CME

Current Clinical Applications of Fat Grafting

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Learning Objectives: After reading this article, the participant should be able to: 1. Understand the theory and principles behind successful avascular fat transfer; 2. Apply these principles into techniques that yield safe and successful fat grafting operations; 3. Identify the well-established indications and limitations of the various fat grafting operations as well as the indications that require additional clinical and translational research.

Summary: In this article, the authors summarize the established principles and techniques of fat grafting, discuss debated topics, and present both the well-established and the novel clinical applications of fat grafting. (*Plast. Reconstr. Surg.* 140: 466e, 2017.)

"The results are amazing but inconsistent." This was the sentiment surrounding free flaps in the 1980s. We discovered a naturally occurring inhibitor of coagulation that prevented anastomotic thrombosis in the laboratory[1] and conducted a double-blinded, controlled, randomized study to assess its benefit in free flaps. Disappointingly, there was no significant effect.[2] When we dissected why free flaps fail, we realized that success depended on multiple factors chain-linked in series, and that the anastomosis was not always the weakest link.[3] Free flaps became a reliable procedure when we abandoned the search for a panacea and realized that success required exacting surgical technique. This history illustrates the concept that, in a multivariable process, optimizing a single variable does not necessarily improve the outcome; the entire process must be taken into consideration.

Similarly, autologous fat transfer has opened many applications in reconstructive surgery with amazing results, but many dismiss it as inconsistent. Although many individual technical factors have been singled out as being responsible for graft take, it has become clear that no single additive or processing method can serve as a panacea.[4–11] Favorable results can be consistently obtained by following established principles and techniques. Fat graft surgery should be approached with the same degree of craftsmanship as microvascular free flap surgery.[12,13] This article reviews the established principles of fat graft survival, elaborates on the surgical techniques that adhere to these principles, and provides an overview of the clinical applications.

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PRINCIPLES OF GRAFT SURVIVAL

What Is Fat?

Over 90 percent of adipose tissue volume consists of adipocytes, but nearly 50 percent of the in vivo adipose tissue total cell number consists of adipose-derived stem cells, fibroblasts, endothelial cells, and pericytes in an extracellular matrix.[14] Although fat was initially thought to be an inert substance for energy storage, recent research has elicited its regenerative capabilities.

Many studies have demonstrated the regenerative potential of autologous fat transfer, presumably because of its adipose-derived stem cell content. This includes angiogenesis,[15] peripheral nerve regeneration,[16] enhancement of dermal thickness and elasticity,[17] reversal of fibrosis (secondary to radiation therapy,[18,19] scarring,[20]

Disclosure: *Roger K. Khouri has equity interest in LipoCosm, the manufacturer of the LipoGrafter. He is the inventor of Brava, the original External Vacuum Expander, but he no longer has any financial interest in Brava, LLC. Roger K. Khouri Jr. has no conflicts of interest to disclose.*

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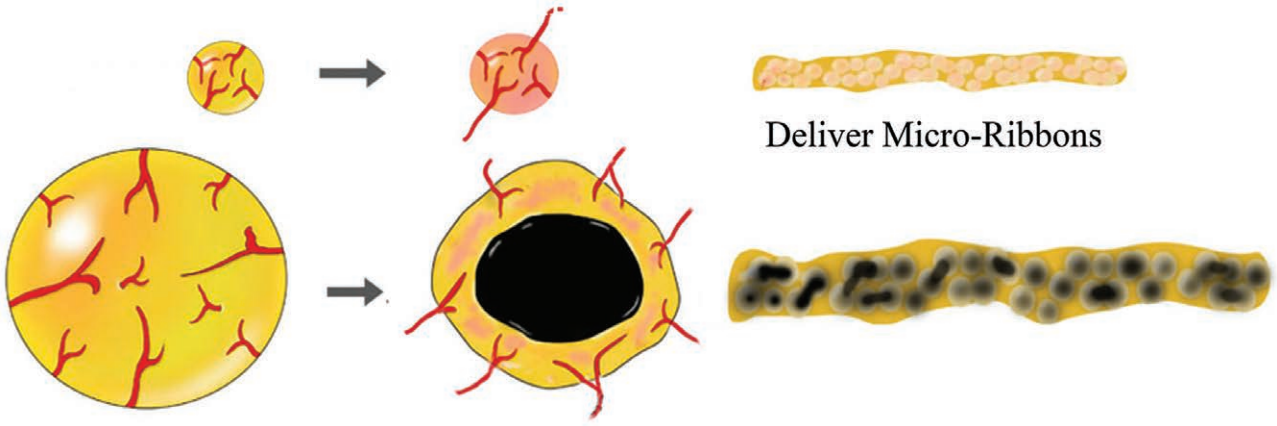


Fig. 1. Only microdroplets with radii less than 1.6 mm = 17 μl ($V = 4/3\ \pi r^3$) will completely revascularize and 100 percent survive. A 1-ml spherical droplet has a radius of approximately 6.2 mm. At best, only its outer 1.6-mm shell will survive, leaving behind a necrotic center with a 4.6-mm radius (volume = 0.41 ml). Therefore, even a tiny 1-ml droplet will have at least 41 percent necrosis. When injected continuously through a cannula, microdroplets become cylindrical microribbons. Ribbons with radii wider than 1.6 mm will inevitably have some central necrosis.

or inflammatory conditions, such as scleroderma),[21,22] treatment of Peyronie's disease,[23] urethral strictures,[24] stress urinary incontinence,[25] rheumatoid arthritis,[26] and osteoarthritis.[27] The challenge is to refine the true indications and harness this potential for the clinical arena.

What Happens to Fat after Being Grafted?

In an avascular fat graft, only the most peripheral layer of adipocytes survive the hypoxia.[28,29] Just below is the regenerative zone, where only adipose-derived stem cells revascularize and regenerate a new adipocyte population. Deep to the regenerative zone is the necrotic zone, where no cells survive. Under ideal circumstances, the maximum depth of the regenerative zone is 1.6 mm.[30] Oxygen diffusion is the rate-limiting step in fat grafting, and only "microdroplets" or "microribbons" in the 3-mm (2 x 1.6 mm) range revascularize and survive (Fig. 1). (**See Video, Supplemental Digital Content 1**, which displays the neovascularization limit. Grafts larger than 3 mm will invariably suffer central necrosis. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C297***.)

Video 1. Supplemental Digital Content 1 displays the neovascularization limit. Grafts larger than 3 mm will invariably suffer central necrosis. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or available at ***http://links.lww.com/PRS/C297***.

How Can Large-Volume Fat Grafts Revascularize?

Revascularization depends on this maximal 1.6-mm graft-to-recipient interface. To optimize it, large graft volumes must be sprinkled inside a recipient in a three-dimensional distribution as a fine mist of microribbons that do not coalesce (Fig. 2).

How Much Fat Can Be Grafted into a Given Site?

Fat graft can be conceptualized in the same fashion as the stoichiometry of a chemical reaction, where a fat droplet (G) combines with a capillary receptor site (R) to result in a revascularized graft-recipient complex (GR). A given amount of recipient site (R) can only accommodate a limited amount of graft (G) before the excess graft coalesces and necroses (Fig. 3).

As microdroplets are carefully inserted without coalescing, the recipient must stretch to accommodate the added volume. The pressure required for stretching the tissues is determined by their mechanical compliance, which varies between

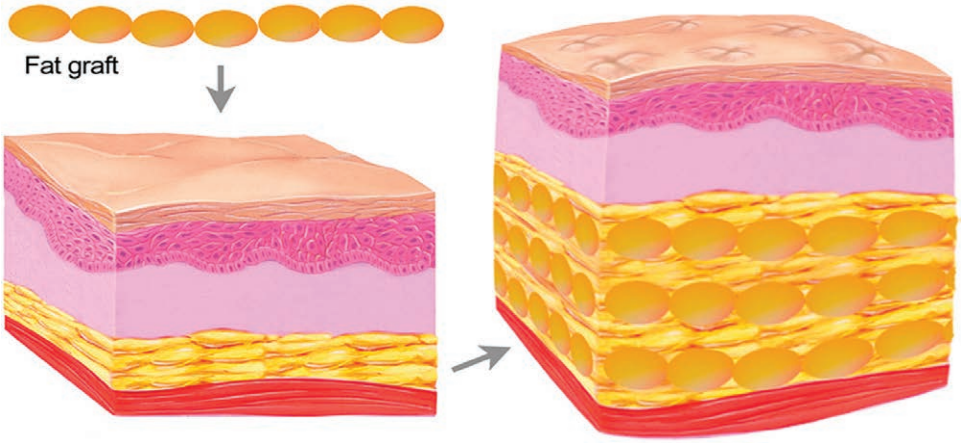


Fig. 2. The sprinkle micrograft delivery. To maximize graft-to-recipient interface, microdroplets smaller than 17 μl or microribbons less than 3.2 mm wide must be distributed in a three-dimensional pattern that avoids coalescence. As the recipient gradually fills up and enlarges to accept more grafts, its mechanical compliance decreases, and its interstitial fluid pressure increases.

tissues and is not linear.[12] For small-volume increases, most tissues are compliant. However, as graft volume increases, interstitial pressure eventually rises to levels that curb capillary perfusion.[30]

Recognizing the limited grafting capacity of a recipient site is crucial, and overzealous grafting is a common pitfall. Just as in two-dimensional grafting, overgrafting beyond the size of the defect is counterproductive; in three-dimensional grafting, we should not graft beyond what the recipient can physiologically stretch to accommodate.

How Should Autologous Fat Transfer Results Be Measured?

Megavolume autologous fat transfer success is commonly measured as percentage graft survival. This erroneous measure tells nothing about what truly matters in volume augmentation, which is meaningful volume increases relative to the original recipient-site volume. Small amounts grafted into a large recipient might have excellent survival but result in minimal augmentation. The relevant measure of success should be percentage volume augmentation (Fig. 4).[31] [**See** Video**, Supplemental Digital Content 2**, which displays the recipient capacity. Under ideal grafting conditions, maximum percentage augmentation (30 to 50 percent) is reached at maximum recipient capacity. Grafting beyond capacity is counterproductive. Preexpansion that increases the maximum recipient capacity also increases the maximum percentage augmentation. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C298***.] This is (permanent *increase* in recipient-site volume)/(original recipient-site volume).

Which Variables Should Be Enhanced?

Although many variables may play a role, there is usually one rate-limiting step to any process. Enhancing other variables has no effect if the rate-limiting step is unchanged. The chain is only as strong as its weakest link.

Elimination of inflammatory cells and molecules has been heralded by some as the key to consistent results. Promoters of this theory tend to market devices that "purify" fat grafts and eliminate harmful substances. Inflammation has not been shown to be a critical variable in fat graft survival. Moreover, the "inflammatory humors" they refer to are unlikely harmful, as they are the natural microenvironments of the harvested fat and of the grafted recipient. Paradoxically, although some advocate removing potential inflammatory agents, others champion adding proinflammatory platelets. Until conclusive evidence with randomized controlled trials exists, we prefer to err on the side of simplicity.

