Breast Reconstruction and Augmentation Using Pre-Expansion and Autologous Fat Transplantation

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The concept of fat grafting for volume enhancement is not a new one. Although surgeons have been injecting fat for years,\textsuperscript{1,2} recent focus by clinicians\textsuperscript{3} and basic science investigators has generated a groundswell of enthusiasm for a “back to the science” approach to fat transplantation. There is much to study to maximize both graft volume and, more importantly, patient safety. This article outlines the authors’ approach to breast deformities using fat grafting, with emphasis on current technique.

FAT GRAFTING: HARVESTING

After Illouz’s\textsuperscript{4} seminal paper describing the ability to remove fat cells from small port incisions using a cannula, liposuction offered surgeons a low-morbidity new supply of autologous filler. Because many of the variables so important to fat grafting were not well understood at that time, early results were disappointing as it related to volume maintenance.

One of the most frustrating outcomes plastic surgeons experience is often in fat grafting. Despite the same surgeon, the same technique, and the same recipient site, there is a wide variability among volumes maintained over time (\textbf{Fig. 1}).

Donor age, donor site, harvesting technique and instrumentation used with harvesting, processing technique, injection technique, and recipient site management both pregrafting and postgrafting are all vitally important to the success of fat grafting and to maintenance of volume.\textsuperscript{5} Looking to the science in the organ transplantation literature may help standardize techniques in this area.

Intuitively, donor (and recipient) age is thought to be a factor in the success of fat grafting. Animal studies in nude mice suggest this to be the case.\textsuperscript{6} Data from human fat over a range of donor ages injected subcutaneously into nude immunocompromised mice, suggested higher volume retention in recipients with fat from younger donors. In practice, autologous fat grafting does not afford the opportunity to control for this variable and this may only serve as a prognosticator for patients preoperatively.

Harvesting techniques vary greatly in liposuction and certainly impact cell survival and graft take. Several studies have demonstrated that less suction results in more viable adipocytes.\textsuperscript{7} Generally, handheld syringe methods are thought to traumatize adipocytes less and are recommended to harvest fat. In addition, smaller-gauge syringes are recommended so as to avoid fat clumping and to ease in reinjection.

Ostensibly, one might think that surgically resected fat, which is then diced with minimal trauma, maintains cellular integrity better than suctioned fat by any method, and results in better graft take.\textsuperscript{8} Ongoing studies are being performed in this area to understand better the role of minimizing graft trauma\textsuperscript{9} and there is an opportunity...
to validate this question and potentially to improve instrumentation in this area.

**FAT PROCESSING**

There have been multiple reports of “percent graft take” by volume. Because of lack of standardization in grafting technique, clinicians must consider rethinking the results of many of these studies. Sixty milliliters of aspirated fat using the tumescent technique decants to a variable aliquot of fat and serum, including blood and crystalloid. Sixty milliliters of aspirate may decant to 30 to 40 mL of fat. When this fat is then centrifuged or rolled on a Telfa pad, two techniques used to concentrate fat further, the resultant fat may reduce to 20 mL by volume. It is not surprising that when fat is grafted, even if all the fat survives, in many cases one has already committed to at best a 30% to 40% volume take, because that is the actual amount of fat that has been inserted by volume.

Although separation by simple decanting uses 1g to separate higher-density blood and crystalloid from adipocytes, a high-speed centrifuge uses much higher gravitational forces (3g–5g) and separates fat from crystalloid extremely well. These centrifuges also require transfer of fat into multiple individual 5- or 10-mL syringes. It has been demonstrated, however, that subjecting adipocytes to 3g to 5g of centrifugation results in a higher degree of cell death. A compromise between these two techniques that the authors use is manual centrifugation. Prototype devices, similar to the geared concept used in salad spinners, can subject larger volumes of adipocytes to 1g to 2g forces to separate out unwanted crystalloid better, without subjecting the fat to excessive (3g–5g forces) trauma or excessive syringe manipulation.

Subjecting adipocytes to air can potentially damage the cells and can decrease their survival. In addition, the time between harvesting and reinjection increases duration of hypoxia and potentially has an effect on adipocyte survival. Such concerns support the argument that fat grafting in large volumes (unlike those performed for lip or nasolabial folds) might best be accomplished with a team approach. Ostensibly, it is recommended that an assistant or several assistants process fat simultaneously while surgical liposuction harvest is performed.

