

Advancements in Autologous Treatments Prove the Future is Now

By Kevin A. Wilson, Contributing Editor

Experiencing rapid advancement, autologous therapy is a hot topic in aesthetic medicine. A good deal of these treatments fall under the category of regenerative medicine, an emerging field aiming to repair or restore lost or damaged tissue function due to aging, disease or injury. For many, the idea of using one's own cells or adipose tissue for the purpose of augmenting therapeutic outcomes or creating entirely new treatments is both controversial and futuristic.



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62 year old female before Tx



62 year old female 3.5 months after 3D face-lift using a fat graft prepared by PureGraft from Cytori Therapeutics
Photos courtesy of Steven R. Cohen, M.D.



Patient before Tx



Patient three months after VASER Hi-Def liposuction and fat transfer to pectoral area
Photos courtesy of John A. Millard, M.D.

Currently, there are basically three modes of therapy available for medical patients: drugs, devices and surgery, with autologous cell therapy developing into a separate, fourth method of treatment. "Cell therapy is an adjunct to existing modalities bringing us completely new therapies as well," said Marc Hedrick, M.D., president of Cytori Therapeutics, Inc. (San Diego, Calif.). "There are clear advantages because the cells are your own; you can't give yourself a disease you don't already have, they're not cultured outside the body, and they're minimally manipulated. This sort of therapy could be relatively inexpensive, and would often be available at the bedside within an hour, so almost any procedure could be augmented with cell therapy of some sort. It will be a powerful and easily available tool for medical and aesthetic procedures."

Few topics have seen as much controversy as the use stem cells. "Stem cells are characterized by their ability to replicate themselves through mitosis and, under certain conditions, differentiate into any of a range of specialized cell types found within the body," explained Spencer A. Brown, Ph.D., director of plastic surgery research at the Nancy L. and Perry Bass Advanced Wound Healing Laboratory, at the University of Texas Southwestern Medical Center (Dallas, Texas). The harnessing of adipose-derived stem cells (ADSC) and adipose-derived regenerative cells (ASRC) for medical use has tremendous potential, and it turns out that the richest source of stem cells is the fat cell. After harvest, ADSC are concentrated through processing into what is called the stromal-vascular fraction (SVF), which contains multiple cell types. "ADSCs are proven to be capable of differentiation, which is what makes them so valuable," he continued, "although the exact mechanism of action by which that happens is not yet fully understood."



Spencer A. Brown, Ph.D.
Director of Plastic Surgery Research
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The fact that the richest source of stem cells is found in fat cells may explain why stem cells and autologous fat transfer (AFT) were quickly joined together. While the first documented autologous fat transfer was performed in 1893, until recently the modality languished behind more exciting, emerging, state-of-the-art technologies such as lasers and injectables. Today these positions have been reversed. "It's safe to say that AFT is the hot topic, and that's even truer when you add stem cells to the mix," said Steven R. Cohen, M.D., medical director of the FACES+ Plastic Surgery, Skin and Laser Center (San Diego, Calif.).



Steven R. Cohen, M.D.
Medical Director
FACES+ Plastic Surgery, Skin and Laser
Center
San Diego, CA

"In the early 21st century there was a brief flurry of clinical studies identifying that stem cells and other regenerative cells may be capable of improving the survivability of fat grafts," Dr. Cohen continued. Through the ensuing five years the work was hidden behind closed doors, but the fruits of that labor are emerging. "AFT requires a skilled hand and high quality, viable fat to work with, but the results you can obtain with the current technology are getting better," as companies worldwide are clamoring to develop technologies using ADSC and ADRC.

PureGraft and Celution from Cytori are separate but complementary technologies for fat grafting and ADSC concentration. "In the simplest terms PureGraft is a sort of fat dialysis," Dr. Hedrick explained. "As in a patient with kidney failure, PureGraft dialyzes liposuction aspirate to remove water and impurities such as anesthetic, blood,

inflammatory cells and extracellular lipid material spilled from ruptured adipocytes leaving basically pure fat. Too much water in transplanted fat makes the result look fuller than it really is."