Augmenting autologous fat transfer with adipose-derived stem cells to enhance the results has been suggested. Kølle and colleagues injected as a subcutaneous bolus into human volunteer arms 30 ml of fat enriched with a tissue culture-expanded preparation containing 20 million adipose-derived stem cells per milliliter (2000 times physiologic levels).[32] The enriched group had 80.9 percent volume retention compared with 16.3 percent in the control. The low retention rate in the nonenriched group was most

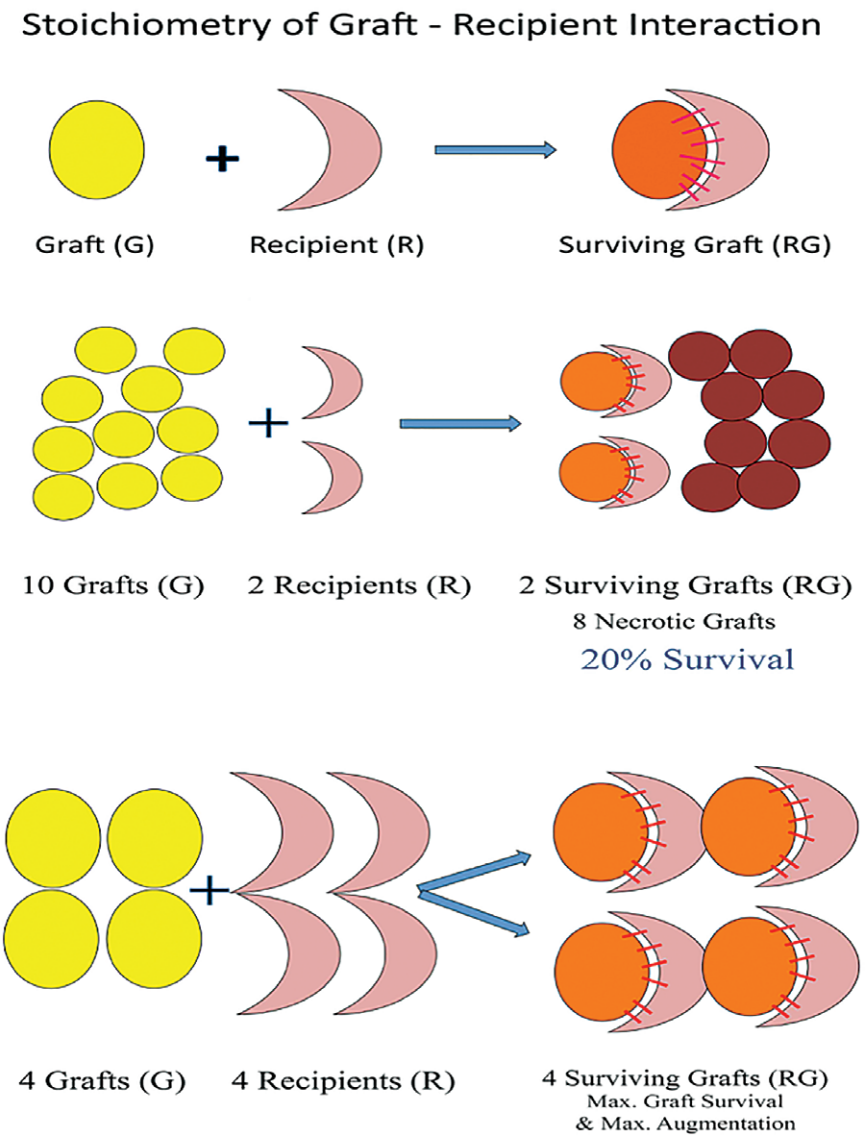


Fig. 3. Stoichiometry of fat grafting. (*Above*) A unit graft (*G*) has to interact with a capillary recipient site (*R*) to yield a surviving graft-recipient complex (*RG*).(*Center*) If only two recipients (*2R*) are available, adding 10 grafts (*10G*) will at best yield two surviving grafts (*2RG*), leaving eight necrotic grafts. Assuming a surviving graft unit adds one unit of total tissue augmentation, the tally in this scenario is 20 percent graft survival, 80 percent necrosis, and 20 percent augmentation. (*Below*) If the recipient can be manipulated such that its two recipients can be expanded and increased to four recipients (*4R*), then carefully adding four grafts (*4G*), the maximum it can now tolerate, will yield four surviving grafts (*4RG*). The tally becomes 100 percent survival, 0 percent necrosis, and 100 percent augmentation. Overgrafting by adding more graft in this case will only cause more necrosis, reduce the percentage survival, and add nothing to the augmentation except for necrotic fat. We cannot increase the reaction yield by adding only more of one of the reagents. The balance has to be maintained.

likely attributable to the poor graft-to-recipient interaction in the bolus injection. The impractical and limited clinical translatability of adding extreme superphysiologic amounts of stem cells barely overcame that rate-limiting step. No large, randomized, controlled, clinical trials comparing adipose-derived stem cell–augmented fat grafts with simple fat graft have found significant differences.[33] We still have no silver bullet.

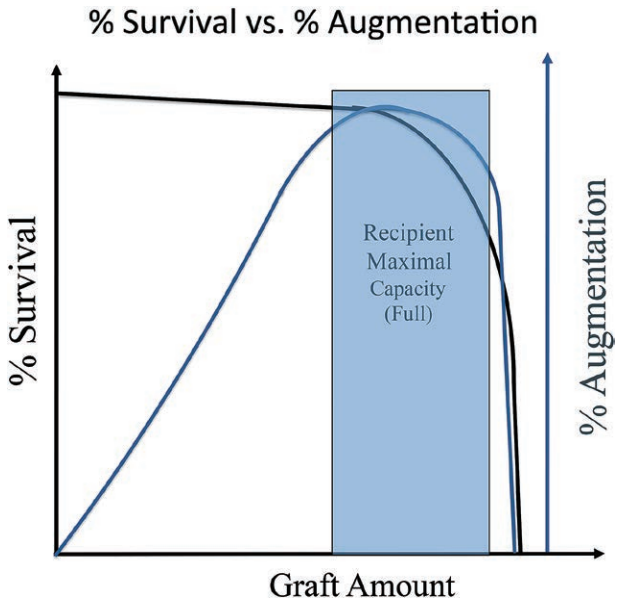
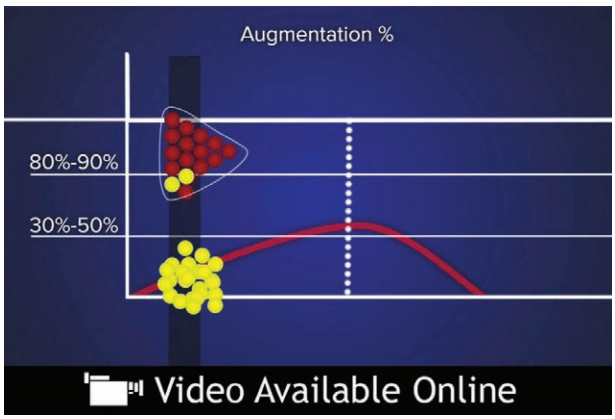


Fig. 4. Percentage augmentation versus percentage survival. With small graft amounts, and with excellent craftsmanship in graft delivery, percentage survival (*black curve*) remains very high until the recipient reaches its maximal capacity. Beyond that point, percentage survival drops dramatically because, even with optimal insertion of sprinkled droplets that do not coalesce, the added grafts will increase the interstitial fluid pressure to levels that choke capillary perfusion. In parallel, with small graft amounts, percentage augmentation (*blue curve*) is modest despite excellent graft survival. With increasing graft amounts, percentage augmentation increases until maximal capacity is reached. Beyond this point, additional grafting is counterproductive. With more grafting, there is more necrosis and a worsening of the augmentation. The challenge, therefore, is to stay as close as possible to the maximal capacity and avoid falling off the cliff of overgrafting. Preexpansion increases the maximal recipient capacity and shifts this curve to the right.



Video 2. Supplemental Digital Content 2 displays the recipient capacity. Under ideal grafting conditions, maximum percentage augmentation (30 to 50 percent) is reached at maximum recipient capacity. Grafting beyond capacity is counterproductive. Preexpansion that increases the maximum recipient capacity also increases the maximum percentage augmentation. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or available at ***http://links.lww.com/PRS/C298***.

In addition to the limited clinical role for enhancing fat grafts, there are major regulatory and scaling issues that limit adipose-derived stem cell translatability. The process of purifying adipose-derived stem cells requires enzymatic digestion and further augmentation requires delicate cell culture work. Moreover, the U.S. Food and Drug Administration views anything more than minimally manipulated adipose tissue as a drug subject to regulations.[34]

Is It Possible to Enhance the Recipient Site?

Yes, and we believe this is a key to successful large-volume autologous fat transfer. External volume expansion can induce adipogenesis, enhance tissue vascularity, and increase recipient capacity and mechanical compliance, thereby priming the recipient site for autologous fat transfer.[35–42] Brava (Brava LLC, Miami, Fla.) was the first clinically available external volume expansion device. Worn like a bra a few hours per day for 2 to 4 weeks, it prepares the breasts for autologous fat transfer. It enhances compliance, making room for more grafts. It also primes the recipient site by increasing its vascularity and presumably the number of available receptors. This device has been the key to success in large-volume autologous fat transfer.[43–47] Preexpansion maximizes percentage augmentation. Preexpansion that triples the original volume doubles the final graft volume (Table 1).[44,45,48–50]

TECHNIQUES THAT ADHERE TO THE PRINCIPLES

The surgeon grafting fat is akin to the farmer planting seeds. The 4S components of a successful crop are as follows: soil (recipient site), seeds (fat graft), sowing (grafting technique), and support (postgraft care).[13] The weakest link in this series of steps will seal the outcome. Animal studies that compare "method A" with "method B" of fat processing by measuring percentage graft survival in the back of a nude mouse are comparing Ferraris to Priuses stuck in a traffic jam. Investing in a non–rate-limiting component is as ineffective as adding horsepower to a car stuck in heavy traffic.

Table 1. Summary of Recent Studies on Breast Augmentation with Autologous Fat Transfer*

	Peltoniemi et al., 2013[49]	Peltoniemi et al., 2013[49]	Spear and Pittman, 2014[48]	Wang et al., 2015[50]	Khouri et al., 2012[44]	Khouri et al., 2014[45]
Preexpansion	No	No	No	No	Yes	Yes
Stem cells added	Yes	No	No	Yes	No	No
Volume grafted	286	300	243	256	277	367
Volume increase	147	160	92	125	233	293
Survival, %	52	53	38	49	84	80
Augmentation, %	16	18	39	33	63	92

*Most published studies report only percentage survival. We derived percentage augmentation from their data. The highest percentage augmentation reported without using preexpansion was by Spear and Pitttman (Spear SL, Pittman T. A prospective study on lipoaugmentation of the breast. *Aesthet Surg J.* 2014;34:400–408). Even with adipose-derived stem cell or platelet-rich plasma supplementation, no series ever reported an augmentation above 40 percent. So far, only preexpansion of the breast has yielded significantly higher percentage augmentations (Khouri RK, Eisenmann-Klein M, Cardoso E, et al. Brava and autologous fat transfer is a safe and effective breast augmentation alternative: Results of a 6-year, 81-patient, prospective multicenter study. *Plast Reconstr Surg.* 2012;129:1173–1187; and Khouri RK, Khouri RK Jr, Rigotti G, et al. Aesthetic applications of Brava-assisted megavolume fat grafting to the breasts: A 9-year, 476-patient, multicenter experience. *Plast Reconstr Surg.* 2014;133:796–807; discussion 808–809).

Soil: Recipient Site and Its Capacity

It is important to determine the capacity of the recipient site to plan the optimal graft amount to be harvested. Recipient capacity is a function of volume and mechanical compliance. This is reasonably approximated by the palm-and-pinch technique. Pinching the tissue estimates laxity and thickness, whereas the palm approximates surface area (the palm size of the average man is 200 cm^2). For example, a typical nonirradiated mastectomy defect with no scarring from previous reconstructions is typically 1.5 palms (300 cm^2). If the tissue thickness is 2 cm, and it is nonirradiated and soft, we can assign it optimal 40 percent compliance. The recipient capacity is then 240 ml (300 cm^2 × 2 cm × 40 percent). Attempting to graft more is counterproductive. Ideally, the patient would be preexpanded, and the recipient size would be doubled. Megavolume grafts require megavolume recipients. When the goal is volume augmentation of a small recipient, the recipient-site capacity is the bottleneck.

Seeds: Graft Harvesting and Preparation

To obtain a nonbloody lipoaspirate that sediments easily, we favor extensive tumescence. To avoid trauma and the high-airflow exposure of vacuum pumps, harvesting is safest with a controlled constant low-pressure syringe (300 mmHg) in a closed system. Harvesting with a thin (2.7-mm) cannula introduced through 14-gauge needle punctures that leave minimal scar allows for multiple entry sites with crisscrossing passes for even harvest. Increasing the number of cannula holes increases its efficiency, with 12 holes being the optimal number; beyond 12, the cannula becomes impractical. (**See Video, Supplemental Digital Content 3**, which displays the sprinkler graft harvesting method. Diffuse and even harvest is achieved by crisscrossing passes of a 12-gauge cannula introduced through multiple needle punctures entry sites that leave minimal scars. Using controlled low pressure and low airflow, the ribbon spring-loaded syringe delivers a constant 300-mmHg vacuum pressure along the entire excursion of the plunger. The routing valves automatically send the lipoaspirate to collection bags where the fat separates by simple gravity sedimentation. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C299***.)

Video 3. Supplemental Digital Content 3 displays the sprinkler graft harvesting method. Diffuse and even harvest is achieved by crisscrossing passes of a 12-gauge cannula introduced through multiple needle punctures entry sites that leave minimal scars. Using controlled low pressure and low airflow, the ribbon spring-loaded syringe delivers a constant 300-mmHg vacuum pressure along the entire excursion of the plunger. The routing valves automatically send the lipoaspirate to collection bags where the fat separates by simple gravity sedimentation. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C299***.