**INJECTION TECHNIQUE**

Injection technique also varies and probably plays a role in fat grafting survival. Bolus injections are to be condemned because they defeat the purpose of oxygen diffusion and usually result in fat liquefaction, necrosis, and oil cysts. Dispersing the fat as evenly as possible into as many interstices as possible in the recipient tissue theoretically gives the donor cells the highest chance of maintaining an oxygen diffusion gradient over the critical 3 to 5 days postgrafting.

There are currently several preferred techniques of grafting fat into the breast. The authors’ preferred technique, the “mapping” technique, involves the use of small (3-mL) syringes handheld and connected directly to a 16-gauge blunt needle. Markings are made in the recipient areas (Fig. 3) to aid in a systematic injection. An exact amount of fat (1–2 mL) is then injected slowly on withdrawal. The needle is then inserted into another adjacent tunnel and the process is repeated. This technique is more deliberate and exact but does take more time. In addition, it requires the operator to deploy the plunger and withdraw the needle at the same time.
A second technique is the “reverse liposuction” method. A 30-mL syringe containing prepared fat is connected to short intravenous extension tubing and is connected to an injection needle. An assistant depresses the plunger at a desired rate (as directed by the surgeon) while the surgeon focuses only on the motion and location of the needle. In this manner, a large volume of fat can be randomly dispersed into the recipient site in a shorter period of time. It is vitally important to keep the needle under motion at all times and to keep the injection speed low to avoid bolus injections. When starting out with fat grafting to the breast the mapping technique is generally advised. To date there are no data suggesting one technique is superior.

Because many reports suggest at best 30% fat take, one controversy in fat grafting has been whether or not to overcorrect. Overcorrection historically seemed alluring because one might reach a desired end point knowing a significant amount of adipocytes would not survive. It is believed, however, that the increased interstitial pressure created in most cases results in lack of oxygen diffusion and cell death, potentially of all the cells.

Indeed, some of the best clinical results in fat grafting have been demonstrated by those who promote small serial volume sessions of fat grafting. The evidence suggests that this approach is successful because it respects the interstitial pressure limitations of the recipient site and in doing so, promotes diffusion during the initial critical days postgrafting.

THE ROLE OF THE RECIPIENT SITE

Recipient site management has only recently been suggested as a potential important variable in fat grafting. From the general surgery trauma literature and from hand and upper extremity trauma, the importance of compartment pressure and grave consequences of interstitial pressure are well understood. If it is possible to increase the volume of the interstitial space before fat grafting, it is potentially feasible to inject a larger volume of graft into the recipient site before reaching high interstitial pressures.

Experience with the vacuum-assisted closure as a means of wound management has proved that microangiogenesis is a direct result of negative mechanical pressure. The extensive vacuum-assisted closure data on vascular in-growth coupled with the MRI findings from BRAVA-expanded breasts support the authors’ thesis that increased microcirculation, combined with the larger interstitial space created by the expansion, may both contribute to the potential for increased fat volumes and increased diffusion gradients. Although such postulates are currently being considered for animal study, mechanical difficulties related to immobilization of vacuum domes on animal subjects remain a significant challenge (Fig. 4).

The BRAVA bra was initially developed in the 1990s to generate a nonsurgical negative pressure breast enhancement. The device generates a negative pressure that creates an inflow of fluid, in this case interstitial fluid, and increased vascularity. The device was typically worn nightly under a low negative pressure, and over 4 to 6 weeks breast enlargement of a cup size on average was achieved. Once the device was discontinued from use, however, breast size regressed to the pre-expansion baseline.

When used as a recipient site modulator before fat grafting, pre-expansion is thought to generate a more supple skin envelope, especially in reconstruction cases and in cases of irradiated tissue. In addition, the increased interstitial space is believed to allow for a larger volume of fat to be grafted while still dispersing the cells with oxygen-rich recipient site tissue. Clinically, the authors aim for a twofold to threefold increase in volume before grafting (Fig. 5).

