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PRELIMINARY RESULTS FROM MULTI-CENTER VOLUME RETENTION STUDY OF VIALITY™ WITH AURACLENS™ LIPOASPIRATE WASH SYSTEM SUPPORT ENHANCED VIABILITY FAT TRANSFER

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Introduction

Autologous fat transfer (AFT) is a minimally invasive medical procedure that includes aspirating adipose tissue from one part of the body and reinjecting the processed fat tissue into a different part of the body with the primary purpose of adding volume or enhancing soft tissue coverage.

AFT is used for various procedures, including breast augmentation or reconstruction, facial rejuvenation, and body contouring. Fat transfer to the breast has become increasingly popular in recent years due to its natural results and low risk of complications. One of the most important factors that determines the success of fat transfer is the quality and viability of the transferred adipose cells.

A 2013 survey of the American Society of Plastic Surgeons indicated that approximately 70% of the responding physicians use AFT[1]. Surgeon adoption of AFT has been facilitated by several FDA-cleared, commercially available systems that are used to harvest, filter, wash and transfer autologous fat tissue. While some authors have concluded that there are potential benefits from the use of these systems[2,3,4,5], they suffer from numerous disadvantages. For example, more than 70% of surgeons in a 2022 survey[9] expressed dissatisfaction with volume retention when performing AFT, despite the same survey identifying it as the most important factor in choosing a fat transfer method. This is borne out in the clinical literature, where long-term volume retention estimates vary widely from 30-70%[11,12], showcasing a lack of predictability in the long-term outcome. Other disadvantages include long processing times, burdensome and complex connections, inadequate processing capacity and lack of efficiency[2].

Pre-clinical and clinical research[7,10] has shown the potential benefits to a technique we refer to as Enhanced Viability Fat Transfer (EVFT), which includes the use of a surfactant (P188) wash in conjunction with filtration and a concentrating step using a super-absorbent foam to improve the long-term survival of fat. In this white paper, we discuss the use of Viality™, the first commercially available EVFT device, including its benefits and impact on the outcomes of the procedure.

The Viality Lipoaspirate Wash System

Viality features a patented processing technology that is designed to enhance the viability and survival of fat cells during the fat transfer process. The specialized device gently and efficiently filters and washes the adipose tissue with a unique lipoaspirate wash called AuraClens™, then concentrates it for reinjection with a super-absorbent foam pad. The process, which takes less than 10 minutes in the operating room, facilitates the removal of unwanted oils and cellular debris from the lipoaspirate while also ensuring that most of the harvested fat cells remain intact, healthy, and viable, thereby, reducing the risk of cell death and resorption after the transfer. The Viality system has the capability of processing from 50 to more than 1,000 milliliters (mL) in a single run. Figure 1 shows the device and the steps involved during its use.

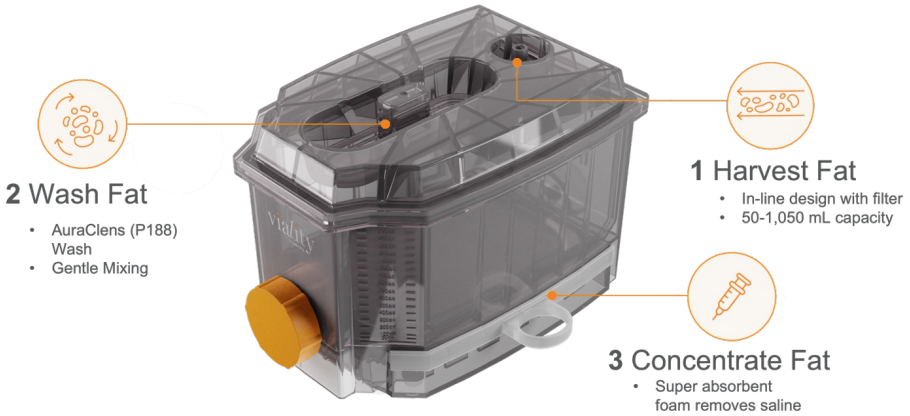


Figure 1 Viality System and Its 3-Step Process

Viality is backed by more than 10 years of research at Massachusetts General Hospital, and by pre-clinical and clinical studies that have shown that Viality produces an average 94% cell viability and 89% average fat concentration with low processing time and increased volume for reinjection[6]. In addition, the AuraClens concentrating wash was shown in a 20-patient study to improve fat retention by more than 70% compared to saline rinse[7].