Celution, approved in Europe for breast augmentation and reconstruction, automates the extraction of stem cells from fat and concentrates them down to 5 cc, in a way that's both safe and clinically useful. "Clinical trials are showing promising results when used during breast reconstruction after radiation and lumpectomy, and to promote growth and healing from severe heart disease," said Dr. Hedrick. In more and more cases physicians are combining these technologies to create a superior fat graft. "You can use PureGraft to obtain a clean, high quality, viable fat sample. Adding Celution-concentrated stem cells back to the fat graft makes for a better implant that's more likely to take because the stem cells and growth factors concentrated in the graft improve vascularization and provide other benefits as well."

"The development of safer and gentler techniques has provided us with higher quality fat for grafting, which was always a big problem from the beginning."

Regardless of stem cells, fat grafting has advanced rapidly as technology has improved liposuction. "The development of safer and gentler techniques has provided us with higher quality fat for grafting, which was always a big problem from the beginning," noted Dr. Cohen.

John A. Millard, M.D., a plastic surgeon in Lone Tree, Colo. considers the VASER Ultrasonic Lipo System from Sound Surgical Technologies, LLC (Louisville, Colo.) the standard in ultrasonic body contouring adjunctive to liposuction. Recent improvements in this device, such as more sensitive monitoring and control of suction pressure, were focused on advancing its ability to harvest fat.



John A. Millard, M.D.
Plastic Surgeon
Lone Tree, CO

The use of VASER for AFT was further enhanced by two adjunctive fat collection systems: Shippert Tissue-Trans and the Origins Collection System. "Shippert was the first large volume collection device out there," Dr. Millard said. "It's extremely fast, effective and collects every drop of viable fat in the aspirate. This is essential when you consider that the future of AFT is harvesting in individuals with less body fat. In those cases every bit of viable fat is precious."



Robert Troell, M.D.
Plastic Surgeon
Las Vegas, NV

Robert Troell, M.D., a plastic surgeon in Las Vegas, Nev., was the first to use the Origins Collection System. "This system is a closed system that allows gravity to separate fat from aspirate without a filter. However, you have the capability of adding a filter in the future if studies show this to be beneficial, which so far they have not," he said. "Fat can be more easily collected than with the Shippert system. When used with VASER's VentX cannulas, fat suctioned at low pressure (< 0.5 atmosphere) is less likely to be injured in transit. It also makes acquisition of fat from the collection container a simple, rapid process for fat grafting."



Patient before Tx



Patient after autologous fat transfer Tx
Photos courtesy of Robert Troell, M.D.

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Patient before Tx



Patient after autologous fat transfer to buttocks
Photos courtesy of Leonard Tachmes, M.D.



Patient after traditional face-lift



Patient after autologous fat transfer Tx
Photos courtesy of Mark Berman, M.D., F.A.C.S.

AquaVage, marketed by M.D. Resource in Livermore, Calif., also relies on gravity to separate fat from liposuction aspirate. According to Leonard Tachmes, M.D., a plastic surgeon in Miami Beach, Fla., "This is a simple but elegantly designed disposable two or five liter container with a filter and you can connect their collection syringe. What's ingenious is that instead of a luer lock system, which is associated with higher pressures, they employ a Toomey syringe system, which has a larger bore diameter for reduced pressure and trauma to the fat."



Leonard Tachmes, M.D.

Plastic Surgeon
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TICKLE LIPO or Nutational Infrasonic Liposculpture is distributed in the U.S. by Medical Alliance Services (Southlake, Texas). This unique and proven technology offers a patented, nutational movement to gently and selectively release and remove unwanted adipose tissue while preserving the important connective tissue, without exposing the fat to excessive vacuum, heat or hydration. TICKLE LIPO places the sterile reusable canister between the aspirator and the nutational infrasonic harvesting cannula to reduce handling of fat. After decanting, the operator may open the release valve at the base of the sterile canister and drain the tumescent fluid, leaving the viable fat in the sterile canister. Without further preparation, sterile fat is drawn into individual luer lock syringes, ready for injection.

