

**Combination Facial Aesthetic Treatment in Millennials
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SUNY DOWNSTATE MEDICAL CENTER

RESEARCH PROTOCOL

PROTOCOL TITLE

Combination Facial Aesthetic Treatment in Millennials

VERSION

1.0 (25 February 2020)

PRINCIPAL INVESTIGATOR

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INTRODUCTION/BACKGROUND INFORMATION

With the destigmatization of cosmetic procedures, minimally invasive procedures have become an additional cosmetic tool in the aesthetic tool-box of the modern-day millennial, defined by the Pew Research Center as individuals born between 1981 and 1996.¹ Per Allergan's 360° Aesthetics Report, "82% of millennial consumers believe injectable treatments to be socially acceptable," with a reported 52% having considered dermal fillers and 60% having considered neuromodulating agents.² Worldwide, millennials are also more likely to consider preventative treatments compared to any other age-group.² The American Academy of Plastic and Reconstructive Surgery's 2018 annual survey further demonstrates the growing demand of cosmetic procedures in this particular consumer group, citing a 24% increase in cosmetic procedures (surgery and/or injectables) in patients under 30 since 2013 (58% to 72%).³ In particular, botulinum toxin, laser hair removal, and soft tissue fillers were reported to be the most popular minimally invasive cosmetic procedures.⁴

These reported findings reveal a notable trend in young adults seeking to enhance their physical appearance via cosmetic procedures as adjunct tools to accompany non-invasive cosmetic products.²⁻⁴ The rise of minimally invasive procedures, particularly injectables, such as fillers and

neuromodulators, is likely multifactorial in nature. Owing to the affordability of cosmetic procedures relative to more invasive plastic surgery, the subtle, yet appreciable results, as well as reasonable recovery times, patients are seeking convenient procedures to achieve their intended aesthetic goals.

Injectables such as fillers and neuromodulating agents have been widely used to achieve a youthful aesthetic. While each patient has their own desired aesthetic goals, the current socially-desirable beauty trend emphasizes the accentuation of one's physical features while maintaining a natural aesthetic.³ Allergan's 360° Aesthetics Report cites the most commonly used terms to describe beauty in millennials include: soft, smooth, and natural, among others.²

Among the latest cosmetic trends in the millennial consumer group is *prejuvenation*, a portmanteau combining the words prevention and rejuvenation.⁵ Prejuvenation utilizes minimally-invasive procedures with the intention of maintaining a youthful appearance and ideally delaying visible signs of aging.⁵⁻⁶ This trend highlights the focus of millennials on early maintenance treatments to produce natural-appearing results in order to avoid or delay more invasive procedures down the line. Cosmetic injectables such as neuromodulators and dermal fillers have become the leading products utilized to achieve these results.⁴ Neuromodulating agents have been used cosmetically to reduce the appearance of dynamic rhytids and fine lines while dermal fillers have been utilized to improve volume distribution and ultimately achieve balanced facial contouring.^{7-8,11} By inhibiting muscles from contracting, neuromodulating agents decrease facial movement and in theory may be used preventatively to suspend the development of wrinkles.⁷⁻⁸ A long-term twin study seeking to evaluate the prevention of wrinkles with neuromodulating agents concluded that long-term onabotulinumtoxinA treatment can effectively prevent facial lines present at rest.⁹ This study, although limited by design, suggests that long-term treatment with neuromodulating agents can lead to the prevention of future wrinkles, providing supporting evidence for prejuvenation. An additional study demonstrated similar results with long-term treatment of glabellar rhytids with onabotulinumtoxinA, further supporting the use of neuromodulators for prejuvenation.¹⁰

Given the subjectivity of beauty standards and desired outcomes, patient satisfaction remains paramount in evaluating the success of aesthetic treatments. The HARMONY study utilized patient-reported outcomes as a primary measure for a multimodal facial aesthetic treatment in a cohort of patients aged 37-65.¹² While the HARMONY study's primary outcome measure focused on patient satisfaction of post-procedural facial appearance, several of their secondary outcome measures were reflective of their cohort being comprised of an older-age group: patient's perceived

age and reduction in facial rhytids, lines, and folds.¹² Because our study seeks to focus on the millennial population, most of whom will show little to no signs of aging, our primary outcome measure will relate to patient satisfaction with their overall facial appearance, without focusing on the reduction in visible signs of aging. A survey evaluating motivation for cosmetic surgery details low self-esteem and low self-rated attractiveness as critical contributory factors.¹³ Given that it is pertinent to evaluate for psychosocial factors in cosmetic procedures, our secondary measures will focus on patient's self-perception, self-esteem, and decision satisfaction to explore the psychosocial impact of minimally invasive cosmetic procedures in millennials.