Ongoing Multi-Center Volume Retention Study with Viality

Sientra is sponsoring a multi-center (13 sites enrolled) prospective study enrolling patients undergoing an aesthetic or reconstructive fat transfer procedure to the breast with or without a breast implant. A total of up to 200 patients will be enrolled in the study in two cohorts of up to 100 patients each: reconstruction and augmentation, meeting the selection criteria for each cohort, as outlined below. All patients receive autologous lipoaspirate processed with the Viality system.

This ongoing study is the only study of its kind to measure long-term retention over multiple sites and multiple types of patients and procedures, with a statistically significant population, and volume calculations performed in a blinded and independent manner, as will be detailed below.

Patients are followed on post-procedure month 1, 3, 6 and 12. Long-term volume retention is evaluated by 3D imaging, using Canfield's Vectra XT or H2, utilizing reproducible settings, including lighting, distance from target area, background, garments, etc.) at each visit, including a baseline scan taken pre-operatively, so that images are suitable for comparison.

The 3D measurements at different timepoints are used to quantify the total breast volume and calculate fat graft retention over time. Volume Retention is defined as the ratio of total breast volume to expected breast volume as calculated by dividing total measured volume at each time point by expected breast volume.

Expected volume was calculated with the following formula:

$$\textit{Expected Volume} = \begin{array}{c}\textit{Baseline Volume-Explanted Implant Volume-Tissue Excised} \\ \textit{+New Implant Volume+Fat Injected}\end{array}$$

At all sites, the volume of explanted implants was recorded at each procedure, and any tissue (skin and/or breast tissue) excised was weighted and recorded. Baseline Volume represents the volume calculated from the baseline, pre-operative, scan.

Volume retention at each timepoint was calculated with the following formula:

$$\textit{Volume Retention \%} = \frac{\textit{(Total Measured Volume Calculated by Canfield)}}{\textit{(Expected Volume)}} \times 100$$

	Inclusion Criteria	Exclusion Criteria
Augmentation	• Female patients > 22 years and <65 years of age • Patients with a BMI < 35 • Patients undergoing an aesthetic fat grafting procedure to the breast (breast augmentation) with or without a breast implant. • Patients must be able to provide written informed consent, understand and be willing to comply with study- related procedures and follow-up visits. • Patients must be non-smokers. • Patients with available/adequate harvest sites for fat grafting. • Anticipated harvested fat volume between 200 and 700 cc. • Anticipated fat injection volume 50-350 cc per breast. • Anticipated breast implant (if used) volume between 200 and 550 cc. • Patients must agree to maintain their weight (i.e., within 5%) by not making any major changes in diet or lifestyle during the study.	• Skin rash in the treatment area. • Patients who smoke or use nicotine products. • Patients with bleeding disorders or currently taking anticoagulants. • Patients with history of trauma or surgery to the treatment area. • Patients with history of breast cancer. • Active, chronic, or recurrent infection. • Compromised immune system • Hypersensitivity to analgesic agents. • Co-morbid condition that could limit ability to participate in the study or to comply with follow-up requirements. • Untreated drug and/or alcohol abuse. • Pregnant or breastfeeding. • Any issue that, at the discretion of the Investigator, would contra-indicate the patient's participation. Patients who do not wish to have the study area (breast) photographed.

	Inclusion Criteria	Exclusion Criteria
Reconstruction	• Female patients> 18 years and <65 years of age • Patients with a BMI < 35 • Patients undergoing a fat grafting procedure to the breast in a second or third stage of a staged breast reconstruction, with or without a breast implant. • Patient is at least 1year post-completion of chemotherapy. • Patients must be able to provide written informed consent, understand and be willing to comply with study- related procedures and follow-up visits. • Patients must be non-smokers. • Patients with available/adequate harvest sites for fat grafting. • Anticipated harvested fat volume between 200 and 700 cc • Anticipated fat injection volume 50-350 cc per breast • Anticipated breast implant (if used) volume between 200 and 550 cc. • Patients must agree to maintain their weight (i.e., within 5%) by not making any major changes in diet or lifestyle during the study.	• Skin rash in the treatment area. • Patients who smoke or use nicotine products. • Patients with bleeding disorders or currently taking anticoagulants. • Patients undergoing active treatment for breast cancer. • Active, chronic, or recurrent infection. • Compromised immune system • Hypersensitivity to analgesic agents. • Co-morbid condition that could limit ability to participate in the study or to comply with follow-up requirements. • Untreated drug and/or alcohol abuse. • Pregnant or breastfeeding. • Any issue that, at the discretion of the Investigator, would contra-indicate the patient's participation. • Patients who do not wish to have the study area (breast) photographed.