Postoperatively, skin grafts are immobilized to promote secure apposition of the donor cells to the recipient wound bed. This promotes an adequate diffusion gradient and greater likelihood that angiogenesis occurs. Searing of the graft or movement of any type in this initial 3 to 5 days can prove fatal for a skin graft. It is believed that immobilization of the transplanted adipocyte can best be accomplished with mild external negative pressure. The authors are currently advocating use of the BRAVA bra for 5 to 7 days postgrafting.
Not only does the mild negative pressure serve to immobilize the fat in its interstitial space, it also may help with angiogenesis as has been demonstrated with the vacuum-assisted closure. Lastly, the domes of the external expander BRAVA unit help protect the newly grafted tissue from external movement and trauma.

**IMPROVED INSTRUMENTATION**

In 1980, when Illouz first described the liposuction technique, 10-mm cannulae were described. Thirty years later, clinicians are now rapidly removing fat using 12-gauge cannulae with multiple side ports, in a less traumatic manner (Fig. 6).

**Fig. 4.** VAC data demonstrate increased circulatory flow with negative pressure (top left). (Data from KCI.) The theoretical effect of negative pressure on breast circulation (top right). MRI of breasts pre-expansion (bottom left). Postexpansion using BRAVA (bottom right). Note the real increase in vessel caliber and number postexpansion.

**Fig. 5.** A threefold to fourfold volume expansion of the recipient site is possible and desirable before fat grafting.
CELL PRESERVATION TECHNIQUES FROM TRANSPLANTATION LITERATURE

In the solid organ transplantation, cell preservation is maximized by hypothermia and extracorporeal perfusion during organ transfer using a variety of solutions. One such solution, University of Wisconsin Solution,\(^\text{13}\) is a highly concentrated potassium solution that reduces cellular metabolism in the solid organ during its period of cellular hypoxia and anoxia, and is thought to reduce cellular death following reperfusion in the recipient site. This highly concentrated potassium solution is not used in vivo, but is used to perfuse the solid organ while in transit and in preparation for transplantation. In general surgery shock and trauma, a variety of solutions are known to improve reperfusion and improve cell survival following resuscitation. These represent just a few starting points for several potential strategies that are suitable for study for possible adoption in maximizing techniques of fat transplantation. Current research is underway to identify optimal solutions in this area.\(^\text{14}\)

BREAST RECONSTRUCTION AND AUGMENTATION: THE EMERGING ROLE OF THE RECIPIENT SITE AND FAT GRAFTING

The State of Mastectomy Surgery in the United States

Annually in the United States, there are approximately 182,000 newly diagnosed cases of breast cancer that require some type of surgical procedure to treat breast cancer.\(^\text{15}\) These generally represent some form of mastectomy or lumpectomy; however, there are approximately 57,000 breast reconstructions performed a year in the United States.\(^\text{16}\) If one assumes that all these reconstructions are performed for immediate (or in the same year of the mastectomy) reconstruction, at best only 31% of patients are receiving some form of breast reconstruction. This number is probably lower because many of the reconstructions are performed on cases diagnosed and surgically treated in prior years. This also means that every decade, approximately 1.2 million women are electing to do nothing about their postsurgical breast deformity. Why do such a high percentage of breast cancer surgery patients elect to do nothing following lumpectomy or mastectomy? One postulate is that the degree of morbidity of the reconstruction outweighs the perceived aesthetic improvement over the existing deformity.

In this orphaned population, a low-morbidity procedure to reconstruct breast defects that results in significant aesthetic improvement represents a large opportunity.

The State of Augmentation Surgery in the United States

An adequate discussion of augmentation with breast implants is beyond the context of this article. It is interesting to consider, however, the risk-reward analysis similar to that outlined in the patient after breast cancer surgery.

Reviewing available statistics, there were approximately 348,500 cosmetic breast augmentations performed in the United States in 2007. In addition, retail data from Consumer Reports suggests that at least 34% of women in the United States own padded bras.\(^\text{17}\) Based on standard assumptions about the United States population and the percent of women of adult age, for every woman who undergoes a cosmetic breast enhancement, there are over 100 women who, for whatever reason, would like their breasts to appear larger in some way. The same rationale for nonsurgery (padded bras) may also exist as it does for breast reconstruction. Besides financial issues, concerns over artificial implants, and other personal concerns, a remaining variable is that the degree of morbidity of the augmentation does not outweigh the aesthetic improvement over the existing aesthetic concern. As in the case of reconstruction, a low-morbidity procedure to augment breasts that results in significant improvement represents a large number of potential patients, much larger than the reconstruction population.