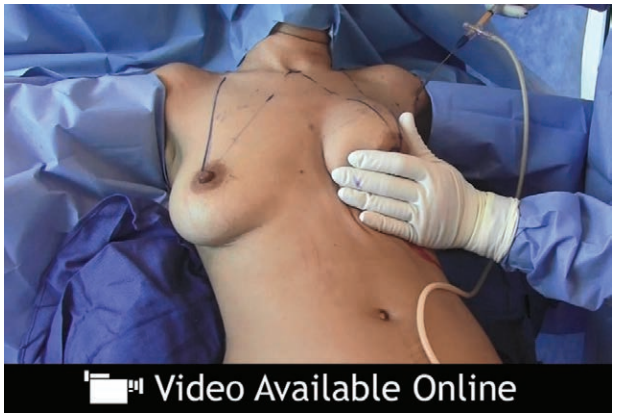
There is little scientific evidence that adding to or removing anything from the graft that might be effective in the laboratory provides any clinical advantage. We therefore leave the seeds and their surrounding microenvironment as minimally manipulated as possible.

Centrifugation might be useful for minor contour correction, but it is not suited for large-volume augmentation; it tends to lyse adipocytes and compact the graft to reduce the possibility of graft-to-recipient interaction.[13] (**See Video, Supplemental Digital Content 4**, which displays a fat graft prepared in a closed system with minimal manipulation by simple gravity sedimentation of the lipoaspirate. After draining the infranatant fluid, the supernatant fat is consolidated into one bag that becomes the lipografting bag. This is a closed system for graft harvesting, preparation, and reinjection. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C300***.)

Sowing: Graft Delivery

Even with the best seeds and the largest most fertile field, the farmer will only get a good crop if he evenly sows the seeds all across the field. In his pioneering work, Coleman used tuberculin syringes to painstakingly deliver the graft through hundreds of different cannula passes as a fine mist of microdroplets,[51] whereas skeptics expeditiously pouring the fat with larger syringes were unable to duplicate his results. Graft delivery craftsmanship

Video 4. Supplemental Digital Content 4 displays a fat graft prepared in a closed system with minimal manipulation by simple gravity sedimentation of the lipoaspirate. After draining the infranatant fluid, the supernatant fat is consolidated into one bag that becomes the lipografting bag. This is a closed system for graft harvesting, preparation, and reinjection. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C300***.



Video 5. Supplemental Digital Content 5 displays a precise injection of less than 0.1 ml of graft per centimeter of cannula excursion that is best done with a 3-ml syringe. Economy of motion saves time, as the two-way tissue valve automatically refills the syringe from the bag after each injection, avoiding multiple syringe switches. Grafting and refilling the syringe are performed with the dominant hand, leaving the nondominant hand free to guide the cannula. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C301***.

is a very important and poorly studied factor.[13] (**See Video, Supplemental Digital Content 5**, which displays a precise injection of less than 0.1 ml of graft per centimeter of cannula excursion that is best done with a 3-ml syringe. Economy of motion saves time, as the two-way tissue valve automatically refills the syringe from the bag after each injection, avoiding multiple syringe switches. Grafting and refilling the syringe are performed with the dominant hand, leaving the nondominant hand free to guide the cannula. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C301***.) We have developed several mottos for fat grafting: "no injection without motion," "injection/motion rate < 0.1 ml/cm," "sprinkle with precision," "smaller syringe → greater precision," and "no two motions in the same direction" (Table 2).

Figure 5 demonstrates the crucial importance of the 0.1-ml/cm limit of graft delivery. These

Table 2. These Easy-to-Remember Mottos Highlight the Key Techniques That Adhere to the Principles of Fat Grafting

"No injection without motion"
"Injection/motion rate <0.1 ml/cm"
"Sprinkle with precision"
"Smaller syringe → greater precision"
"No two motions in the same direction"

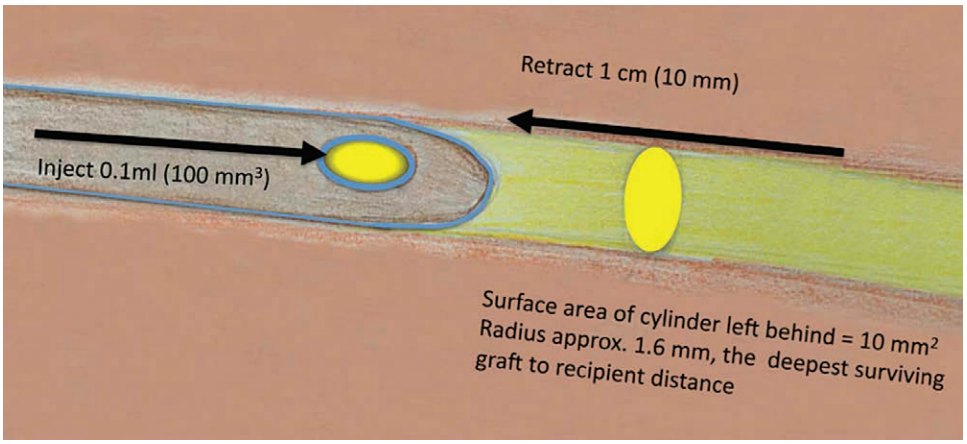


Fig. 5. The most important factor in graft delivery is maintaining optimal graft-to-recipient interface. The surgeon driving the cannula forward and retracting it creates tunnels through the tissues. Injection during retraction fills the tunnels with fat ribbons. Injecting without motion delivers a blob, whereas injecting the same volume while retracting along the tunnel leaves behind a ribbon. The size of the delivered ribbon is a function of the injection volume delivered per centimeter of cannula retraction. Based on the 1.6-mm maximal graft-to-recipient interface distance, and using the formula Area = πr^2, the maximum cross-sectional area of a cylindrical microribbon delivered should be approximately 8 mm^2, which can be rounded to 10 mm^2. Therefore, to deliver 1 ml (1000 mm^3) along a cylinder with a 10-mm^2 base surface, the length of the retraction cylinder should be 10 cm (100 mm). This calculated limit is crucial to fat graft delivery. The injection rate should not exceed 0.1 ml per 1 cm of cannula motion. Simple physics therefore dictates that the size of graft ribbon delivered depends mostly on the rate of injected volume per distance of motion covered while injecting. Contrary to the beliefs of many, the size of the delivered ribbon has very little to do with the pressure of injection, the rate of injection flow (in milliliters per minute), the caliber of the cannula, or the size of its hole. To avoid blob delivery and cavity formation, there should be no injection without motion. Any cavity where the graft can coalesce into a large lobule will curtail the optimal graft-to-recipient interface. It is also important that the cannula makes a new, different tunnel with every stroke. Otherwise, it will be refilling the same tunnel. There should be no two motions in the same direction. The mechanically driven reciprocating cannula delivery devices give a false sense of better dispersion as they mostly plow through back and forth in the same channel.

precisely delivered microribbons best survive when meticulously sprinkled as diffusely as possible in three dimensions using multiple sprinkler heads, each delivering a fine mist in all planes and all directions. As with sprinkled grains of salt, we achieve evenness through randomness. We favor fine 2.4-mm cannulas inserted through small needle pricks that leave minimal scars. A curved cannula is better at following the curved contour of the body and at going through different paths. By keeping the tip pointing up, we reduce the risk of inadvertent body cavity penetration.

Some oppose the concept of microribbons because of the shear forces caused by the thin cannula. Others emphasize the pressure used to inject the grafts and the high speeds at which high-volume grafts can be delivered. However, at 0.1 ml/cm of cannula motion, the pressure and shear forces are minimal, and the graft is delivered as thin ribbons.

Performing large-volume autologous fat transfer while efficiently sprinkling microribbons with a 3-ml syringe requires hundreds of syringe switches. To save the time lost switching syringes, we use a two-way large-bore tissue valve (Lipografter; Lipocosm, Miami, Fla.) that automatically transfers fat from the collection bag to the patient.

Support: Postgrafting Care

As with any graft, immobilization is crucial to engraftment. We postoperatively immobilize the graft for a few weeks by external volume expansion at 20 mmHg to preserve the swelling, or by applying over the breast a conforming adherent splint that prevents deflation. The postgrafting care should immobilize the graft and prevent the

natural recoil shrinking because chronic edema is adipogenic.[38,41] By adhering to these straightforward principles and techniques, we maximize the odds for obtaining consistently favorable results.

CLINICAL APPLICATIONS

Tissue Augmentation

A contour concavity is not only a tissue deficiency; there is a fibrous network tethering down its uneven surface. Simply pumping fat will not correct the defect. For the procedure to succeed, the tethering fibers need to be released by jackhammer grafting and needle meshing (Fig. 6).[13,52] Overzealous release destroys the fibrovascular recipient framework and creates cavities where the graft will die. To better release tethering scars, we often place these fibers under tension by injecting tumescent fluid. The previously discussed principles and techniques of fat grafting must then be followed. Estimate the recipient capacity, and realize that some defects may require more than one grafting session. Fat is not an expander. Even with meshing, tissues can hardly accommodate a greater than 50 percent volume increase. Repeated sessions result in exponential gains.

Breast Applications

Augmentation

Early attempts at breast augmentation with liposuctioned fat were disastrous. Using techniques that adhere to the principles of autologous fat transfer, surgeons found that external volume expansion before grafting yielded safe, consistent, impressive results.[43–45,47] Today, breast augmentation with autologous fat transfer is a well-accepted breast augmentation alternative (Fig. 7). (**See Video, Supplemental Digital Content 6**, which displays how tissues have limited capacity to enlarge and accommodate the graft.

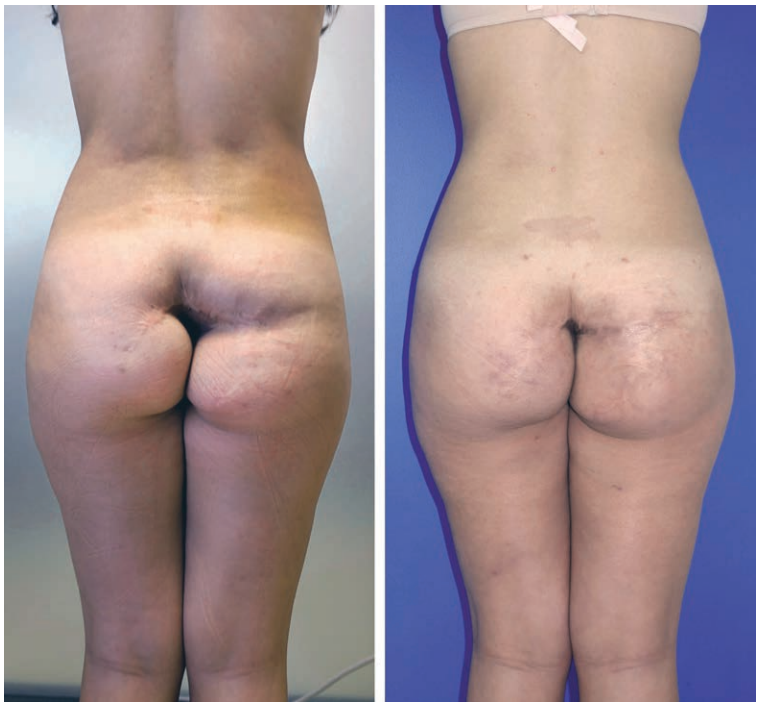


Fig. 6. Three-dimensional mesh scar release. (*Left*) A 14-year-old girl presented with a contracted scarred buttock deformity from tumor excision and skin grafting in infancy. To turn the restrictive cicatrix block into a graft recipient matrix, we tightly tumesced it with saline containing epinephrine, and then created microcavities that mesh-expanded in three dimensions. This was achieved through multiple puncture entry points and a fine blunt cannula that opened hundreds of tunnels in multiple directions and at multiple levels. The tumescent tunneling release was then supplanted with a needle Rigottomy of remaining tensed fibers. The resultant matrix was then filled with diffusely sprinkled fat grafts. (*Right*) One year after a second similar grafting session. The contour is improved and the majority of the missing tissue has been regenerated.

