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PRELIMINARY RESULTS FROM THE PROSPECTIVE MULTICENTER VOLUME RETENTION STUDY OF VIALITY™ LIPOASPIRATE WASH SYSTEM SUPPORT THE EFFECTIVENESS OF 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 adipose tissue into a different part of the body for the primary purpose of adding volume or enhancing soft tissue coverage.

AFT is used for various purposes such as breast augmentation, facial rejuvenation, body contouring and breast reconstruction. Fat transfer to the breast has become increasingly popular in recent years due to the natural results and low risk of complications associated with the procedure. In breast reconstruction, fat transfer is becoming the standard of care for adjuvant soft tissue augmentation; in particular for implant-based methods. The quality and viability of transferred adipose cells is a critical factor contributing to the success of fat transfer.

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 process and transfer autologous fat tissue. While some authors have concluded that there are potential benefits to using these systems[2,3,4,5], there are also limitations, especially those leading to unpredictable outcomes. More than 70% of surgeons in a 2022 survey[9] expressed some degree of dissatisfaction with volume retention when performing AFT. Volume retention was noted as the most important factor when choosing a fat transfer method in the survey. The variability of long-term volume retention is also well documented in the clinical literature with rates ranging from 30-70%[11-12]. Additionally, there exists dissatisfaction with the current range of commercially available processing systems. These disadvantages include burdensome intra-operative work flows, long processing times, complex equipment connections, inadequate processing capacity, and lack of overall efficiency[2].

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

The Viality Lipoaspirate Wash System with AuraClens

Viality features a patented processing technology that is designed to enhance the viability and survival of fat cells during the fat transfer process. This specialized device atraumatically and efficiently combines the surfactant wash (AuraClens), with subsequent filtration of the adipose tissue, along with further concentration on a super-absorbent foam pad for reinjection. 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 facilitating stabilization of the adipose cell membranes which are prone to injury during harvest[10]. This ensures that the majority of harvested fat cells remain viable, thereby, reducing early cell death and resorption during engraftment[13]. 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.

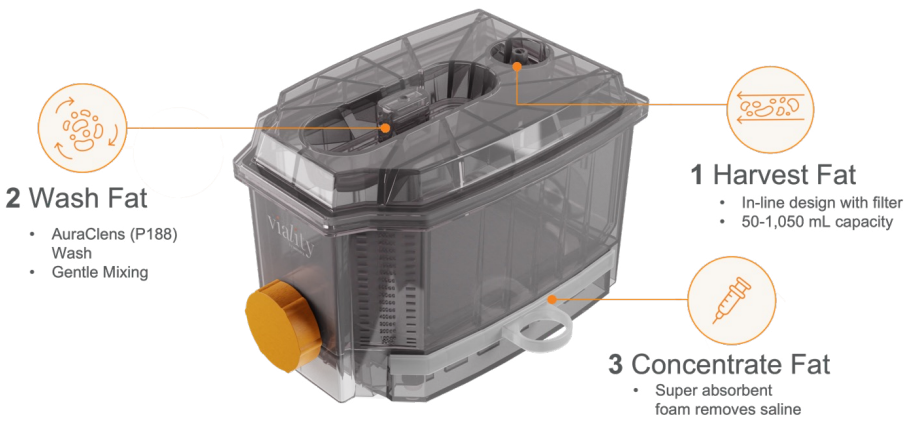

Figure 1 Viality System and Its 3-Step Process

Viality is backed by more than 10 years of research at Massachusetts General Hospital, including: pre-clinical bench top and animal studies, followed by clinical studies, that have shown Viality produces 94% average cell viability and 89% average fat concentration[2,7,10]. This in combination with a low processing time and high capacity for large volume reinjection[6] support efficiency and reliability of the system. 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 prospective multicenter (14 participating sites) study enrolling patients undergoing an aesthetic or reconstructive fat transfer procedure to the breast with or without a breast implant. Up to 200 patients will be enrolled in two study cohorts: reconstruction and augmentation. Selection criteria for each cohort is outlined in Table 1. All patients receive autologous lipoaspirate processed with the Viality system.

This ongoing study is the only study of its kind to measure long-term volume retention across multiple types of patients and procedures. It is powered to determine statistical significance. The primary endpoint is long-term volume retention, with volume measurements performed by an independent central core laboratory utilizing clinically obtained 3D Canfield Vectra images at defined time intervals.

Patients are followed on post-procedure months 1, 3, 6 and 12. Long-term volume retention is derived by 3D imaging, using Canfield's Vectra XT or H2 systems. The system utilizes reproducible parameters including: lighting, distance from target area, background, and garments. The software picks the defined points on the images in a standardized fashion. In addition, images are acquired in a standardized manner at each visit, including a baseline scan taken pre-operatively, for comparison. Prior to volume analysis, acceptability of images is confirmed by the core laboratory based on the standardized parameters.