Patient Evaluation: Medical

The patient presenting for breast reconstruction or augmentation with autologous fat grafting should be evaluated for associated medical conditions that might otherwise exclude them from safely undergoing a liposuction procedure. Acutely, the liposuction aspect of the intervention is probably higher in morbidity than that of the breast fat grafting. Smokers are generally not advised as candidates for breast reconstruction with fat grafting with pre-expansion. Donor site fat is evaluated for the likely availability of fully processed fat.
Irradiated patients have been successfully treated using BRAVA pre-expansion. In irradiated reconstructions, the skin envelope expands more slowly and serial expansion and injection sessions are required. It is generally advised to begin breast reconstruction in nonirradiated mastectomy patients and first become familiar with these techniques before embarking on treating irradiated defects. The assessment of the opposite breast is addressed with the same principles as for any breast reconstruction.

**Patient Evaluation: The Role of Compliance**

Animal studies with negative pressure pre-expansion are challenging because of difficulties maintaining a device in animal subjects. The same can be said for patients with regards to BRAVA pre-expansion. There is no substitute for sustained moderate to high negative pressure pre-expansion to maximize pre-fat grafting volume of the recipient site. Indeed, the earliest versions of the negative pressure pumps were low-voltage battery-operated devices that exerted a low negative pressure. These patients exhibited less dramatic pregrafting expansion when compared with more powerful pumps currently used. These pumps are similar in negative pressure and in terms of size and portability as the vacuum-assisted closure pump, and have demonstrated a dose response curve with regards to both pre-expansion volume and to overall fat volume results postgrafting.

Based on experience with the dose response data, the authors believe there is no substitute for adequate pre-expansion. The degree and extent of pregrafting expansion is directly proportional to the amount of grafting possible to maintain a physiologic interstitial pressure. Last minute “cramming” on part of the patient has been experienced and does not result in successful preparation. It is ultimately the responsibility of the surgeon adequately to select, educate, coach, and troubleshoot their patients to ensure adequate and optimal pre-expansion. Patients should spend as much time in-office the first time they use their bras to ensure they are properly educated and motivated to use the device.

**BASELINE VOLUME CONSIDERATIONS**

The more breast and subcutaneous tissue there is to begin with, the easier it is to volume expand with negative pressure. In addition, the less scar damaged (nonirradiated) the tissue is, the easier it is to expand with negative pressure. The following cases serve as extreme examples (Box 1).

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**Box 1 Examples of baseline volume considerations**

**Case A: Augmentation**
Existing breasts, 250 mL size. Desired final breast volume, 500 mL. Plan: pre-expansion to desired volume, then graft. Percent expansion = \( \frac{500 - 250}{250} = 100\% \).

**Case B: Reconstruction**
Existing breast skin, subcutaneous fat 50 mL size. Desired volume, 500 mL. Plan: pre-expansion to desired volume, then graft. Percent expansion = \( \frac{500 - 50}{50} = 900\% \).
The number of sessions for Case A may be one, whereas the number may be four to five for Case B.

**Preferred Techniques**

**BRAVA: recipient site preparation**
In cases of mastectomy and for augmentation, the BRAVA dome is placed for 3 to 4 weeks and is worn 12 hours daily. For the last 4 to 5 days before fat grafting, it is advised to wear the domes 24 hours a day. Circumferential pressure at the edges of the domes can create skin sensitivity and this should be explained to patients who should reduce the degree of negative pressure. Nonirradiated skin and subcutaneous tissue has greater potential for parenchymal expansion than cases performed in irradiated tissue, which requires more serial sessions (Fig. 7).

The location and degree of body fat available is analyzed to evaluate the existence of an adequate amount of donor fat. Because there are so many variables (amount of tumescence, degree of bleeding, time allowed for tumescent solution to set) it is impossible to formulate a standard ratio of aspirate to actual processed fat by volume. As a conservative rule, four to five times the desired volume of fat needed for grafting should be available to be harvested as aspirate. For example, if reconstruction using 400 mL of fat is planned, the patient should be able to render at least 1600 to 2000 mL of aspirate to ensure adequate donor material.