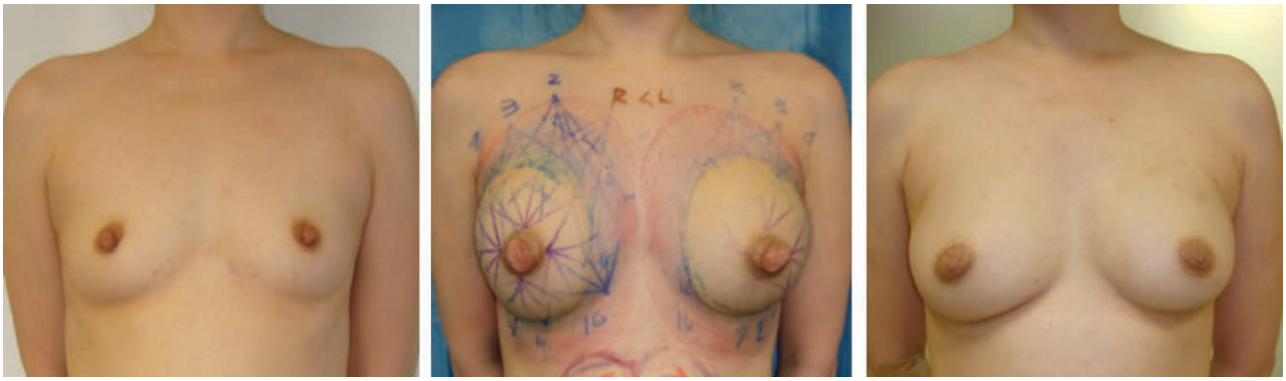
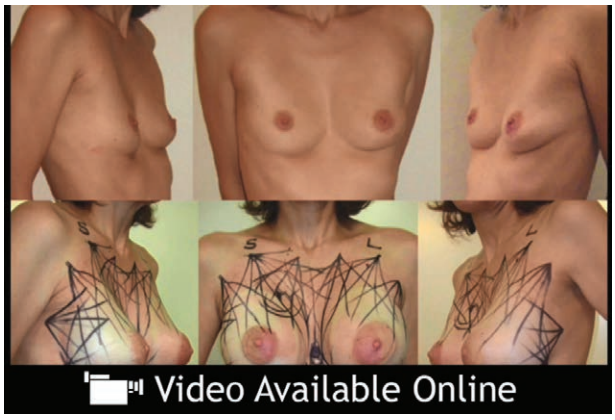
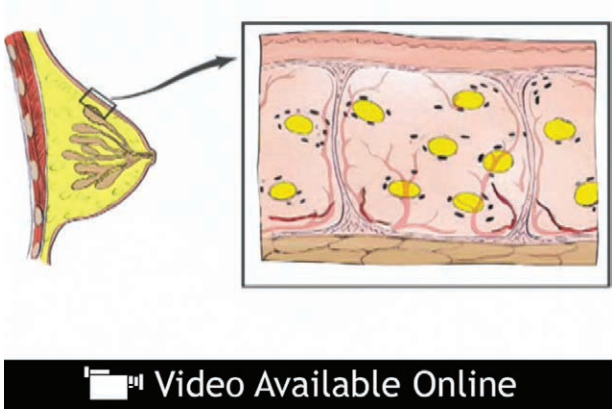


Fig. 7. Breast augmentation. A 30-year-old nulliparous Asian woman presented for primary breast augmentation. (*Left*) Her small breasts and tight skin would not allow for large-volume fat grafting. (*Center*) Immediate pregrafting view shows how external vacuum expansion temporarily more than tripled her breast size, allowing us to graft 400 ml per breast in one session. (*Right*) One year postoperatively, her breasts are more than double their original size and magnetic resonance imaging confirms that the augmentation is attributable to normal appearing fat without necrotic cysts.

Fat is not an expander; it cannot augment the recipient-site capacity. External vacuum expansion expands that capacity, allowing the diffusely injected graft to simply occupy the expanded scaffold. Pregrafting tripling of the volume through external vacuum expansion typically results in doubling of the original breast volume. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C302***. **See Video, Supplemental Digital Content 7**, which displays the sprinkler grafting method. Just as multiple fine sprinkles achieve evenness through randomness, the graft is sprinkled through multiple circum-mammary needle entry sites. A 2.4-mm cannula delivers less than 0.1 ml/cm of excursion as it sweeps through multiple contiguous passes in multiple planes. The subcutaneous, preglandular plane is most expanded by external vacuum expansion and is the preferred grafting plane, as golf balls placed beneath a blanket give more projection than if



Video 6. Supplemental Digital Content 6 displays how tissues have limited capacity to enlarge and accommodate the graft. Fat is not an expander; it cannot augment the recipient-site capacity. External vacuum expansion expands that capacity, allowing the diffusely injected graft to simply occupy the expanded scaffold. Pregrafting tripling of the volume through external vacuum expansion typically results in doubling of the original breast volume. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C302***.



Video 7. Supplemental Digital Content 7 displays the sprinkler grafting method. Just as multiple fine sprinkles achieve evenness through randomness, the graft is sprinkled through multiple circum-mammary needle entry sites. A 2.4-mm cannula delivers less than 0.1 ml/cm of excursion as it sweeps through multiple contiguous passes in multiple planes. The subcutaneous, preglandular plane is most expanded by external vacuum expansion and is the preferred grafting plane, as golf balls placed beneath a blanket give more projection than if placed beneath a mattress. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C303***.

placed beneath a mattress. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C303***.)

Reconstruction

Breast reconstruction is more challenging than primary augmentation because its smaller recipient site has less compliance and vascularity. Furthermore, radiation therapy and scars create a hostile environment for graft survival. Still, the same principles and techniques apply.[46,52] Breast reconstruction with external vacuum expansion plus autologous fat transfer is in vivo tissue engineering. The expansion generates a vascularized recipient scaffold that we seed with fat. To reconstruct a mastectomy that is nonirradiated and unscarred from previous reconstruction failures usually requires three successive outpatient grafting sessions 3 months apart. An irradiated mastectomy will usually require two more sessions to overcome radiation damage, and additional scars from prior failed reconstructions might require more (Fig. 8). (**See Video, Supplemental Digital Content 8**, which displays postmastectomy breast reconstruction with external vacuum expansion and autologous fat transfer, which is in vivo tissue engineering. External vacuum expansion generates a skin envelope and a vascularized recipient scaffold

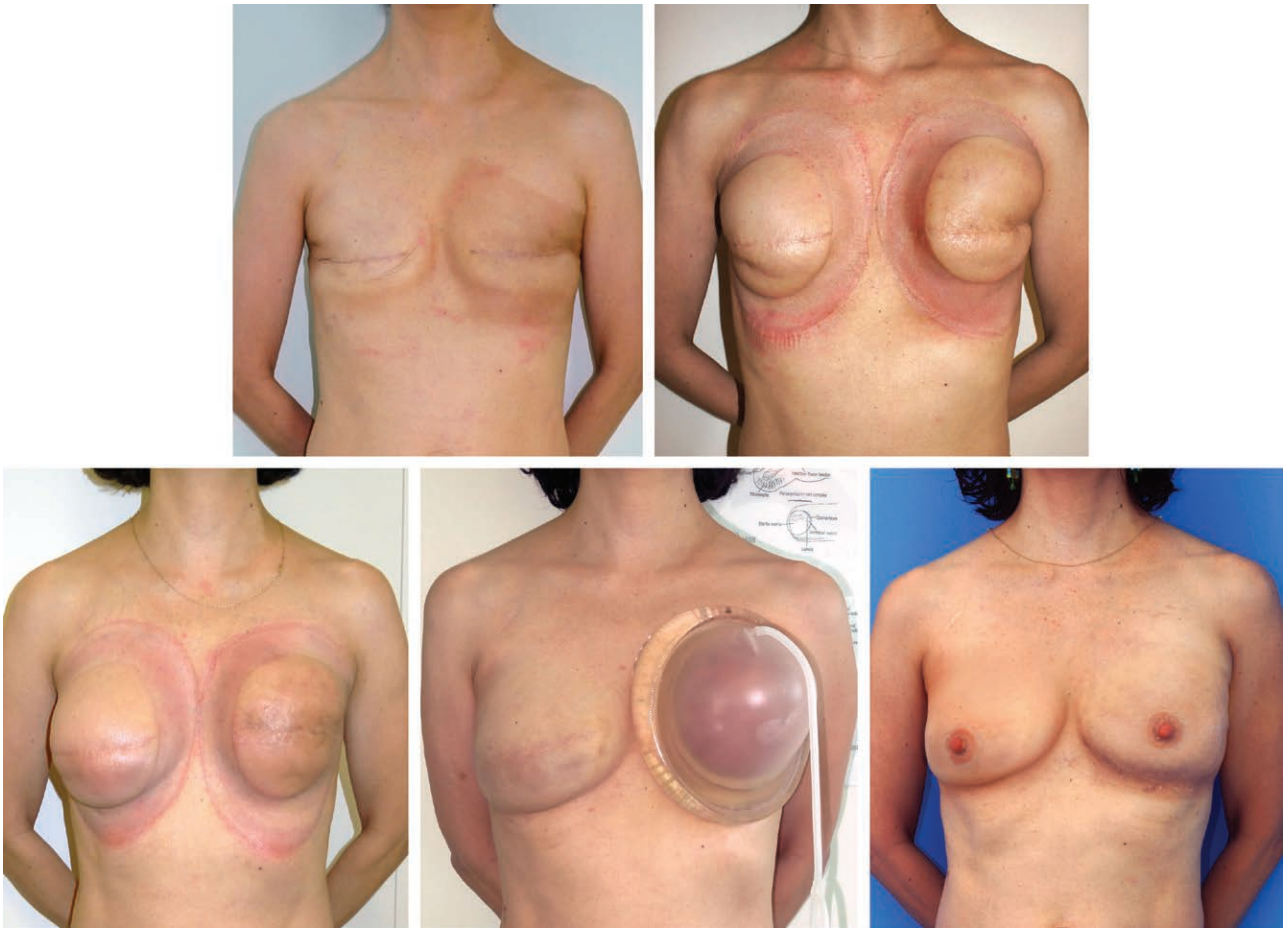


Fig. 8. Breast reconstruction. (*Above*, *left*) A 38-year-old woman 1 year after a bilateral mastectomy and left breast irradiation. She was not interested in having implants or flaps for her reconstruction and remained without reconstruction until she learned of this new minimally invasive in situ breast regeneration alternative. (*Above*, *right*) Just before the first grafting session, external vacuum expansion generated a cutaneous envelope and a recipient scaffold, allowing us to disperse more graft without crowding or tension. (*Below*, *left*) Three months later, just before the second grafting session. External vacuum expansion created a larger scaffold with room for more graft. (*Below*, *center*) Three more months later, just before the third grafting session. Note that we expanded only the left irradiated breast. She was already satisfied with her right breast result, and we only needed to graft the irradiated left breast at this third grafting session. (*Below*, *right*) One-year follow-up final result. She required five external vacuum expansion plus autologous fat transfer sessions for the left breast and only two for the nonirradiated right breast. She truly feels she has regained her lost breasts; they feel soft and natural, and have recovered light touch sensation over their entire surface.

Video 8. Supplemental Digital Content 8 displays postmastectomy breast reconstruction with external vacuum expansion and autologous fat transfer, which is in vivo tissue engineering. External vacuum expansion generates a skin envelope and a vascularized recipient scaffold that is seeded with autologous fat transfer to result in a natural appearing, soft, sensate breast mound that is histologically and radiographically indistinguishable from native fat. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C304***.

that is seeded with autologous fat transfer to result in a natural appearing, soft, sensate breast mound that is histologically and radiographically indistinguishable from native fat. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C304***.) A sensate breast is what women miss the most after breast reconstruction.[53] Reconstructions with external vacuum expansion plus autologous fat transfer result in sensate, soft, natural appearing and feeling breasts that truly restore the loss with a few minimally invasive procedures.

Implant-to-Fat Conversion

Implants stretch tissue. Removing the implants leaves behind some tissue laxity that can make room for more graft. Removing the implant and fat grafting in the same session has many advantages. The cavity left behind by the implant allows the surgeon to precisely graft the immediate subcapsular plane by digitally controlling the cannula tip. This plane is an ideal recipient and can bulge inward to obliterate the cavity. Immediately after implant removal, tissues are lax and maximally compliant to accommodate the added fat. Over time, this compliance dissipates. If the implant is removed and the cavity is left empty, the excess skin might fold over to create deep wrinkles. Deep surface wrinkles are difficult to correct. For all of these reasons, we highly recommend performing implant removal and fat grafting in the same operation.