Palomar Medical Technologies, Inc. (Burlington, Mass.), is entering the fat collection arena with an unnamed device, revealed Mark Berman, M.D., F.A.C.S., a plastic surgeon in Los Angeles, Calif., and immediate past president of the *American Academy of Cosmetic Surgery*. "It is basically a centrifuge with a suction pressure pump, which isn't so new; however, they developed 60 cc custom syringes that fit into the closed system. These syringes have a weighted piston system (instead of a plunger) and a filter within. You suction the aspirate into the centrifuge, separate it and harvest fat from the middle section – where the best adult fat cells and highest concentration of stem cells exist. Then you implant the fat. This device is very easy-to-use."



Mark Berman, M.D., F.A.C.S.

Plastic Surgeon
Los Angeles, CA

Breast enhancement has long been a key focus of aesthetic medicine, and related AFT modalities are no exception. While the benefits of such techniques seem obvious, augmentation of the breast via AFT and/or infusion of adult stem cells for aesthetic or reconstructive purposes have been considered an unstable idea until recently. "There was a serious concern that infusing the breast with stem cells, for any reason, might accelerate tumorigenesis," Dr. Cohen explained. Some believe undiagnosed cancer could be exacerbated; as well, there is additional unease since these procedures would help reconstruct breasts post-mastectomy, a case where latent cancer cells are even more likely to reside. "The community wavered on this issue for the past several years, but when you look at the science, this phenomenon has just not been seen," he added.



Klaus Ueberreiter, M.D.

Plastic Surgeon
Berlin, Germany

For AFT breast augmentation, Klaus Ueberreiter, M.D., a plastic surgeon in Berlin, Germany uses another prominent liposuction device for AFT: Body-Jet water-assisted liposuction (WAL) with its adjunctive LipoCollector system from human med, Inc. (Dallas, Texas). Body-Jet uses pulses of fluid instead of

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Patient before Tx



Patient after autologous fat transfer Tx
Photos courtesy of Mark Berman, M.D., F.A.C.S.



Patient before Tx



Patient six months after second BEAULI Tx
Photos courtesy of Klaus Ueberreiter, M.D.

laser, ultrasound or other energy sources to gently dislodge fat for easy removal. LipoCollector filters the fat from the water and other components for a more pure grafting sample.

Dr. Ueberreiter's technique, termed BEAULI, utilizes a thin cannula for harvesting and an even thinner cannula (2 mm) for injection. "Implants always look artificial," he said. "Through a single tiny puncture I can implant microdroplets of fat into all layers of the breast for a very natural shaping result. BEAULI can create more volume than one would expect (maybe half a cup size on average), but unlike implants you can significantly influence breast shape. The process may take up to four sessions, especially with reconstruction." Dr. Ueberreiter is currently conducting a clinical trial of the BEAULI technique and his results will be showcased in an upcoming publication. The study measured increases in breast volume through MRI and volumetry at six months post treatment. "We are seeing about a 75% success rate on average, with an extremely low amount of complications."

Currently, the technical standard for fat implantation is the Lipostructure microdroplet technique developed by Sydney Coleman, M.D., a plastic surgeon in New York, N.Y.



Sydney Coleman, M.D.
Plastic Surgeon
New York, NY

Fat is implanted at various locations and depths in small aliquots to encourage graft viability and promote a natural looking result. "This technique started as aesthetic but has moved into the field of reconstructive surgery. It's more than just AFT as a filler; there is neovascularization, which possibly leads to what I consider improved skin

quality. The procedure is not only used as a primary procedure for rejuvenation, but also to reverse radiation damage to skin and surrounding tissues after cancer therapies. In just the past few months, the number of peer-reviewed articles about fat grafting, stem cell content and their regenerative properties has skyrocketed."