With 63% of consumers willing to consider investing in facial aesthetics and 73% of consumers worldwide expecting to invest in aesthetic treatments in the upcoming year,² it is imperative to explore patient satisfaction and psychosocial impact of a multimodal aesthetic treatment in a millennial cohort.

AIMS & OBJECTIVES

Primary objective:

- To evaluate changes in patient's satisfaction with their appearance following a combination facial aesthetic treatment, using the FACE-Q Satisfaction with Facial Appearance Overall Scale, at 2 months after the procedure compared to baseline

Secondary objectives:

- To assess the motivating factors, concerns, and treatment preferences of millennials who seek facial aesthetic treatment
- To assess patient expectations regarding the impact of facial aesthetic treatment on their lives, using the FACE-Q Expectations Scale
- To assess changes in psychosocial factors after facial aesthetic treatment, using FACE-Q Social Function Scale and FACE-Q Psychological Function Scale
- To assess changes in self-perceived age after facial aesthetic treatment, using the FACE-Q Patient-Perceived Age Visual Analogue Scale and FACE-Q Aging Appraisal Scale
- To assess changes in patient satisfaction with their appearance after facial aesthetic treatment, using the FACE-Q Aesthetic Scales

- To assess patient satisfaction with facial aesthetic treatment, using the FACE-Q Satisfaction with Outcome Scale
- To evaluate clinician assessment of patient's aesthetic appearance using the Global Aesthetic Improvement Scale (GAIS), as completed by a blinded evaluator at 2 months after facial aesthetic treatment

HYPOTHESES

We hypothesize that a combination approach to facial aesthetic treatment in a millennial cohort will result in increased patient-reported satisfaction in multiple areas, including perception of aging concerns and quality of life.

METHODS

OVERVIEW OF THE STUDY DESIGN

This is a single-center, prospective, rater-blinded, pilot study to evaluate patient satisfaction with facial aesthetic treatment using a combination of botulinum toxin and dermal fillers. The three types of injectables are **Botox Cosmetic** (onabotulinumtoxinA), **Juvéderm Voluma XC** (hyaluronic acid gel filler), and **Juvéderm Volbella XC** (hyaluronic acid gel filler). Twenty individuals who belong to the millennial generation (i.e., born between January 1, 1981 and December 31, 1996)¹ and meet eligibility criteria will be enrolled. Study participants will receive all three injectables during a single procedure, with an optional touch-up treatment at 2 weeks. The primary endpoint is the change in satisfaction after facial aesthetic treatment, using the FACE-Q Satisfaction with Facial Appearance Overall Scale. Other outcome measures include various FACE-Q Aesthetic scales, digital skin imaging analysis, photographs, and rater-blinded clinical assessment using the Global Aesthetic Improvement Scale (GAIS).

STUDY POPULATION

INCLUSION AND EXCLUSION CRITERIA

Inclusion Criteria

- Date of birth between January 1, 1981 and December 31, 1996
- Naiveté to facial injections of botulinum toxin and dermal filler
- Desire to receive all three facial cosmetic injectables in the study
- Suitable candidate to receive facial injectables, as determined by clinician judgment
- Provision of written informed consent for all study procedures
- Stated willingness to comply with all study procedures and availability for the duration of the study

Exclusion Criteria

- Desire to receive only one or two of the facial injectables
- Dermatologic or medical conditions at the injection sites that may be exacerbated by the study procedures (e.g., severe acne, active infection, open sores or lesions, history of cold sores)
- Pre-existing cardiovascular disease (e.g., heart failure, coronary artery disease)
- Pre-existing swallowing or respiratory disorders (e.g., dysphagia, asthma, COPD)
- Peripheral motor neuropathy disease, amyotrophic lateral sclerosis, or neuromuscular junctional disorders (e.g., myasthenia gravis, Lambert-Eaton syndrome)
- Known hypersensitivity or allergies to any of the components of the administered drugs/devices in the study (e.g., Gram-positive bacterial proteins, lidocaine)
- History of anaphylaxis or multiple severe allergies
- History of a bleeding or coagulation disorder
- Pregnant or breast-feeding
- Current and/or scheduled use of the following medications: immunosuppressants, anticoagulants (e.g., warfarin, heparin, rivaroxaban), antiplatelets (e.g., clopidogrel, ticagrelor, NSAIDs), antibiotics (e.g., aminoglycosides), anticholinergics, muscle relaxants
- Procedures or treatments to the face in the past 14 days (e.g., chemical peel, laser surgery, microdermabrasion)