In implant-to-fat conversion, the order of operations is crucial. First, graft the immediate subdermal plane surrounding the implant. Keeping the implant in this first step maintains the tissue stretched taut for smoother cannula excursions. Second, remove the implant through a lateral thoracic incision. Reopening the original implant incision will preclude grafting across this scar and will further depress it. Third, graft the subcapsular plane with a finger inside the cavity guiding the cannula. If the implant is subglandular, carefully graft the posterior muscle. Fourth, without creating a cavity, expand the intermediate plane by mesh-releasing the taut vertical fibers that prevent swelling while preserving the loose horizontal fibers of the recipient scaffold. Inject the fat into the potential space of this intermediate plane.

Implant-to-fat conversion is the lowest hanging fruit for autologous fat transfer to the breast and is probably the best solution to implant problems (Figs. 9 through 11). (**See Video, Supplemental Digital Content 9**, which displays details of implant-to-fat conversion, part 1. First, inject an even 3-mm layer of graft in the immediate subcutaneous plane while it is still stretched taut by the implant. Next, remove the implant through an extramammary incision and inject another thin layer in the immediate subcapsular plane with a finger inside the cavity to guide the cannula and prevent intracapsular injections. Third, though multiple passes of the cannula, release the vertical fibers to mesh-expand the intervening plane and recreate the breast mound. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C305***. **See Video, Supplemental Digital Content 10**, which displays implant-to-fat conversion, part 2. Grafting the deeper planes after implant removal is a two-handed procedure. Injecting the graft and refilling the plunger is done with the dominant hand while the nondominant hand guides the cannula from the inside of the cavity. A two-way valve makes this motion practical to achieve. A dilute lipoaspirate is preferred, as it places the vertical fibers under tension to facilitate their release with the spatulated tip of the grafting cannula. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C306***. **See Video, Supplemental Digital Content 11**, which displays implant-to-fat conversion, part 3. Replacing implants with the patient's own fat is the answer to many of the implant problems and is the low-hanging fruit for autologous fat

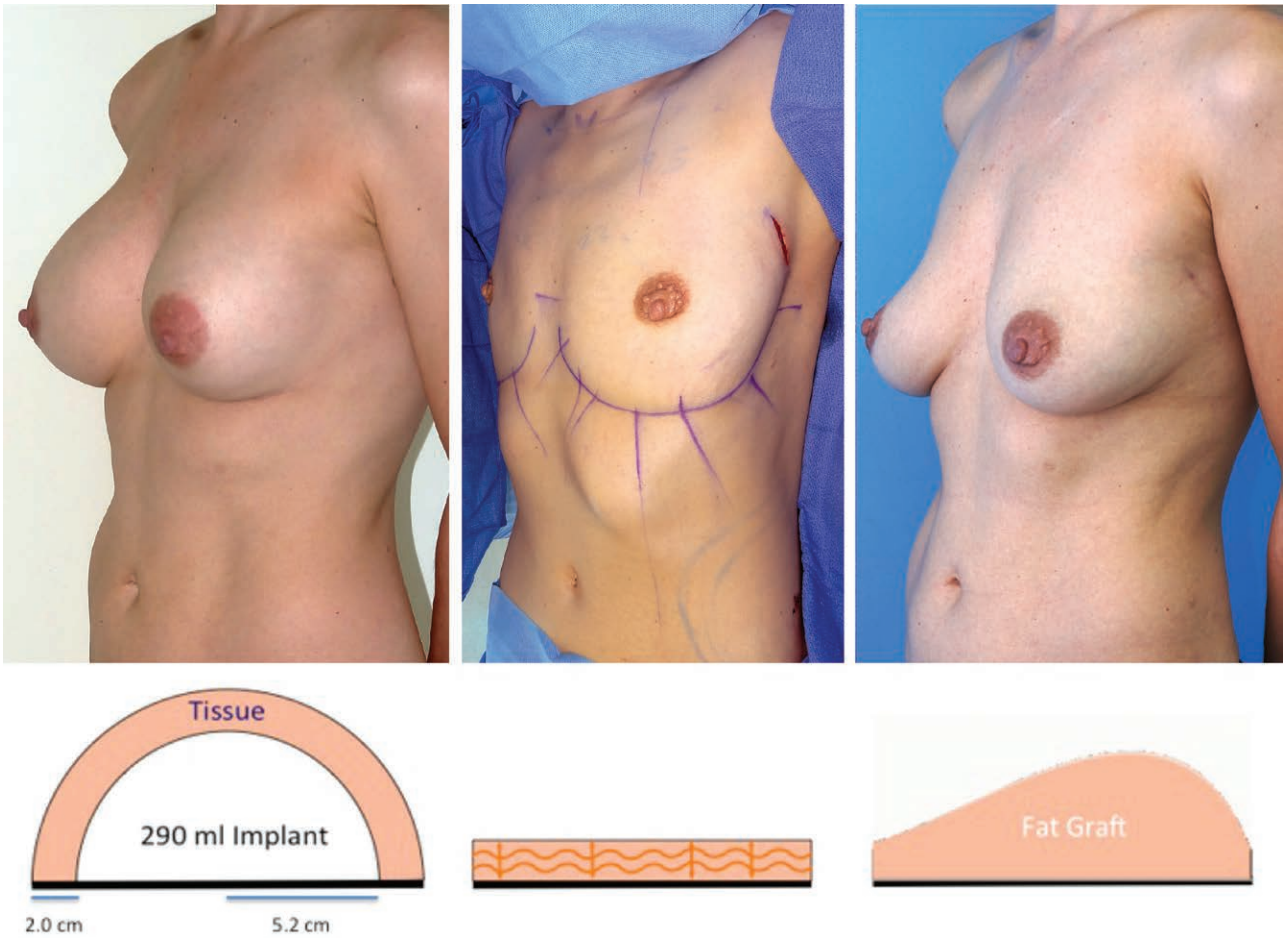


Fig. 9. (*Above*, *left*) A 36-year-old woman with painful capsular contractures from her 290-ml implants. (*Below*, *left*) Approximating the 290 ml implant as a hemisphere, the radius would be approximately 5.2 cm [$V = (2\pi/3) \times r^3$]. If the thickness of her breast tissue surrounding the implant is approximately 2 cm, her dome-like stretched breast has a volume of approximately 480 ml: $V = [(2\pi/3) \times (r + 2)^3] - [(2\pi/3) \times r^3]$. (*Above*, *center*) Once the implant is removed, the dome collapses into a flaccid disk that is still 2 cm thick because the intrinsic vertical tissue fibers prevent ballooning and expansion. (*Below*, *center*) The collapsed disk will still have the same radius of 5.2 cm and the same 2-cm thickness because the intrinsic vertical tissue fibers prevent its ballooning. However, its flaccid volume is now 170 ml ($V = \pi r^2 \times$ height). She therefore has 310 ml (480 ml to 170 ml) of potential tissue laxity to be grafted. (*Above*, *right*) Grafting while releasing the vertical fibers in a mesh pattern that leaves no cavity restores a natural appearing, aesthetically pleasing breast. At 1-year follow-up, autologous fat transfer has successfully replaced the silicone augmentation with improved aesthetics and minimal volume loss.

transfer to the breast. Autologous fat transfer can plump up the laxity left behind after implant removal, and the reverse abdominoplasty and fat transfer purse-string procedure can recruit an additional 100 ml of perimammary tissue, collapse the implant cavity, define the breast folds, and mushroom up a breast mound. With proper technique, much of the implant volume can be replaced with fat. With the reverse autologous fat transfer addition, the resultant breast is slightly smaller but much more natural appearing. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C307***.)

Gluteal Augmentation

Buttock augmentation with autologous fat transfer is a well-established procedure. The much larger buttocks can accommodate much more graft than the breasts.[54] Fat necrosis and oil cysts are also much less of a problem in the buttocks. Furthermore, even without grafting, liposuction of the flanks, thighs, and waists improves the contour of the buttocks. Fatal fat emboli have occurred from inadvertent bolus injections in the large gluteal vein plexus. The best way to prevent this is to follow the principles of injection grafting described earlier under Sowing: Graft Delivery (refer to Table 2).

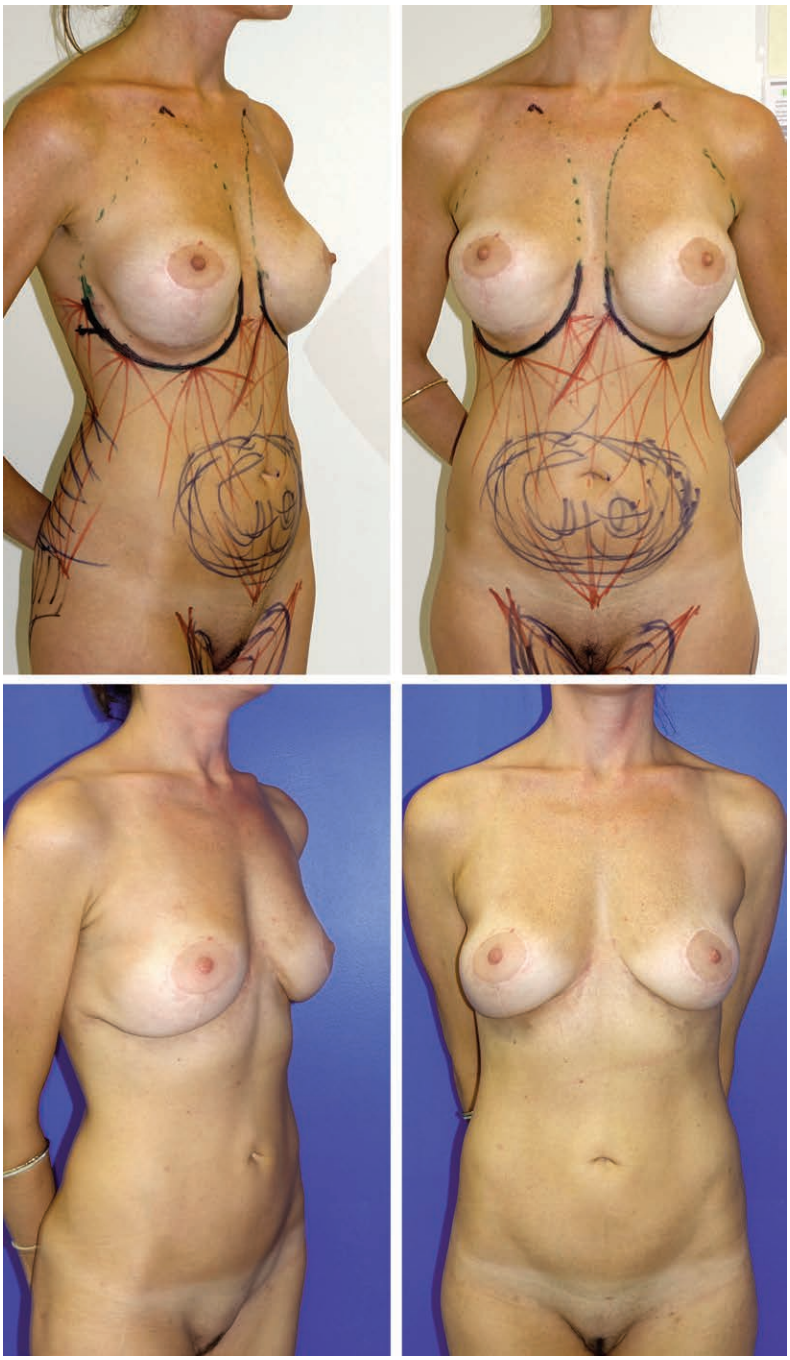


Fig. 10. (*Above*) A 46-year-old woman with a history of multiple capsulectomies, implant exchanges, and mastopexies presented with recurrent implant contractures, pseudoptosis from inferior migration of her implants, and loss of the inframammary folds. *Black markings* around the breast represent the subdermal course of the reverse abdominoplasty and fat transfer (RAFT) suture that will be inserted just under the clavicle and pursue a deeper course along the *green dotted lines*. Purse-string tightening of this suture and suspending it to the pectoralis will redefine the new mammary folds and recruit an additional 100 ml of perimammary tissue. (*Below*) One-year postoperatively, the pseudoptosis is corrected, and the breast has a more natural shape. Magnetic resonance imaging demonstrates that the 260-ml implants are replaced with approximately the same volume of normal appearing fat. Flank and waist donor sites in this relatively slim patient also improved her buttock contour.