Richard Ellenbogen, M.D., a plastic surgeon in Beverly Hills, Calif., has taken the concept of stem cell facial rejuvenation one step further with the stem cell activated face-lift. "I was the first to add fat to face-lifts in what I call the volumetric face-lift," he stated. "Using an emerging proprietary technology from Adistem Ltd. (Wan Chai, Hong Kong, China), we harvest and then irradiate ADSC with low-level laser light for biostimulation, which may increase graft persistence and improve the overall result in numerous visible, but little-understood ways. I am hesitant to make claims beyond that, because we still have a lot of research ahead of us."



Richard Ellenbogen, M.D.
Plastic Surgeon
Beverly Hills, CA



Per Hedén, M.D., Ph.D.
Plastic Surgeon
Stockholm, Sweden

Some believe that AFT results are better achieved by implanting segments of donor fat. Per Hedén, M.D., Ph.D., a plastic surgeon in Stockholm, Sweden, is developing Resitu, a disposable device for the minimally invasive harvesting of fat segments from the body. "This is basically a cylinder with a round cutting knife

for safe and easy harvesting. With Resitu you can implant segments in places where traditional AFT doesn't work, such as the lips or nose," he explained. A version of Resitu for excising larger amounts of fat for implantation in the body is in development.

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Richard Ellenbogen, M.D. preparing stem cells for stem cell face-lift.



Patient before Tx



Patient six months after second BEAULI Tx
Photos courtesy of Klaus Ueberreiter, M.D.

Stem cells and growth factors can also be concentrated from other sources, such as autologous blood. Sabine Zenker, M.D., a dermatologist in Munich, Germany pointed out that injections of biostimulating platelet-rich plasma (PRP) to rejuvenate and regenerate the skin are becoming popular in Europe, where mesotherapy is more widely practiced than it is in the U.S. Two major offerings include Selphyl from Aesthetic Factors, LLC (Princeton, N.J.), and MyCells from Kaylight Corporation (Kreuzlingen, Switzerland). Each involves the use of a disposable kit to derive and collect platelets from a patient's blood, thereby concentrating the naturally occurring growth factors for re-injection.



Sabine Zenker, M.D.
Dermatologist
Munich, Germany

As with mesotherapy, PRP is implanted with numerous superficial injections. The only downside is very mild bruising or hematoma, which is mostly invisible. "This is not a replacement for dermal fillers, although some patients use it as an alternative," she said. "With regular injection, PRP revitalizes the skin in ways that are visible to an observer, but harder to prove scientifically. The presence of concentrated growth factors seems to cause matrix stimulation, neovascularization, neocollagenesis and epithelialization, for example. PRP gives facial skin a very healthy, naturally beautiful glow. The results are outstanding."

The difference between the two products lies in the harvesting method, Dr. Zenker continued. "MyCells uses a special harvesting technique after the platelets are separated from the plasma for more stability, and they have proven a consistently high platelet recovery rate. With Selphyl the plasma is activated extracorporeally, so it clots rapidly if not quickly implanted. Nevertheless, Selphyl is the only product to my knowledge that has a solid peer-reviewed paper behind it."

Although not yet approved for use in the U.S., ReCell from Avita Medical, Ltd. (Woburn, Mass.), also harnesses the power of growth factors, but for the treatment of wounds, burns, scarring and skin defects. According to the company's website¹, the ReCell kit facilitates the harvest of a split thickness skin biopsy and processes it into an autologous cell population for spray application (a process which takes approximately 30 minutes) to cover up to 80 times the area of the donor biopsy. According to Aamer Khan, M.D., medical director of the Harley Street Skin Clinic (London, U.K.), quoted in a November 2010 press release: "Results with ReCell have been exceptionally encouraging. Extremely difficult cases have shown significant improvement with respect to visual scarring, texture, pigmentation and contour."