- Plan to undergo elective cosmetic procedure on the face (e.g., laser surgery, plastic surgery, physician-strength chemical peel) during the study
- Any medical condition(s) that could be compromised by participating in the study

SAMPLE SIZE

20

METHOD FOR SCREENING FOR ELIGIBILITY

At the in-person screening visit, the research team will screen potential study subjects by asking about demographics, medical history pertinent to the eligibility criteria, and prior and concomitant medications. On the case report form titled “Eligibility Checklist,” all inclusion criteria boxes must be marked *yes* and all exclusion criteria boxes must be marked *no* for a potential study subject to be eligible to enroll and participate in the study.

INCLUSION OF VULNERABLE POPULATIONS

Vulnerable populations will not be included in this study.

STATISTICAL CONSIDERATIONS

ANALYSIS PLAN

Statistical analyses will be performed using SAS version 9.4 statistical package (SAS Institute, Cary, NC, USA) or similar. Efficacy analyses will be conducted on the modified intent-to-treat population (mITT). Statistical analysis will be modeled after the HARMONY study.¹² The raw scores of the primary outcome measure (FACE-Q Satisfaction with Facial Appearance Scale) will be transformed by the Rasch measurement method into a 0-to-100 point scale.¹⁴⁻¹⁵ Data will be analyzed using a paired *t*-test. Secondary outcome measures will also be analyzed using paired *t*-tests. Categorical variables will be presented as proportions. Pearson χ^2 tests will be used to compare categorical variables between subgroups. A *p*-value < 0.05 is considered to be statistically significant.

Subgroup analysis will be performed on participants that have demonstrated significant improvement on outcome measures, as defined by post-treatment scores falling outside the 95% confidence intervals for baseline scores.

Adverse events (AE) will be categorized into general, product-related, or procedure-related AEs. These will be summarized by severity of reported event, timing of reported event, and percentage of participants with each reported event.

SAMPLE SIZE JUSTIFICATION

This is a pilot study that is designed to evaluate differences in satisfaction with facial appearance before and after the study intervention. No power analysis was performed to determine a target sample size.

PROCEDURES AND DATA COLLECTION

All study procedures will take place in Dr. Jared Jagdeo's Photomedicine Research Clinic, located in Suite C of University Hospital of Brooklyn, or the Clinical and Translational Science Center (CTSC) at SUNY Downstate Medical Center. All study participants must provide written informed consent before any study related procedures are performed. The study will be conducted as outlined in the schedule of assessments (Table 1).

SCREENING

At the screening visit, potential study participants will be asked to provide the following information to be recorded in the case report forms: demographics (date of birth, sex, race, ethnicity); medical history pertinent to the eligibility criteria; prior and concomitant medications. The research team will determine whether potential study participants meet the inclusion and exclusion criteria specified in the "Eligibility Checklist" case report form. Subjects who meet all of the inclusion criteria and none of the exclusion criteria will be eligible for study entry.

FACIAL AESTHETIC TREATMENT

Study participants will undergo an elective, minimally invasive cosmetic procedure involving the administration of botulinum toxin and dermal fillers. All procedures will be performed by Dr. Jared Jagdeo (principal investigator), a board-certified dermatologist and cosmetics expert.

DRUG & DEVICE DESCRIPTION

The three types of facial injectables to be used are Botox Cosmetic (onabotulinumtoxinA), Juvéderm Voluma XC (hyaluronic acid gel filler), and Juvéderm Volbella XC (hyaluronic acid gel filler). The U.S. Food and Drug Administration (FDA) classifies Juvéderm Voluma XC and Juvéderm Volbella XC as devices, and Botox Cosmetic as a drug. Botox Cosmetic is an acetylcholine release inhibitor and a neuromuscular blocking agent. Juvéderm Voluma XC and Juvéderm Volbella XC are gel implants consisting of cross-linked hyaluronic acid.

The FDA has approved these treatments for the following indications:

- Botox Cosmetic: injection into muscle to temporarily improve the appearance of frown lines between the eyebrows and crow's feet lines in adults
- Juvéderm Voluma XC: deep (subcutaneous and/or supraperiosteal) injection for cheek augmentation to correct age-related volume deficit in the mid-face in adults
- Juvéderm Volbella XC: injection into the lips for lip augmentation and for correction of perioral lines in adults

DOSAGE AND ADMINISTRATION

The products will be administered by intramuscular injection according to the manufacturer's prescribing information/package insert. The injection sites, treatment areas, and volumes/dosages of each product used will be documented in the appropriate case report form. The lot number and expiration date for each product will also be recorded.