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:

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

The volume of any explanted implants was recorded at each procedure, and any excised tissue (skin and/or breast tissue) was also weighed and recorded.

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

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

Table 1. Study Selection Criteria

	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.
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

All volume analysis is performed by Canfield Core Lab using the Vectra Analysis Module to ensure consistency across sites and avoid bias in volume calculation from the 3D image. Each site is trained to capture the images in a consistent standardized manner. No image evaluation, including point selection, is performed by sites. All images are assigned random tracking numbers which blind the Canfield Core Lab Image Analysis Technicians (IATs) to site name, patient ID, 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 timepoints 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, or 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 patient (e.g., identifiable skin features on sternum which can be matched per patient). Where it is not possible to match both specific baseline AOI placement and anatomical AOI position, preference is given to the anatomical AOI position.

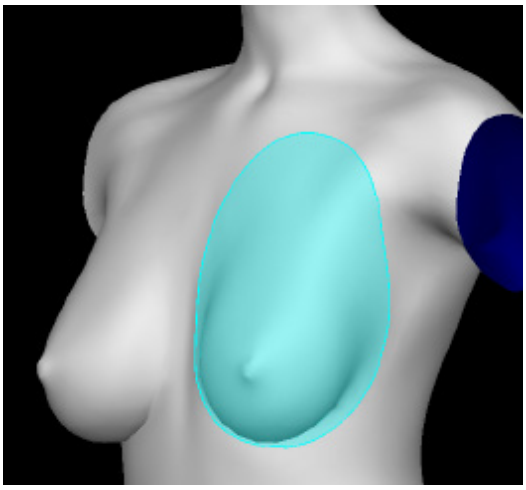

Figure 2 Breast AOI

All images undergo a Quality Control (QC) process. An IAT, independent of the IAT who performed registration and AOI placement for an image, reviews the image registration (baseline image to the x, y, z axis; follow up image to the baseline image) 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 in the event that corrections or improvements can be made.

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

Preliminary Analysis

A preliminary data analysis was performed using data collected on September 23, 2023. This analysis includes 102 patients (46 reconstruction, 56 augmentation) for a total of 193 breasts (88 reconstruction, 105 augmentation) from 12 sites followed for at least 3 months post-procedure. Average fat transfer volume was 149 cc (20-425 cc range). Table 2 lists the patient cohorts included in this analysis as well as average fat transfer volumes per breast.

Table 2. Preliminary Analysis Cohorts + Average Fat Transfer Volume

	All	Reconstruction	Augmentation
Patient (N)	102	46	56
Breasts (N)	193	88	105
Average volume fat transfer per breast and range	149 cc (20-425 cc)	113 cc (20-300 cc)	177 cc (36-425 cc)

Results

In the current assessment, data analysis was performed for all patients, as well as for reconstruction and augmentation cohorts separately. A sample size of 50 breasts per cohort (breast reconstruction or breast augmentation) is sufficient to provide greater than 90% power that volume retention is greater than 70%. It is assumed that for each cohort, 70% volume retention will be achieved, this being the hypothesis tested. At study completion, data will be assessed using a right-tailed hypothesis test, with alpha 0.05. Volume retention values >110% (8 values at various timepoints) were excluded from this analysis to guard against potential overestimation of volume retention. These values will be further evaluated for validity prior to the final analysis.

Table 3 details the volume retention results for this preliminary assessment. Figures 3 and 4 show the distribution of the datapoints, along with a paired analysis for breasts with volume retention values at 3, 6, and 12 months.

Table 3. Preliminary Volume Retention Results

Timepoint	Cohort	Breasts (N)	Average Volume Retention (%) ± SD	P value*
3 months	All	193	82.7 ± 12.7	<0.001
	Reconstruction	88	84.9 ± 11.7	0.001
	Augmentation	105	80.9 ± 13.3	0.007
6 months	All	144	84.0 ± 11.7	<0.001
	Reconstruction	65	86.3 ± 11.0	0.002
	Augmentation	79	82.1 ± 12.1	0.009
12 months	All	34	81.0 ± 12.7	NA
	Reconstruction	12	82.1 ± 13.0	NA
	Augmentation	22	80.4 ± 12.7	NA

*P value represents statistical significance for average volume retention greater than 70%. A minimum sample size of 50 breasts is required to calculate p value.