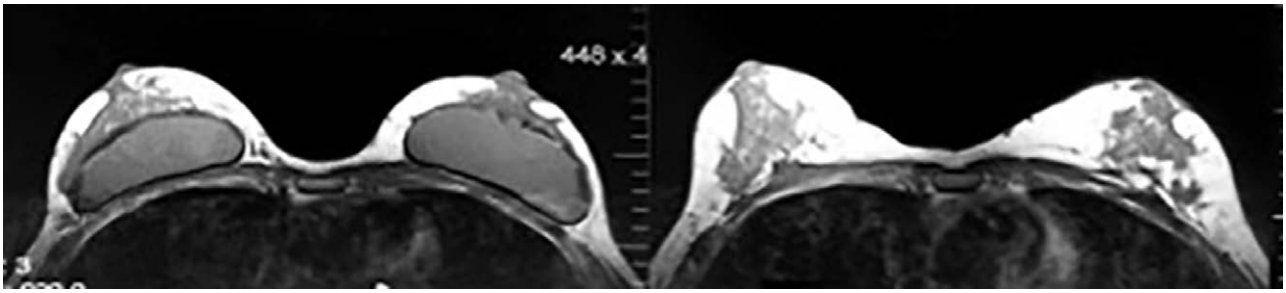


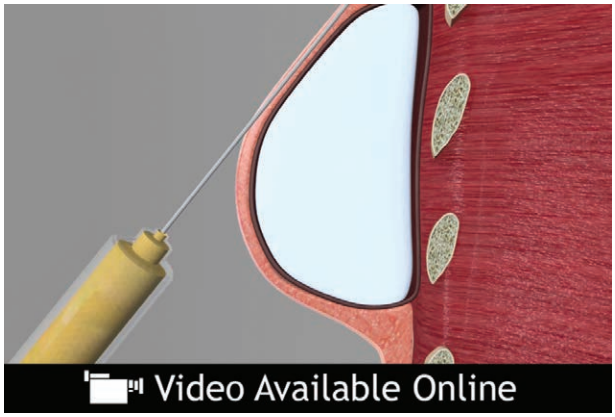
Fig. 11. (*Left*) Preoperative magnetic resonance imaging scan of the patient in Figure 10 . (*Right*) One-year postoperative magnetic resonance imaging scan shows replacement of the implant with normal appearing fat.

Fibrosis and Scar Treatment

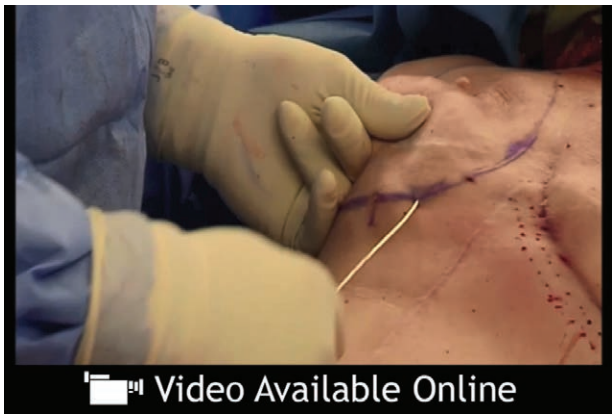
Fat is the soft-tissue alternative to fibrous scar. Judicious lipofilling turns the fibrous scar into a recipient matrix. What was once a dense fibrous scar becomes the loose supporting fibrous scaffold for fat grafts. The cicatrix-to-matrix concept explains how autologous fat transfer can turn tight and stiff into loose and soft.

Scar Contractures

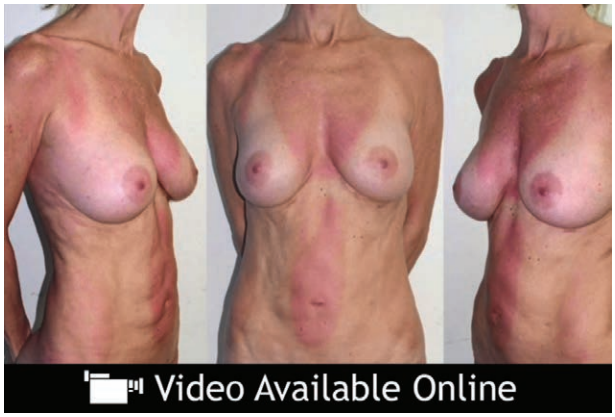
Percutaneous aponeurotomy and lipofilling (PALF) has emerged as a regenerative alternative to flap surgery for treatment of scar contractures.[52] Percutaneously meshing the restrictive scar and expanding the resultant microcavities with fat injection expands the cicatrix into a fat-filled matrix. For proper three-dimensional release, nicks must be staggered in multiple planes in multiple directions wherever restrictive fibers prevent expansion. We named the technique "Rigottomy" after its originator. This percutaneous meshing expands the restrictive block of scar tissue to create a larger three-dimensional recipient scaffold for autologous fat transfer. The loosened grafted scar becomes softer and closer to the normal surrounding fat tissue. Repeating the process a few months later leads to substantial tissue volume gain and can eliminate the scar to replace it with normal fat. The Rigottomy is useful when grafting fat into scarred tissue to correct a volume deficiency. It transforms a restrictive cicatrix into a regenerative matrix.[13,46] (**See**



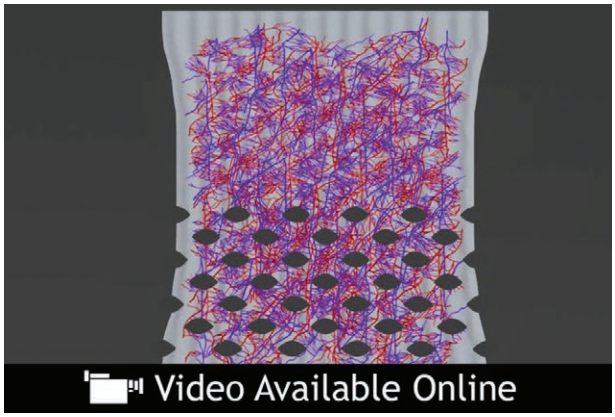
Video 9. Supplemental Digital Content 9 displays details of implant-to-fat conversion, part 1. First, inject an even 3-mm layer of graft in the immediate subcutaneous plane while it is still stretched taut by the implant. Next, remove the implant through an extramammary incision and inject another thin layer in the immediate subcapsular plane with a finger inside the cavity to guide the cannula and prevent intracapsular injections. Third, though multiple passes of the cannula, release the vertical fibers to mesh-expand the intervening plane and recreate the breast mound. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C305***.



Video 10. Supplemental Digital Content 10 displays implant-to-fat conversion, part 2. Grafting the deeper planes after implant removal is a two-handed procedure. Injecting the graft and refilling the plunger is done with the dominant hand while the nondominant hand guides the cannula from the inside of the cavity. A two-way valve makes this motion practical to achieve. A dilute lipoaspirate is preferred, as it places the vertical fibers under tension to facilitate their release with the spatulated tip of the grafting cannula. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C306***.

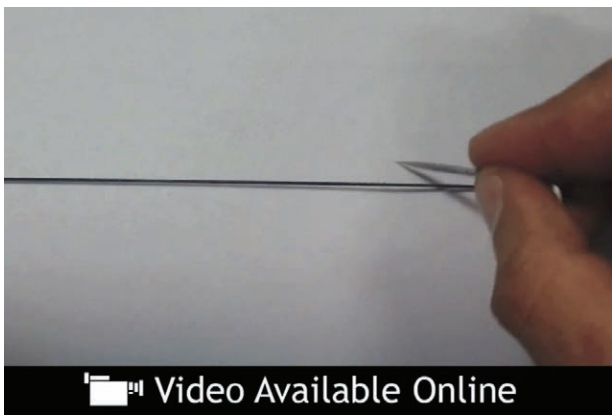


Video 11. Supplemental Digital Content 11 displays implant-to-fat conversion, part 3. Replacing implants with the patient's own fat is the answer to many of the implant problems and is the low-hanging fruit for autologous fat transfer to the breast. Autologous fat transfer can plump up the laxity left behind after implant removal, and the reverse abdominoplasty and fat transfer (RAFT) purse-string procedure can recruit an additional 100 ml of perimammary tissue, collapse the implant cavity, define the breast folds, and mushroom up a breast mound. With proper technique, much of the implant volume can be replaced with fat. With the RAFT addition, the resultant breast is slightly smaller but much more natural appearing. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C307***.



Video 12. Supplemental Digital Content 12 displays percutaneous aponeurotomy and lipofilling (PALF). PALF is the regenerative alternative to flaps. Flaps are needed when primary defect reconstruction is not possible. However, as an alternative, we can place the tissues around the defect under tension and inflict a pattern of alternating staggered slits that mesh-expand these tissues. The pattern of slits is performed with a needle that leaves no cutaneous scar, and the slit gaps can be seeded with autologous fat transfer to regenerate the defect. Tissues can regenerate across only very small gaps, and fat grafts require high graft-to-recipient interface, and thus it is important to avoid excessive meshing that creates larger cavities that will result in scar and fat necrosis. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C308***.

Video, Supplemental Digital Content 12, which displays PALF. PALF is the regenerative alternative to flaps. Flaps are needed when primary defect reconstruction is not possible. However, as an alternative, we can place the tissues around the defect under tension and inflict a pattern of alternating staggered slits that mesh-expand these tissues. The pattern of slits is performed with a needle that leaves no cutaneous scar, and the slit gaps can be seeded with autologous fat transfer to regenerate the defect. Tissues can regenerate across only very small gaps, and fat grafts require high graft-to-recipient interface, and thus it is important to avoid excessive meshing that creates larger cavities that will result in scar and fat necrosis. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C308***.)



Video 13. Supplemental Digital Content 13 shows how tension is the key to the safe percutaneous release of contracture. This video demonstrates how a needle cuts the tight violin strings but not the looser string. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C309***.

Radiation Damage

Radiation kills cancer cells but also kills the adipose-derived stem cells responsible for tissue upkeep and for engraftment capacity. Liposuctioned fat is rich in adipose-derived stem cells. Although initially poor to engraft because of the hostile environment, the little graft that takes in the first round makes it easier for more to engraft in the second round. From there on, the advantage is exponential, with more grafting rendering the tissue richer in normal cells and

Video 14. Supplemental Digital Content 14 displays how release of the Dupuytren contracture with percutaneous aponeurotomy and lipofilling (PALF) is a minimally invasive regenerative alternative to flaps and extirpative surgery. The key to the procedure is a strong digital extension retractor that places the restrictive fibers under tension. The selective cutting of a needle for structures under tension divides the Dupuytren fibers that prevent extension while preserving the neurovascular bundles. The procedure is safe and particularly suited for multidigit contractures. Lipofilling the meshed cord treats the subcutaneous atrophy and helps prevent recurrence of the fibrosis. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C310***.

more like nonirradiated tissue. Rigotti made the seminal observation that fat grafting can reverse radiation damage; this has opened the field of radiation damage reversal with autologous fat transfer.[18] Autologous fat transfer is best immediately after radiation treatment while the tissues are still inflamed and before fibrosis sets in; it tends to soothe the inflammation and reduce the fibrosis.[46]

Dupuytren and Other Hand Contractures

Needles preferentially cut tensed fibers while leaving intact the looser structures. Forceful digital extension tenses the Dupuytren cords before healthy neurovascular structures become tight. (**See Video, Supplemental Digital Content 13**, which shows how tension is the key to the safe percutaneous release of contracture. This video demonstrates how a needle cuts the tight violin strings but not the looser string. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C309***. **See Video, Supplemental Digital Content 14**, which displays how release of the Dupuytren contracture with percutaneous aponeurotomy and lipofilling is a minimally invasive regenerative alternative to flaps and extirpative surgery. The key to the procedure is a strong digital extension retractor that places the restrictive fibers under tension. The selective cutting of a needle for structures under tension divides the Dupuytren fibers that prevent extension while preserving the neurovascular bundles. The procedure is safe and particularly suited for multidigit contractures. Lipofilling the meshed cord treats the subcutaneous atrophy and helps prevent recurrence of the fibrosis. This video is available in the "Related Videos" section of the full-text article on PRSJournal.com or at ***http://links.lww.com/PRS/C310***.) Steadily applied strong extension allows needles to cut these restrictive fibers and avoid damage to the neurovascular structures. Multiple percutaneous