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\text{Aspirate} = 5 \times \text{Graft};
\]

\[
2000 \text{ mL} = 5 \times 400 \text{ mL}
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Considering the pre-expansion effort the patient must tolerate, it is always better to have more than less fat available.

In the case of augmentation with 300 mL of fat on each side, a minimum of 3000 mL of aspirate is recommended. Patients with body mass indexes as low as 23 to 24 have been successfully
treated. The lower the body mass index, the greater the number of donor sites (abdomen, knees, thighs, and so forth) that must be entered to harvest adequate amounts of aspirate and fat.

**Lipografting: preoperative planning**
On the day of surgery patients are photographed and marked as usual for liposuction. Markings are made for injection sites on the breasts and lines are made on the breast mound to ensure proper dispersion of the fat grafts. Patients are brought into the operating room still wearing the BRAVA bra to maximize expansion closer to the point of injection. Once all the fat is harvested and processed, the Bra is removed, the site is prepared and redraped, and injection takes place.

**Harvesting and collection**
Fat is harvested using a 12-gauge blunt cannula with multiple side ports. Syringe aspiration is used as opposed to high negative pressure machine techniques. To avoid desiccation,
a closed system is used, transferring the fat from the syringe directly into an empty sterile intravenous bag by an extension tubing setup (Fig. 8).

**Processing**

Once an adequate amount of aspirate is harvested, the collected intravenous bags are decanted of unwanted fluid and are placed into a manual centrifuge. This manual centrifuge further separates fluid from the adipocytes without subjecting the cells to excessive handling, desiccation, or trauma, as is postulated with high-speed centrifugation in small syringes.

Once the fat is properly processed in this manner, the fat is then drawn back into 3- or 5-mL syringes from the intravenous collection bags using a three-way stopcock, and grafting begins.

**Recipient site techniques: needle band release**

Multiple radial needle insertions are made around the breast mound to disperse the grafted adipocytes maximally and to ensure as many different planes as possible. Before grafting the fat, if there are breast shaping issues that need to be addressed these can be performed at this time.

In many breasts, fibrous ligamentous tissue or bands distort the breast mound, such as in constricted inframammary folds or in the case of tubular breast deformities. Because expansion of the parenchymal space places these bands under high tension, it facilitates the transaction of these bands using an 18-gauge needle, simply by inserting the needle in the area of the band and through proprioception, “feeling” the blade of the needle cut the band. In this manner, it is possible to “expand” or “release” these constrictions further internally in a manner similar to the external release of a burn scar contracture. The inframammary fold can be lowered in constricted inframammary folds, and the constricted bases of tubular breasts can be widened in this manner. It is important not to overrelease these bands, because too large a dead space might ensue. This reduces the interstices of the tissue and reduces the surface-to-volume characteristics of the recipient site.

**Injection technique**

Bolus injections are to be condemned because they defeat the purpose of oxygen diffusion and usually result in fat liquefaction and necrosis.

The mapping technique previously described involves the use of small (3-mL) syringes handheld and connected directly to a 16-gauge blunt needle. Through the multiple radial needle insertions around the breast mound, the needle is advanced in the subcutaneous plane and an exact amount of fat (1–2 mL) is then injected slowly on withdrawal. The needle is then inserted into another adjacent tunnel and the process is repeated.

Injection into the prepectoral fat and the subcutaneous fat is performed in as many different depth planes as the recipient tissue tolerates. In the case of mastectomy, the first session of grafting allows fewer planes of grafting and reasonable volumes during the first session (150–250 mL) should be planned. For subsequent sessions, there are more potential planes, because a thicker interstitial space exists. Generally, the more parenchyma one has to begin with, the larger volumes of fat that can be grafted. For first session reconstruction after mastectomy, 150 to 250 mL of fat can be expected. For augmentation or in subsequent grafting sessions in reconstruction, 200 to 300 mL can be planed. For irradiated cases, one should be extremely careful not to overgraft and should expect a minimum of four to five sessions.

In no cases (breast augmentation, treating a lumpectomy defect, breast asymmetry, or any other cases where any breast tissue remains) is it ever recommended to inject fat directly into breast tissue.

