in a split-abdomen controlled study, DiBernardo, a paid consultant to Cynosure, treated 10 patients with laser-assisted liposuction and suction-assisted liposuction. He reported a statistically significant effect on skin shrinkage and tightening of the skin in the abdominal area.[37] He also published a series of 10 patients with thigh cellulite treated with a single session of 1440-nm pulsed laser therapy. He reported an improved appearance of cellulite that persisted at least 1 year after treatment, with minimal adverse effects.[37] A study by Sasaki was unable to produce skin tightening, although increasing surface temperatures (40° to 42°C) demonstrated changes in reticular collagen.[38] Using the combined 1064-nm/1320-nm neodymium:yttrium-aluminum-garnet laser with a cannula liposuction phase, he demonstrated improvement in skin tightening.[39] Fakhouri et al. provide a current and comprehensive review of the current state of laser lipolysis.[40] They review the evolution of the field and its current status. They conclude that despite the effectiveness of different laser wavelengths to selectively target adipocytes and reticular collagen, certain unique disadvantages exist. Finally, they report that there are no randomized controlled studies comparing laser-assisted liposuction with traditional liposuction that report significant clinical advantages to the laser-assisted liposuction. Furthermore, lack of standardization between machines, differing amounts of time and energy applied to anatomical areas, and isolating the effect of laser alone on the outcome make it difficult to quantify and compare published results in this evolving field. Figures 1 and 2 list currently available technologies for noninvasive and minimally invasive fat reduction and/or skin tightening.

Complications

All plastic surgeons that perform liposuction should be familiar with the risks, untoward sequelae, and complications associated with the procedure. Fortunately, most complications of liposuction are minor in nature and tend to resolve spontaneously (untoward sequelae). Hughes demonstrated that complication rates increase when liposuction is combined with other procedures.[41] Devastating injuries, including internal organ perforation, are reported but are exceedingly rare.[42,43] Kim et al. recently reviewed a series of 2398 patients who underwent superficial liposuction over 14 years,[36] ostensibly to enhance skin tightening. Patients were divided into three groups: power-assisted liposuction alone, power-assisted liposuction with ultrasound, and power-assisted liposuction with external ultrasound and postoperative Endermologie (LPG Systems, Valence, France). Mean aspirate volume in all groups was 5045 cc. They reported a total complication rate of 8.6 percent, with contour irregularities being the most common complications reported (3.0 percent).[36]

Venous thromboembolism following surgical procedures continues to generate a great deal of attention in the professional and lay media. Few large-scale formal studies exist that evaluate the incidences of deep vein thrombosis or pulmonary embolism in patients undergoing liposuction.[44] A recent article cited the incidence of deep vein thrombosis to be less than 1 percent.[45] Newall et al. reported a 0 percent deep vein thrombosis rate in a retrospective series of patients who underwent large-volume liposuction and received chemoprophylaxis with low-molecular-weight heparin.[46] Miszkiewicz et al. published a systematic review in 2008 that captured 11 articles and reported rates of deep vein thrombosis in patients undergoing liposuction between 0 and 0.59 percent.[47]

Plastic surgeons are becoming familiar with the Davison-Caprini model for thromboembolism risk assessment.[48] Ideal risk assignment and prophylaxis for the prevention of deep vein thrombosis/pulmonary embolism in liposuction patients remains a challenge. One obstacle is that the widely adopted American College of Chest Physicians Guidelines applies to inpatients only. No high-level data exist to inform recommendations for venous thromboembolism prophylaxis in outpatient liposuction, but it is worthwhile for all plastic surgeons to consider adopting a clear system for their own practices.[48]

In July of 2011, the American Society of Plastic Surgeons published the "Evidence-based Practices for Thromboembolism Prevention: A Report from the ASPS Venous Thromboembolism Task Force." The Task Force selected the 2005 Caprini scale as its reference point because it was formally validated to stratify plastic surgery patients based on their individual risk factors. Risk stratification guidelines were limited to include patients who required general anesthesia. Recommendations were that inpatients should complete a 2005 Caprini risk-assessment model (or equivalent scale) and outpatients should consider completing a 2005 Caprini risk-assessment model (or equivalent scale). Prevention guidelines applicable to liposuction patients were extrapolated from data generated by patients undergoing body contouring procedures that lasted more than 60 minutes. Their highest level recommendation (grade B) is that patients with a Caprini score of 3 or more should consider using postoperative low-molecular-weight heparin or unfractionated heparin. Patients with a Caprini score of 7 or more should *strongly consider* using postoperative low-molecular-weight heparin or unfractionated heparin.[49]