As with any technology, there are those who caution against jumping on the bandwagon. Val Lambros, M.D., a plastic surgeon in Newport Beach, Calif., isn't so much against these technologies; he's just not overwhelmingly impressed. "Medicine is constantly changing, but there are always fads and trends. People are typically dazzled by technology and what may often be unproven or even outlandish claims," he began. "This year's laser, which usually costs more than \$100,000, is supposedly better than last year's model, but is it really much improved, and does that justify buying a new machine just because patients will pay for it? In my 25 years of practicing aesthetic medicine this is the third go-round for PRP, for example. I don't think it really does anything particularly useful to make people look better or younger. If well-promoted they will all make money, then it may go away again quietly once people realize that it didn't live up to expectations."

“As a community we have to be cautious, but with what we’re seeing, autologous therapies are exciting for a reason. Regenerative medicine is moving us toward markedly reduced scarring and improved outcomes across the board, among other things.”



Patient before Tx



Patient after autologous fat transfer Tx using fat collected with TICKLE LIPO from Medical Alliance Services
Photos courtesy of Ralph Craig Saunders, M.D.

Dr. Lambros himself uses modest amounts of AFT. “I’ve been using AFT for more than 20 years and was one of the original users. It’s a genuinely useful tool in the armamentarium and an essential component of my face-lift protocol, but in my opinion it’s becoming overhyped and seriously misunderstood,” he stressed. “It’s very technique dependent, more so than people seem to believe. Not every physician has the sculptor’s touch with a syringe. Results are still highly variable; sometimes it doesn’t work well, sometimes it works too well. Also, it’s a biological material, which means that not only can it go away, but it can grow, especially if you put on weight. Five or ten years later you might have a fat face, and the grafts will look terrible. I’ve seen this more and more.” In the case of complications, Dr. Lambros said the best way to rectify them is to remove the fat with a needle and syringe. “You have to know the location and depth of the graft, which adds to the difficulty level.”

According to Dr. Lambros, part of the problem is the science. “Aesthetic medicine really has more to do with the beauty business than science, and in the beauty business you can say whatever you want. Marketing is a huge part of this business model, proof is not; it is lacking in peer reviewed science,” he stated. “I’m not saying that it’s necessarily dishonest, but there are many studies showing results that are hard to see and difficult to prove, and presentations at meetings where you look at the pictures and you can’t tell the difference. Just because two or even 22 people think they see something doesn’t mean it’s there and worth publishing. Hope springs eternal; when you do something you think is great but just can’t prove, and you get that warm and fuzzy feeling – that feeling is probably all inside your head.”

Establishing regenerative treatments as the relevant, scientifically strong field of medicine that it should be is exactly the goal of the *Cell Society*, recently formed with financial backing from Cytori. “The *Cell Society* is the only international scientific organization dedicated to the safe advancement of adult stem cell therapies,” said Dr. Cohen who is co-founder and executive director of the *Cell Society*. “There are so many misconceptions out there about adult stem cells versus embryonic stem cells, for example. We are organizing a clearing house of information about these treatments and the science behind them. We’re not a research organization so much as a force for education and a forum for sharing and presenting clinical applications of established and emerging therapies.”

Whatever the final verdict, it is clear that the emergence and refinement of autologous therapies is to be taken seriously. Its implications are astounding. “As a community we have to be cautious, but with what we’re seeing, autologous therapies are exciting for a reason,” Dr. Cohen explained. “Regenerative medicine is moving us toward markedly reduced scarring and improved outcomes across the board, among other things. In most cases we’re taking cells from a patient and either concentrating them or diluting them, for example, which is relatively safe compared to what medical science has been willing to subject patients to throughout history. The reality is that autologous therapies require intense scientific scrutiny just the same. That’s what the *Cell Society* is all about.” ■

References:

1. <http://www.avitamedical.com/index.php?ob=1&id=15>, accessed 10 January 2011