Image Analysis Workflow

To ensure consistency across sites and avoid bias in volume calculation from the 3D image, all data analysis is performed by Canfield using the Vectra Analysis Module. Sites are trained to capture the images in a consistent manner. No data manipulation, including point selection, is performed at the sites. All images are assigned random tracking numbers which blind the Image Analysis Technicians (IATs) to Site Name, Patient Name, Visit Date and Treatment Group. Each image is assigned a blinding visit designation of "BL" for Baseline or "FU" for Follow-up. All volume measurements are independent to the image being analyzed; there are no measurements for which one visit will be directly measured against another. Images are matched to ensure consistent positioning and orientation in the 3D space. The IAT uses anatomical features (e.g., sternal notch, ribs below the breasts) outside of the treatment area on both Baseline and Follow-up to precisely match the position and orientation of the Follow-up image to that of the Baseline. Both Baseline and Follow-up images may be cropped to remove unnecessary areas of the image (e.g., below the navel, above the neck, the full length of the arm).

Area of Interest (AOI) Definition

An IAT draws one AOI per breast on the Baseline image for a total of two AOIs per image, which cannot touch. The AOIs are drawn superiorly between visible pectoral curvature and/or breast tissue and the clavicle, medially along the sternum and medial mammary fold, and inferiorly including a small margin below the inframammary fold. Laterally the AOIs include the lateral breast curvature as far as can be accommodated up to the mid-axillary line (as seen on Figure 2).

The IAT draws AOIs on Follow-up images to match as closely as possible both the anatomical Baseline AOI definition (which matches the positioning and orientation of the baseline and follow-up images) and the specific Baseline AOI placement for that subject (e.g., identifiable skin features on sternum which can be matched per subject). Where it is not possible to match both specific Baseline AOI placement and anatomical AOI position, preference is given to the anatomical AOI position.

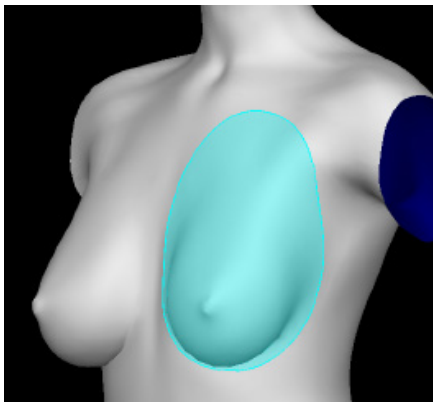


Figure 2 Breast AOI

All images undergo a Quality Control (QC). A second IAT, independent of the IAT who performed registration and AOI placement for an image, reviews the image registration (Baseline to the x, y, z axis; Follow-up to the Baseline) to check that it is optimal. The QC IAT also reviews the AOI to ensure it is placed accurately and optimally. The QC IAT adjusts image registration and/or AOI placement if corrections or improvements can be made. The QC of all images ensure consistency and remove bias; if images do not meet the required criteria, the sites are instructed to retake the images.

After AOI is determined, the volume calculated for each breast in each image is interpolated and expressed in mL.

Preliminary Results as of January 7th, 2023

A preliminary data analysis was performed by Canfield on January 7th, 2023. To that date, the study registered 68 patients enrolled with baseline images, representing 134 breasts; 28 patients with 3-month images, representing 53 breasts; and 10 patients with 6-month images, representing 20 breasts. A total of 9 different surgeons and sites treated the 68 patients, with the number of treated patients per site ranging from 1 to 12, with 6 sites treating at least 5 patients each. Table 1 details the total number of images per timepoint and per cohort.