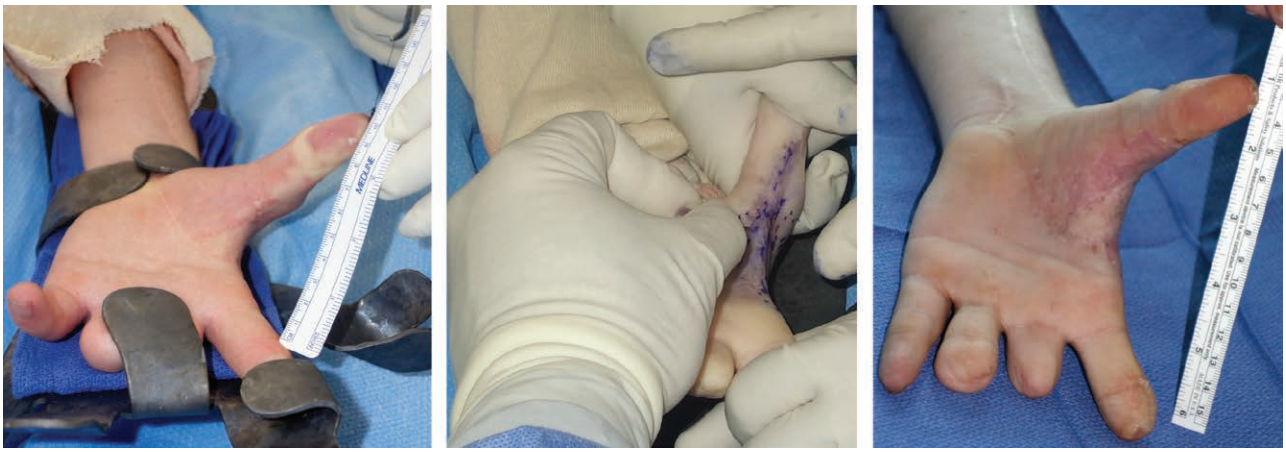


Fig. 12. A 16-year-old boy with multidigit amputations from a firework blast with recurrent first webspace contracture following a prior radial forearm flap release. Forceful intraoperative extension opened the web to only 3.5 inches. After placing the contracture under tension, it is mesh-released and fat grafted with the PALF technique just like a Dupuytren contracture. At 6-month follow-up, the web actively opens up to 4.5 inches. Active extension is shown at 6 months postoperatively.

aponeurotomies mesh-expand the fibrous cord and turn it into a recipient for fat.[55] Furthermore, abdominal fat has been shown to be inhibitory to Dupuytren fibroblasts.[56] A randomized controlled trial demonstrated that percutaneous aponeurotomy and lipofilling performed at least as well as the standard limited fasciectomy and had faster recovery and less morbidity.[57] Percutaneous aponeurotomy and lipofilling can also replace flaps in releasing traumatic scar contractures (Fig. 12).

Scleroderma/Systemic Sclerosis

Magalon et al. and Sautereau et al. found that subcutaneous perioral microfat injection in patients with systemic sclerosis is beneficial in the treatment of facial handicap, skin sclerosis, mouth opening limitation, sicca syndrome, and facial pain.[21,22] Effects on scleroderma of the hand are also impressive.

Facial Contour

Facial rejuvenation often requires a face fill along with the face lift. In contrast to the large volumes required for body contour, a thin layer of strategically placed fat can yield impressive results. The thin graft layer has an excellent graft-to-recipient interface, resulting in excellent survival. This is where compacted, centrifuged fat might be more advantageous than the loose slurry preferred in large-volume grafting. Autologous fat transfer is the preferred treatment alternative for Romberg syndrome, facial lipodystrophy, and posttraumatic craniofacial defects.[58–60]

Additional Potential Uses

Fat grafting has valuable trophic effects on the recipient tissues. It has been shown to increase dermal thickness and elasticity.[17] Interestingly, adipose-derived stem cell supplements did not increase the effectiveness of simple fat grafting. For still poorly understood reasons, fat grafting also has a beneficial effect on neuroma pain and on nerve regeneration. Fat grafting improves the symptoms of Raynaud phenomenon.[61] Early phase I clinical trials have demonstrated safety and potential efficacy for adipose-derived stem cells in the treatment of arthritis[62] and postprostatectomy erectile dysfunction,[63] but larger clinical studies are needed. There are also reports of a beneficial effect on chronic wounds, which might be attributable to the antifibrotic and angiogenic effect of fat grafts.[64]

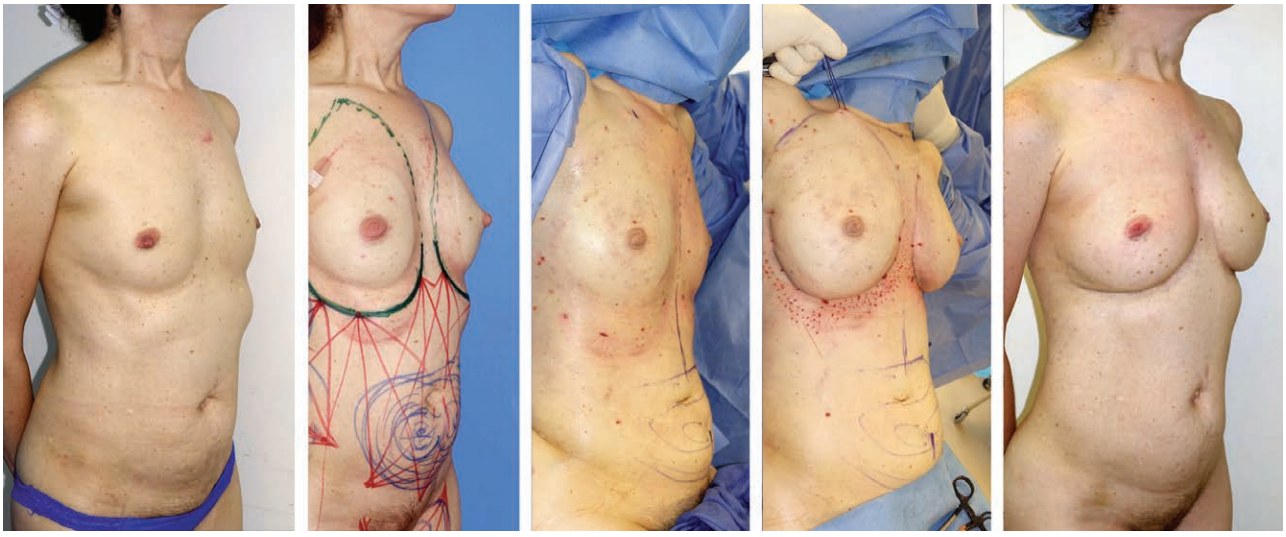


Fig. 13. (*Left*) A 35-year-old woman with AA breast cups asked for maximal possible augmentation in one grafting session. We resorted to the reverse abdominoplasty and fat transfer (RAFT) to recruit her lax upper abdominal panniculus and to use tissue molding to cement the immediate postoperative volume and shape. (*Second from left*) Effect of external vacuum expansion on fibrovascular scaffold just before autologous fat transfer. (*Center*) Intraoperatively, after injecting 350 ml of dilute fat. Note that there is only moderate augmentation. (*Second from right*) Intraoperatively, after inserting and tightening the RAFT purse-string suture. This mushroomed out the breast and reoriented the fibrovascular skeleton. A conforming, adhesive splint was then applied as a mold and kept for a total of 8 weeks after grafting. (*Right*) One year postoperatively, tissue molding at the end of the procedure has preserved the immediate postoperative shape and volume.

Limitations of Fat Grafting

Although fat grafting has great therapeutic potential for a growing number of conditions, the risks and concerns must also be addressed. The most commonly expressed concern regarding fat grafting the breast is oncologic risk. However, many studies have failed to show any increased risk.[46,65–70] Another commonly expressed concern regarding fat grafting the breast is difficulty in distinguishing fat necrosis from potentially malignant lesions on mammography. However, Rubin showed that the calcifications from fat grafting were less problematic than the calcification from the well-accepted breast-reduction procedures.[71] The most well-established serious risk from fat grafting is embolization causing fatal pulmonary emboli, strokes or blindness. This occurs from inadvertently injecting large boluses of fat into veins, most commonly the large gluteal plexus. The best way to prevent this is to follow the principles of injection grafting described earlier under Sowing: Graft Delivery. Even if a vein is inadvertently cannulated, delivering a fraction of a microribbon will not cause significant morbidity.

New Horizons

The applications above show that we not only enlarge soft tissues with autologous fat transfer but—as we enlarge the scaffold with external volume expansion, reorient its fibers, and mesh-expand them—also reshape the tissues. Fat can be seen as the epoxy glue that permeates and cements the modified supportive fibrovascular structure. A conforming adhesive splint that holds the construct in place until it cures completes our ability to mold tissue and to become true "plastic" surgeons (Fig. 13).

Future Steps

Autologous fat transfer is a safe, reliable, and efficacious procedure for many common clinical conditions. With the principles and techniques of fat grafting well established, scientists and clinicians will need to more thoroughly investigate the indications in question and better translate the basic science research into the clinical setting.

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REFERENCES

1. Lantieri LA, Ozbek MR, Deune EG, et al. Prevention of microvascular thrombosis by topical application of recombinant tissue factor pathway inhibitor. *Plast Reconstr Surg.* 1996;97:587–594.
2. Khouri RK, Sherman R, Buncke HJ, et al. A phase II trial of intraluminal irrigation with recombinant human tissue factor pathway inhibitor to prevent thrombosis in free flap surgery. *Plast Reconstr Surg.* 2001;107:408–415; discussion 416–418.
3. Khouri RK. Avoiding free flap failure. *Clin Plast Surg.* 1992;19:773–781.
4. Khouri RK Jr, Biggs TM. Fat grafting & the philosopher's stone. *J Plast Reconstr Aesthet Surg.* 2016;69:e17–e18.
5. Khouri RK Jr, Khouri RK. Commentary on: Prospective 1-year follow-up study of breast augmentation by cell-assisted lipotransfer. *Aesthet Surg J.* 2016;36:191–192.
6. Cleveland EC, Albano NJ, Hazen A. Roll, spin, wash, or filter? Processing of lipoaspirate for autologous fat grafting: An updated, evidence-based review of the literature. *Plast Reconstr Surg.* 2015;136:706–713.
7. Gupta R, Brace M, Taylor SM, Bezuhly M, Hong P. In search of the optimal processing technique for fat grafting. *J Craniofac Surg.* 2015;26:94–99.
8. Gabriel A, Champaneria MC, Maxwell GP. Fat grafting and breast reconstruction: Tips for ensuring predictability. *Gland Surg.* 2015;4:232–243.
9. Strong AL, Cederna PS, Rubin JP, Coleman SR, Levi B. The current state of fat grafting: A review of harvesting, processing, and injection techniques. *Plast Reconstr Surg.* 2015;136:897–912.
10. Tocco I, Widgerow AD, Lalezari S, Banyard D, Shaterian A, Evans GR. Lipotransfer: The potential from bench to bedside. *Ann Plast Surg.* 2014;72:599–609.
11. Ross RJ, Shayan R, Mutimer KL, Ashton MW. Autologous fat grafting: Current state of the art and critical review. *Ann Plast Surg.* 2014;73:352–357.
12. Khouri RK, Rigotti G, Cardoso E, Khouri RK Jr, Biggs TM. Megavolume autologous fat transfer: Part I. Theory and principles. *Plast Reconstr Surg.* 2014;133:550–557.
13. Khouri RK, Rigotti G, Cardoso E, Khouri RK, Biggs TM. Megavolume autologous fat transfer: Part II. Practice and techniques. *Plast Reconstr Surg.* 2014;133:1369–1377.
14. Yoshimura K. Cell-assisted lipotransfer for breast augmentation: Grafting of progenitor-enriched fat tissue. In: Shiffman M. eds., *Autologous fat transfer.* Springer: Berlin, Heidelberg, 2010.
15. Rubina K, Kalinina N, Efimenko A, et al. Adipose stromal cells stimulate angiogenesis via promoting progenitor cell differentiation, secretion of angiogenic factors, and enhancing vessel maturation. *Tissue Eng Part A* 2009;15:2039–2050.
16. Walocko FM, Khouri RK Jr, Urbanchek MG, Levi B, Cederna PS. The potential roles for adipose tissue in peripheral nerve regeneration. *Microsurgery* 2016;36:81–88.
17. Charles-de-Sá L, Gontijo-de-Amorim NF, Maeda Takiya C, et al. Antiaging treatment of the facial skin by fat graft and adipose-derived stem cells. *Plast Reconstr Surg.* 2015;135:999-1009.
18. Rigotti G, Marchi A, Galiè M, et al. Clinical treatment of radiotherapy tissue damage by lipoaspirate transplant: A healing process mediated by adipose-derived adult stem cells. *Plast Reconstr Surg.* 2007;119:1409–1422; discussion 1423–1424.
19. Sun W, Ni X, Sun S, et al. Adipose-derived stem cells alleviate radiation-induced muscular fibrosis by suppressing the expression of TGF-β1. *Stem Cells Int.* 2016;2016:5638204.