Administration of low-molecular-weight heparin (i.e., enoxaparin) has resulted in a decreased incidence of venous thromboembolism, although there is concern that the risk of bleeding may be increased (**Level of Evidence: Risk, II**).[50] In January of 2012, the Plastic Surgery Foundation–funded Venous Thromboembolism Prevention Study examined whether receipt of postoperative enoxaparin prophylaxis changed 60-day reoperative hematoma rates (in a variety of plastic surgery procedures). They concluded that postoperative enoxaparin does not produce a clinically relevant or statistically significant increase in observed rates of reoperative hematoma.[51] Large-scale trials to help elucidate which patients undergoing which procedures require pharmacologic, mechanical, or other deep vein thrombosis prophylaxis are necessary and underway.

Laboratory research also supports the need for increased attention to deep vein thrombosis/pulmonary embolism in liposuction patients. Prado et al. used thromboelastography, a method of testing the efficiency of the coagulation of blood, to demonstrate that patients undergoing suction-assisted liposuction have decreased initial clotting time, decreased time to full clot formation, increased clot rigidity, and a hypercoagulable state.[52] Franco et al. demonstrated that fat emboli (pulmonary fat embolism syndrome, not deep vein thrombosis/pulmonary embolism) occur in animal studies after liposuction and hypothesized they are likely underdiagnosed in human patients.[53] Gravante et al. reported that resection of less than 1500 g of tissue volume decreases the likelihood of pulmonary embolus when liposuction is combined with abdominoplasty.[9]

Autologous Fat Transfer/Stem Cells

Although peripherally related to liposuction, the topic of fat transfer is among the most current and still controversial topics in plastic surgery despite initial investigations going back more than 25 years.[54] Numerous studies have looked at the ideal extraction method of fat, how it should be processed, how it should be injected, and the depth of injection. It is likely that no one method will apply to all autologous fat transfer procedures. Fat transfer may be performed as a primary procedure (e.g., breast or buttock augmentation), as an adjunct (e.g., face-lift surgery or breast reconstruction), or for the potential of "stem cell" therapy. Contributing to the discrepancy in conclusions, cell therapy as an aspect of fat grafting is receiving a lot of attention. The American Society of Plastic Surgeons and the American Society for Aesthetic Plastic Surgery recently published a position paper on the topic of stem cell therapy to address the growing concern surrounding unsupported claims of stem cell treatments in aesthetic surgery. They determined that terms such as "stem cell therapy" or "stem cell procedure" should be reserved to describe those treatments or techniques where the collection, concentration, manipulation, and therapeutic action of the stem cells is the primary goal, rather than a passive result, of the treatment. For example, standard fat grafting procedures that happen to transfer some stem cells that are naturally present within the tissue should be described as fat grafting procedures, not stem cell procedures. Furthermore, they concluded that the marketing of stem cell procedures as advantageous in aesthetic surgery is not adequately supported by clinical evidence at this time, and that all use of stem cell therapy in aesthetic and reconstructive surgery should be conducted within clinical studies under institutional review board approval.[55]

Future Directions in Adipocyte Biology

Previously considered relatively metabolically inert compared with other cells, adipocytes are recognized as metabolically active and hormonally sensitive cells with considerable biological activity, resulting in renewed research enthusiasm. Brown fat has garnered much attention because of its unique physiologic properties. Specifically, it burns calories at a much higher rate than white fat. Researchers are currently characterizing brown fat and have already determined that it exists in greater quantities in young people, is activated when people get cold, and burns white fat (as opposed to glucose) to fuel itself. Moreover, a form of brown fat can be created from ordinary white fat by exercise.[56] A Swedish group identified a protein, irisin, which is capable of turning white fat into brown fat. This molecule is being studied by adipocyte biologists and may one day provide a truly noninvasive method of decreasing fat.[57]

CONCLUSIONS

When liposuction was first introduced and popularized in the early 1980s, it indelibly altered the field of body contouring surgery and redefined plastic surgery for future generations of surgeons. With 203,106 operations performed in 2010 (up from 198,251 in 2009),[58] and many more performed by nonplastic surgeons, liposuction continues to rank among the most frequently performed plastic surgical and indeed one of the most common of all elective surgical operations.[59] Unless a "cure" for obesity is discovered, or a tectonic shift in human nature, lifestyle, or fashion trends occurs, it is likely than our concerns with lipodystrophy will persist unabated. Moreover, as more practitioners and manufacturers become involved in this area and research continues into the understanding of adipocyte physiology (where previously there was little interest), the fields of liposuction, lipolysis, obesity, and fat cell metabolism will continue to gain more interest and realize more advancement.

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