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**Fig. 8.** Closed system method of collection and fat replantation.
POSTOPERATIVE MANAGEMENT

Patients are instructed to wear the BRAVA bra 5 to 7 days postgrafting. This potentially helps with graft immobilization, potentiates neovascularization, and definitely protects the breast from external pressure or trauma.

REPRESENTATIVE RESULTS

Breast Reconstruction

The patient in Fig. 9 had bilateral mastectomy (radical on the right) and had four serial sessions of BRAVA pre-expansion and fat grafting sessions of 150 mL each time.

Breast Reconstruction for Severe Asymmetry

The 20-year-old patient in Fig. 10 had a giant congenital nevus excised as a child and demonstrated hypomastia on the left, documented by MRI. She underwent 3 weeks of BRAVA pre-expansions to increase her parenchymal space and to increase the vertical skin envelope deficiency. She underwent a single session with grafting of 300 mL into the left breast. Her postoperative result at 6 months reveals retention of grafted fat volume.

Breast Augmentation: Postpartum Deflation

The 33-year-old patient shown in Fig. 11 desired larger breasts after having several children and experiencing some mild deflation. Although she wore a padded bra and desired a cup size increase in volume, she did not wish to have breast augmentation with implants. She underwent 3 weeks of BRAVA pre-expansions to increase her parenchymal space bilaterally. She underwent a single session with grafting of 250 mL into

Fig. 9. Patient with bilateral mastectomy and BRAVA pre-expansion reconstruction; three sessions, 600 mL total.
Fig. 10. (A) Patient with severe breast asymmetry and BRAVA pre-expansion reconstruction. (B) BRAVA pre-expansion increases parenchyma and skin envelope. (C) Six months after 280 mL of fat transplanted into the left breast.
each breast. At 9 months postgrafting, she demonstrates adequate volume maintenance.

**A COMPARISON OF BREAST RECONSTRUCTION USING THREE TECHNIQUES**

Table 1 helps delineate some of the main differences between currently popular reconstruction options and breast reconstruction using pre-expansion and autologous fat transplantation.

**CONTROVERSIAL TOPICS**

At the time of this communication, it is early days in breast augmentation and reconstruction using fat transplantation. There are more questions than there are answers, and it is easier to ask than to answer the questions. The following represent some of the biggest controversies and challenges facing this technique in the near, medium, and long term.

**Imaging and Detection of Breast Cancer**

In 1987, the American Society of Plastic Surgeons position paper strongly condemned fat grafting to the breast suggesting fat grafting would distort the ability of breast cancer detection. Breast fat grafting has been demonstrated to sometimes result in microcalcifications. Although many of these calcifications are believed to be distinguishable from calcifications of higher grade that are suggestive of malignancy, unnecessary biopsies have resulted from this effect.

**Risk of Cancer: The Aromatase Question**

It is well known that one in nine women experience breast cancer in their lifetime. Although it takes a nearly impossible study size to prove causality or statistical significance, the question has been raised that aromatase, a breakdown product of adipocyte necrosis, might cause breast cancer. The validity of this is unknown.

### Table 1

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<tr>
<td><strong>Tissue Expander/Implant</strong></td>
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What is known is that surgeons have performed thousands of procedures over the past 20 years in large numbers that cause fat cell necrosis. Despite thousands of TRAM flaps, with a high degree of fat necrosis in zone II and III, breast liposuctions, and breast reductions, there is no evidence, retrospective or prospective, that these procedures are associated with a higher degree of breast cancer. Such facts should not be sufficient, however, as to ignore the question of safety. Although there are currently models being developed to evaluate this carcinogenic potential in an animal model, the reality is that the answer in humans will not be available before the widespread use of this technique. Any patients entertaining any breast fat grafting, including reconstruction patients and breast augmentation patients, must be given full informed consent as to the unknown risks of the technique. Although many suggest this technique not be performed without the approval of an internal review board, the reality is that the technique is already being performed.

There is an unmet clinical need for more institutional review board–approved, multisite studies that can demonstrate reproducible and safe results by many independent surgeons. Such collective data in the literature will eventually help delineate the safety issues as they relate to carcinogenesis and cancer detection.

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