Average volume retention results were greater than 80% at all time points and in all cohorts analyzed, with a range of 80.4%-86.3%. Additionally, volume retention values are highly consistent within each analysis cohort as standard deviations for all timepoints and cohorts are between 11.0% and 13.3% (Table 3) and no difference in retention value distribution observed between reconstruction and augmentation (Figures 3 and 4).

Volume retention achieved with the Viality system at 3 and 6 months is significantly greater than 70%, with p values <0.001 for all breasts and <0.01 for both reconstruction and augmentation cohorts when analyzed separately (Table 3). P values are not available for volume retentions at 12 months in this preliminary analysis as the sample size is under 50 breasts. A paired sample analysis of breasts with data at 3, 6, and 12 months shows that this sample (N=30) is consistent over time and is also consistent with the volume retentions observed for all breasts at 3 and 6 months (Figure 4). The paired analysis supports that breasts followed to 12 months are a representative sample and results from this group are likely indicative of anticipated results from the full cohort at 12 months.

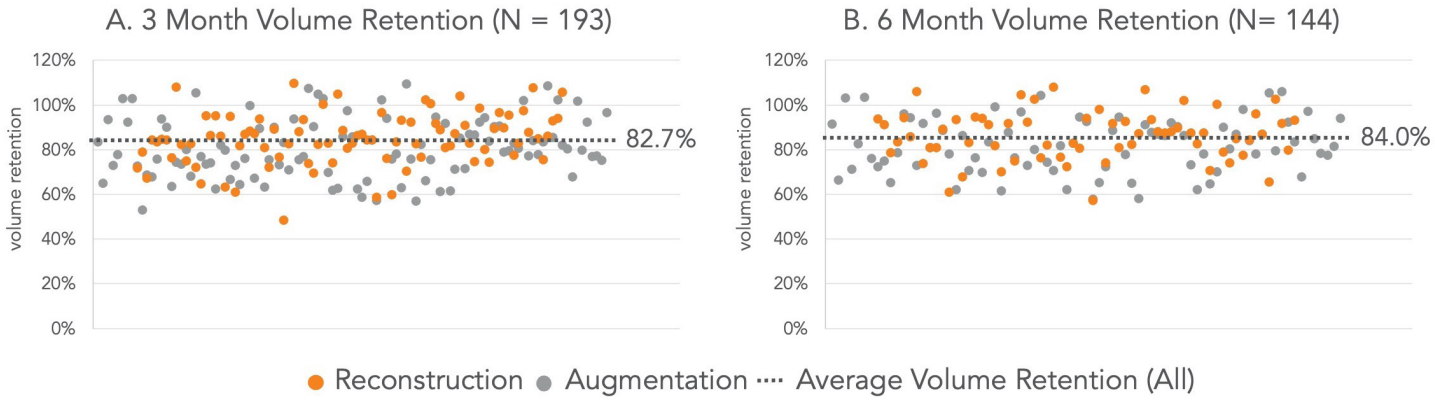

Figure 3. Volume Retention Values at 3 and 6 months.

Scatter plot for volume retentions at 3 months (A.) and 6 months (B.). Orange markers represent breasts from the reconstruction cohort while gray markers represent breasts from the augmentation cohort. The dotted line shows the average volume retention for all breasts at each timepoint.

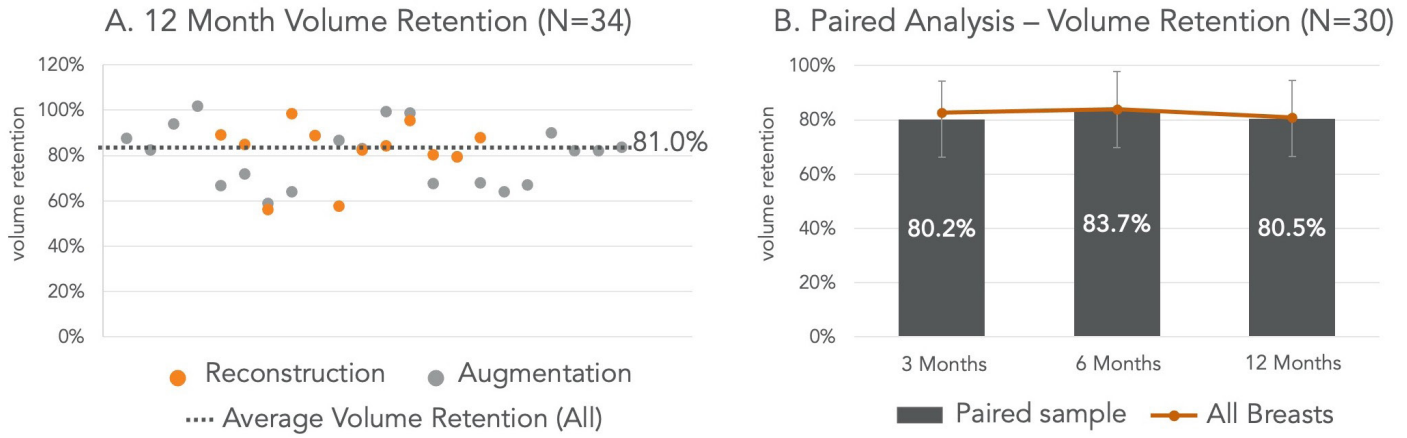

Figure 4. Volume Retention Values at 12 months and Paired Sample Analysis Over Time.