Table 1. Number of Images per Timepoint and Cohort

	TIMEPOINT	N (breasts)
ALL	1 MONTH	122
	3 MONTHS	53
	6 MONTHS	20
PRIMARY OR REVISION AUG (FAT ONLY)	1 MONTH	48
	3 MONTHS	25
	6 MONTHS	12
MASTOPEXY/REVISION (IMPLANT + FAT OR FAT ONLY)	1 MONTH	14
	3 MONTHS	6
	6 MONTHS	2
MASTOPEXY/REVISION (EXPLANT AND FAT ONLY)	1 MONTH	16
	3 MONTHS	6
	6 MONTHS	4
RECON AT EXCHANGE	1 MONTH	16
	3 MONTHS	10
	6 MONTHS	2
RECON 3RD STAGE	1 MONTH	22
	3 MONTHS	6
	6 MONTHS	0

Results

From the 53 breast images at the 3-month timepoint, and the 20 at the 6-month timepoint, 3 images had volume retention calculations above 105% at both timepoints. To avoid introducing discrepancies in the preliminary results, these breasts were not included in the preliminary data analysis; data discrepancies will be assessed later when the study is concluded.

In the current assessment, data analysis was performed only for aggregated data from all cohorts, since no cohort had a sample size at 3-months greater than 50 breasts. A sample size of 50 per indication (breast augmentation or breast reconstruction) is sufficient to provide greater than 90% power that adipose retention is greater than 70%. It is assumed that for each indication, 70% adipose retention will be achieved, this being the hypothesis being tested. At study completion, data will be assessed aggregated and separated per cohort, using a right-tailed hypothesis test, with alpha 0.05.

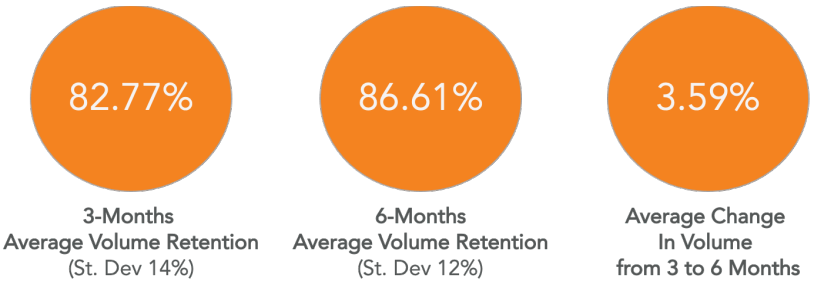
Table 2 details the volume retention results for this preliminary assessment. Figures 3 and 4 show the distribution of the datapoints.

Table 2. Preliminary Results as of January 7th, 2023

Timepoint	Sample Size (# breasts)	Average Volume Retention (%)	Standard Deviation (%)	Average Graft Volume per Breast (mL)
3 months	50	82.77	14	150.92
6 months	17	86.61	12	179.25

It can be concluded with statistical significance that the 3-month volume retention using Viality is greater than 70%, with a p-value of 0.024. No statistical analysis was performed for the 6-month timepoint due to the sample size.

For the 17 breasts with 6-month data, there was no evidence of volume loss from 3-months to 6-months, represented by an actual increase of 3.59% on average, representing stability of volume. This preliminary data is encouraging, since it is supportive of the well-established clinical observation and published data[8] that show that fat grafts retained at 3-months will tend to retain over time, unless significant weight changes occur. The initial 3-months post procedure is when the resorption of all non-adipose tissue injected, as well as of the non-viable fat cells, is believed to occur. As the study progresses, this hypothesis will be confirmed, and if held true, volume retention greater than 70% at 6-months when using Viality for fat transfer is expected to be shown to be statistically significant.