20. Yun IS, Jeon YR, Lee WJ, et al. Effect of human adipose derived stem cells on scar formation and remodeling in a pig model: A pilot study. *Dermatol Surg.* 2012;38:1678–1688.
21. Magalon G, Daumas A, Sautereau N, Magalon J, Sabatier F, Granel B. Regenerative approach to scleroderma with fat grafting. *Clin Plast Surg.* 2015;42:353–364, viii.
22. Sautereau N, Daumas A, Truillet R, et al. Efficacy of autologous microfat graft on facial handicap in systemic sclerosis patients. *Plast Reconstr Surg Glob Open* 2016;4:e660.
23. Castiglione F, Hedlund P, Van der Aa F, et al. Intratunical injection of human adipose tissue-derived stem cells prevents fibrosis and is associated with improved erectile function in a rat model of Peyronie's disease. *Eur Urol.* 2013;63:551–560.
24. Castiglione F, Dewulf K, Hakim L, et al. Adipose-derived stem cells counteract urethral stricture formation in rats. *Eur Urol.* 2016;70:1032–1041.
25. Zhao W, Zhang C, Jin C, et al. Periurethral injection of autologous adipose-derived stem cells with controlled-release nerve growth factor for the treatment of stress urinary incontinence in a rat model. *Eur Urol.* 2011;59:155–163.
26. Lopez-Santalla M, Menta R, Mancheño-Corvo P, et al. Adipose-derived mesenchymal stromal cells modulate experimental autoimmune arthritis by inducing an early regulatory innate cell signature. *Immun Inflamm Dis.* 2016;4:213–224.
27. Wu L, Cai X, Zhang S, Karperien M, Lin Y. Regeneration of articular cartilage by adipose tissue derived mesenchymal stem cells: Perspectives from stem cell biology and molecular medicine. *J Cell Physiol.* 2013;228:938–944.
28. Eto H, Kato H, Suga H, et al. The fate of adipocytes after nonvascularized fat grafting: Evidence of early death and replacement of adipocytes. *Plast Reconstr Surg.* 2012;129:1081–1092.
29. Kato H, Mineda K, Eto H, et al. Degeneration, regeneration, and cicatrization after fat grafting: Dynamic total tissue remodeling during the first 3 months. *Plast Reconstr Surg.* 2014;133:303e–313e.
30. Khouri RK Jr, Khouri RE, Lujan-Hernandez JR, Khouri KR, Lancerotto L, Orgill DP. Diffusion and perfusion: The keys to fat grafting. *Plast Reconstr Surg Glob Open* 2014;2:e220.
31. Khouri RK, Khouri RK. Percentage augmentation: The more meaningful index of success in fat grafting. *Plast Reconstr Surg.* 2015;135:933e–935e.
32. Kølle SF, Fischer-Nielsen A, Mathiasen AB, et al. Enrichment of autologous fat grafts with ex-vivo expanded adipose tissue-derived stem cells for graft survival: A randomised placebo-controlled trial. *Lancet* 2013;382:1113–1120.
33. Marks PW, Witten CM, Califf RM. Clarifying stem-cell therapy's benefits and risks. *N Engl J Med.* 2017;376:1007–1009.
34. U.S. Food and Drug Administration. Human cells, tissues, and cellular and tissue-based products (HCT/Ps) from adipose tissue: Regulatory considerations. Available at: http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/ucm427795.htm. Accessed July 5, 2017.
35. Pietramaggiori G, Liu P, Scherer SS, et al. Tensile forces stimulate vascular remodeling and epidermal cell proliferation in living skin. *Ann Surg.* 2007;246:896–902.
36. Chin MS, Ogawa R, Lancerotto L, et al. In vivo acceleration of skin growth using a servo-controlled stretching device. *Tissue Eng Part C Methods* 2010;16:397–405.
37. Heit YI, Lancerotto L, Mesteri I, et al. External volume expansion increases subcutaneous thickness, cell proliferation, and vascular remodeling in a murine model. *Plast Reconstr Surg.* 2012;130:541–547.
38. Lancerotto L, Chin MS, Freniere B, et al. Mechanisms of action of external volume expansion devices. *Plast Reconstr Surg.* 2013;132:569–578.
39. Chin MS, Lujan-Hernandez J, Babchenko O, et al. External volume expansion in irradiated tissue: Effects on the recipient site. *Plast Reconstr Surg.* 2016;137:799e–807e.
40. Myung Y, Kwon H, Pak C, Lee H, Jeong JH, Heo CY. Radiographic evaluation of vessel count and density with quantitative magnetic resonance imaging during external breast expansion in Asian women: A prospective clinical trial. *J Plast Reconstr Aesthet Surg.* 2016;69:1588–1597.
41. Lujan-Hernandez J, Lancerotto L, Nabzdyk C, et al. Induction of adipogenesis by external volume expansion. *Plast Reconstr Surg.* 2016;137:122–131.
42. Khouri RK, Schlenz I, Murphy BJ, Baker TJ. Nonsurgical breast enlargement using an external soft-tissue expansion system. *Plast Reconstr Surg.* 2000;105:2500–2512; discussion 2512–2514.
43. Khouri R, Del Vecchio D. Breast reconstruction and augmentation using pre-expansion and autologous fat transplantation. *Clin Plast Surg.* 2009;36:269–280, viii.
44. Khouri RK, Eisenmann-Klein M, Cardoso E, et al. Brava and autologous fat transfer is a safe and effective breast augmentation alternative: Results of a 6-year, 81-patient, prospective multicenter study. *Plast Reconstr Surg.* 2012;129:1173–1187.
45. Khouri RK, Khouri RK, Rigotti G, et al. Aesthetic applications of Brava-assisted megavolume fat grafting to the breasts: A 9-year, 476-patient, multicenter experience. *Plast Reconstr Surg.* 2014;133:796–807; discussion 808–809.
46. Khouri RK, Rigotti G, Khouri RK Jr, et al. Tissue-engineered breast reconstruction with Brava-assisted fat grafting: A 7-year, 488-patient, multicenter experience. *Plast Reconstr Surg.* 2015;135:643–658.
47. Del Vecchio DA, Bucky LP. Breast augmentation using pre-expansion and autologous fat transplantation: A clinical radiographic study. *Plast Reconstr Surg.* 2011;127:2441–2450.
48. Spear SL, Pittman T. A prospective study on lipoaugmentation of the breast. *Aesthet Surg J.* 2014;34:400–408.
49. Peltoniemi HH, Salmi A, Miettinen S, et al. Stem cell enrichment does not warrant a higher graft survival in lipofilling of the breast: A prospective comparative study. *J Plast Reconstr Aesthet Surg.* 2013;66:1494–1503.
50. Wang L, Luo X, Lu Y, Fan ZH, Hu X. Is the resorption of grafted fat reduced in cell-assisted lipotransfer for breast augmentation? *Ann Plast Surg.* 2015;75:128–134.
51. Coleman SR. Facial recontouring with lipostructure. *Clin Plast Surg.* 1997;24:347–367.
52. Khouri RK, Smit JM, Cardoso E, et al. Percutaneous aponeurotomy and lipofilling: A regenerative alternative to flap reconstruction? *Plast Reconstr Surg.* 2013;132:1280–1290.
53. Rabin RC. After mastectomies, an unexpected blow: Numb new breasts. *The New York Times.* January 30, 2017. Available at: https://www.nytimes.com/2017/01/29/well/live/after-mastectomies-an-unexpected-blow-numb-new-breasts.html?_r=0. Accessed July 5, 2017.
54. Rosique RG, Rosique MJ, De Moraes CG. Gluteoplasty with autologous fat tissue: Experience with 106 consecutive cases. *Plast Reconstr Surg.* 2015;135:1381–1389.
55. Hovius SE, Kan HJ, Verhoekx JS, Khouri RK. Percutaneous aponeurotomy and lipofilling (PALF): A regenerative approach to Dupuytren contracture. *Clin Plast Surg.* 2015;42:375–381, ix.
56. Verhoekx JS, Mudera V, Walbeehm ET, Hovius SE. Adipose-derived stem cells inhibit the contractile myofibroblast in Dupuytren's disease. *Plast Reconstr Surg.* 2013;132:1139–1148.
57. Kan HJ, Selles RW, van Nieuwenhoven CA, Zhou C, Khouri RK, Hovius SE. Percutaneous aponeurotomy and lipofilling (PALF) versus limited fasciectomy in patients with primary

Dupuytren's contracture: A prospective, randomized, controlled trial. *Plast Reconstr Surg.* 2016;137:1800–1812.
58. Jianhui Z, Chenggang Y, Binglun L, et al. Autologous fat graft and bone marrow-derived mesenchymal stem cells assisted fat graft for treatment of Parry-Romberg syndrome. *Ann Plast Surg.* 2014;73(Suppl 1):S99–S103.
59. Fontdevila J, Serra-Renom JM, Raigosa M, et al. Assessing the long-term viability of facial fat grafts: An objective measure using computed tomography. *Aesthet Surg J.* 2008;28:380–386.
60. Pezeshk RA, Stark RY, Small KH, Unger JG, Rohrich RJ. Role of autologous fat transfer to the superficial fat compartments for perioral rejuvenation. *Plast Reconstr Surg.* 2015;136:301e–309e.
61. Bank J, Fuller SM, Henry GI, Zachary LS. Fat grafting to the hand in patients with Raynaud phenomenon: A novel therapeutic modality. *Plast Reconstr Surg.* 2014;133:1109–1118.
62. Pers YM, Rackwitz L, Ferreira R, et al.; ADIPOA Consortium. Adipose mesenchymal stromal cell-based therapy for severe osteoarthritis of the knee: A phase I dose-escalation trial. *Stem Cells Transl Med.* 2016;5:847–856.
63. Haahr MK, Jensen CH, Toyserkani NM, et al. Safety and potential effect of a single intracavernous injection of autologous adipose-derived regenerative cells in patients with erectile dysfunction following radical prostatectomy: An open-label phase I clinical trial. *EBioMedicine* 2016;5:204–210.
64. Condé-Green A, Marano AA, Lee ES, et al. Fat grafting and adipose-derived regenerative cells in burn wound healing and scarring: A systematic review of the literature. *Plast Reconstr Surg.* 2016;137:302–312.
65. Rigotti G, Marchi A, Stringhini P, et al. Determining the oncological risk of autologous lipoaspirate grafting for post-mastectomy breast reconstruction. *Aesthetic Plast Surg.* 2010;34:475–480.
66. Petit JY, Lohsiriwat V, Clough KB, et al. The oncologic outcome and immediate surgical complications of lipofilling in breast cancer patients: A multicenter study. Milan-Paris-Lyon experience of 646 lipofilling procedures. *Plast Reconstr Surg.* 2011;128:341–346.
67. Seth AK, Hirsch EM, Kim JY, Fine NA. Long-term outcomes following fat grafting in prosthetic breast reconstruction: A comparative analysis. *Plast Reconstr Surg.* 2012;130:984–990.
68. Brenelli F, Rietjens M, De Lorenzi F, et al. Oncological safety of autologous fat grafting after breast conservative treatment: A prospective evaluation. *Breast J.* 2014;20:159–165.
69. Kronowitz SJ, Mandujano CC, Liu J, et al. Lipofilling of the breast does not increase the risk of recurrence of breast cancer: A matched controlled study. *Plast Reconstr Surg.* 2016;137:385–393.
70. Silva-Vergara C, Fontdevila J, Descarrega J, Burdio F, Yoon TS, Grande L. Oncological outcomes of lipofilling breast reconstruction: 195 consecutive cases and literature review. *J Plast Reconstr Aesthet Surg.* 2016;69:475–481.
71. Rubin JP, Coon D, Zuley M, et al. Mammographic changes after fat transfer to the breast compared with changes after breast reduction: A blinded study. *Plast Reconstr Surg.* 2012;129:1029–1038.