A. Scatter plot for volume retentions at 12 months. Orange markers represent breasts from the reconstruction cohort while gray markers represent breasts from the augmentation cohort. The dotted line shows the average volume retention for all breasts at 12 months. B. Paired analysis includes breasts with volume retention values at 3, 6, and 12 months (N=30), along with a volume retention reference line for all breasts included in this preliminary analysis at each timepoint (3 months: N=193, 6 months: N=144, and 12 months: N=34).

Discussion

The Viality study is the first of its kind to assess long-term volume retention after fat transfer in a controlled and systematic manner. This preliminary analysis presents robust clinical evidence from multiple investigational sites with heterogeneous patient and procedure types, and with standardized volume assessments completed by an independent central core laboratory in blinded fashion.

The preliminary results support the effectiveness of Enhanced Viability Fat Transfer with the Viality system as average volume retentions were greater than 80% for all cohorts and timepoints analyzed. The consistency of the Viality system is also evident in this analysis with data points narrowly distributed around the average retention value, which is especially remarkable as fat transfer has historically been plagued by unpredictable results. These results demonstrate a higher precision with lower variability than previously published results or meta-analysis. This predictability is further showcased in the graphical representation of volume retention over time (Figure 5), with minimal change in average volume retention between 3, 6, and 12 months.

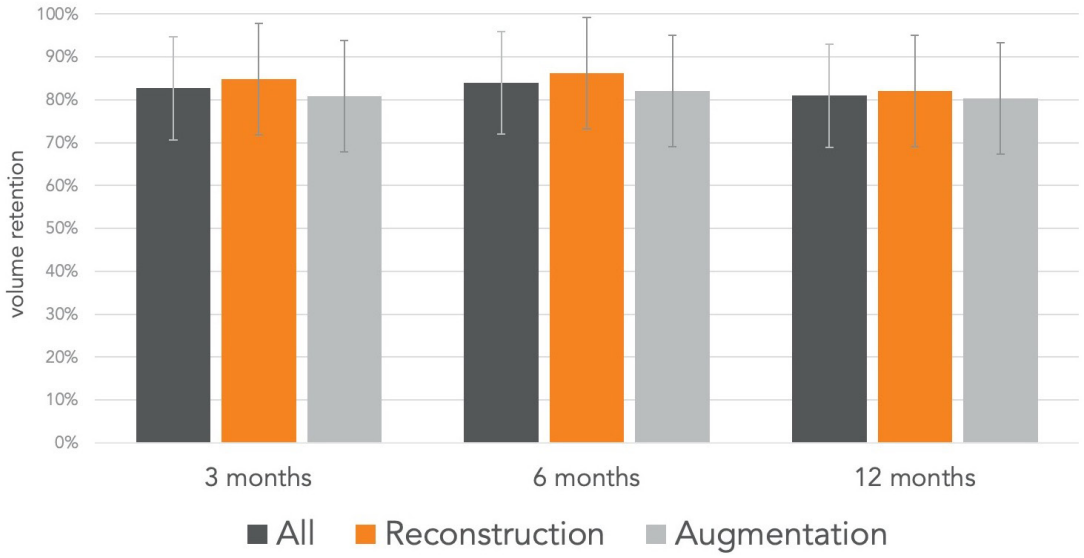

Figure 5. Summary of Volume Retention Over Time

Average volume retention percentage and standard deviation for all breasts and breasts separated by reconstruction and augmentation cohorts is graphically represented at 3, 6, and 12 months, demonstrating consistency both among and between cohorts over time.

Conclusion

As evidenced by the existing pre-clinical data, clinical data, and the preliminary results described above, Viality offers an extraordinary approach to fat transfer, providing industry-leading clinical outcomes and predictability. We anticipate the final results from this groundbreaking study will establish a new standard for evidence in fat transfer, continuing Sientra's tradition of transparency and investment in evidence-based innovation.

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Disclaimers

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

Drs. Calobrace, Medina, and Shridharani, are speakers and consultants for Sientra.

As with any surgical procedure, it is important to consult with a qualified and experienced plastic surgeon.

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