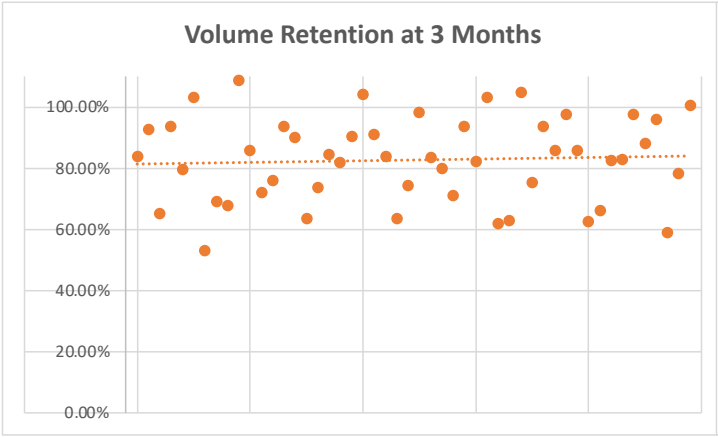


Figure 3

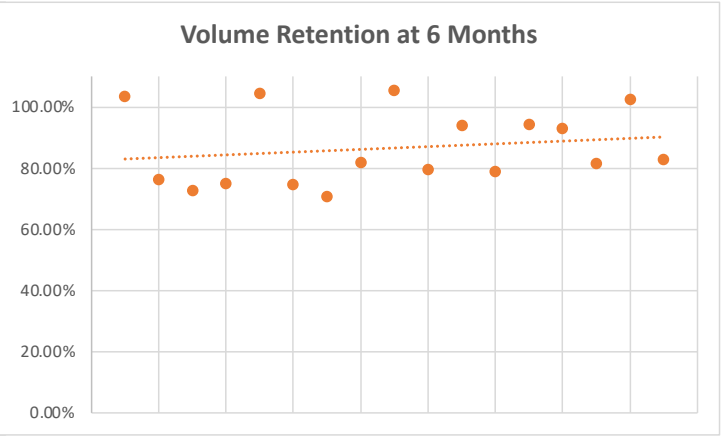


Figure 4

Conclusion

Enhanced Viability Fat Transfer is a safe and effective procedure that can provide natural-looking results for a variety of aesthetic and reconstructive purposes. The use of Viality by Sientra can further enhance the viability and survival of the transferred fat cells, resulting in better outcomes, with predictable results.

The preliminary results from the Viality multi-center clinical study, shows more than 80% volume retention at both the 3- and 6-month timepoints, with a standard deviation of 14% and 12% respectively. In addition, volume changes from 3 to 6 months were on average only 3.59%, representing stability of volume.

Even though the sample size per cohort or per site are not large enough to perform statistical analysis, the preliminary data does not show evident discrepancies between cohorts or between sites, suggesting consistency and predictability of outcomes using Viality. Table 3 shows the preliminary results separated by type of procedure.

Table 3. Results by Type of Procedure

	TIMEPOINT	N (breasts)	AVG RETENTION	ST. DEV
ALL	3 MONTHS	50	82.77%	14%
	6 MONTHS	17	86.61%	12%
PRIMARY OR REVISION AUGMENTATION (FAT ONLY)	3 MONTHS	23	76,56%	13%
	6 MONTHS	10	80.09%	8%
MASTOPEXY/REVISION (IMPLANT + FAT OR FAT ONLY)	3 MONTHS	6	95.00%	9%
	6 MONTHS	2	103.98%	1%
MASTOPEXY/REVISION (EXPLANT + FAT)	3 MONTHS	6	89.41%	14%
	6 MONTHS	3	88.95%	14%
RECONSTRUCTION AT EXCHANGE	3 MONTHS	9	89.13%	9%
	6 MONTHS	2	98.32%	6%
RECONSTRUCTION 3RD STAGE	3 MONTHS	6	78.20%	14%
	6 MONTHS	0	N/A	N/A

The study design, which includes multiple surgeons, multiple type of procedures, as well as independent and blinded volume calculation, makes the study robust and one-of-a-kind. Once completed, this will be the first multi-center study to assess long-term volume retention post-fat transfer in a controlled and systematic manner.

As evidenced in the existing pre-clinical data, clinical data, and the preliminary results described above, Viality offers an extraordinary approach to fat transfer, providing better predictability and long-term results. We anticipate that the results of this first-of-its-kind study will establish a new standard for evidence in fat transfer, continuing Sientra's tradition of transparency and evidence-based development.

Disclaimers

Sientra is sponsoring the clinical study, and both patients and surgeons receive financial compensation.

Dr. Calobrace is a speaker for Sientra; no financial disclosures for Sientra. Dr. Shridharani is a speaker and consultant for Sientra.

As with any surgical procedure, it is important to consult with a qualified and experienced plastic surgeon to determine if fat transfer is right for you and to discuss the benefits and risks of using Viality by Sientra.

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