Each participant will receive all three products using standard injection technique during a single procedure:

1. **Botox Cosmetic (onabotulinumtoxinA)**: up to 50 units in the following three anatomic regions

- a. Frontalis (forehead): up to 20 units
 - b. Lateral canthal area (crow's feet lines): up to 10 units on each side
 - c. Glabella (between eyebrows): up to 10 units
2. **Juvéderm Voluma XC**: up to 2 cc to the mid-face (cheeks)
 3. **Juvéderm Volbella XC**: up to 2 cc to the lips *and/or* perioral area, per participant preference and physician judgment

Study participants will be given the option to receive a touch-up at approximately 2 weeks after the initial procedure. At the optional 2 week touch-up visit, participants may elect to receive additional injections of any of the products, depending on their treatment preferences and the clinician's judgment.

REVERSAL AGENTS

Hyaluronidase will be available to dissolve fillers that have been placed incorrectly, excessively, or unevenly. If indicated and necessary, hyaluronidase will be injected in the affected areas according to the manufacturer's package insert.

POST-PROCEDURE INSTRUCTIONS

Study participants will be counseled on post-procedure care and precautions according to standard clinical practice following facial aesthetic injectable treatment. In addition to the verbal instructions given after the procedure, written instructions will also be provided (*Post-Procedure Instructions: Dermal Fillers and Botulinum Toxin Therapy*). A member of the research team will contact each participant the day after the procedure to assess for the occurrence of any AEs or concerns.

STORAGE AND HANDLING

All products will be stored according to the manufacturer's guidelines in a secure area with restricted access. The drug (Botox Cosmetic) will be stored in the Investigational Drug Pharmacy at University Hospital of Brooklyn and dispensed prior to each cosmetic procedure by the Research Pharmacist.

Botox Cosmetic: Botox Cosmetic is a vacuum-dried powder supplied in a single-dose 50U vial. Unopened vials of Botox Cosmetic are stored in a refrigerator 2°C to 8°C. Reconstituted Botox Cosmetic will be administered within 24 hours.

Juvéderm Voluma XC: Juvéderm Voluma XC injectable gel is supplied in individual treatment syringes with 27G ½” or 25G 1” needles for single-patient use and ready for injection. Juvéderm Voluma XC is stored at room temperature (up to 25°C/77°F).

Juvéderm Volbella XC: Juvéderm Volbella XC injectable gel is supplied in individual treatment syringes with 30G or 32G needles for single-patient use and ready for injection. Juvéderm Volbella XC is stored at room temperature (up to 25°C/77°F).

CONCOMITANT TREATMENTS

Study participants will not be allowed to undergo any elective cosmetic procedures on the face during the study, defined as the time period between the baseline visit and the final 2 month follow-up visit. Elective cosmetic procedures on the face include, but are not limited to: plastic surgery (e.g., surgical facelift or thread lift), laser surgery, physician-strength chemical peels, dermabrasion, phototherapy, neuromodulators, dermal fillers.

EFFICACY ASSESSMENTS

Efficacy assessments are conducted at baseline (prior to undergoing the facial aesthetic treatment) and at the follow-up study visits scheduled at 2 months after the procedure. Participants will be asked to attend the study visits without facial make-up or to remove any facial make-up prior to the assessments.

SATISFACTION QUESTIONNAIRES - BASELINE

At the baseline visit, participants will be asked to complete several validated questionnaires to evaluate their current level of satisfaction with various facial areas, as well as psychosocial attitudes and perceptions regarding facial aesthetic treatments. The following surveys/questionnaires will be administered prior to the procedure:

- Millennial Facial Aesthetics Survey
- FACE-Q Aging Appraisal
- FACE-Q Patient-Perceived Age VAS
- FACE-Q Expectations
- FACE-Q Satisfaction with Facial Appearance

- FACE-Q Social Function
- FACE-Q Psychological Function
- FACE-Q Appraisal of Lines: Overall
- FACE-Q Appraisal of Lines: Between Eyebrows
- FACE-Q Appraisal of Lines: Forehead
- FACE-Q Appraisal of Lines: Crow's Feet
- FACE-Q Satisfaction with Cheeks
- FACE-Q Appraisal of Lines: Lips *and/or* FACE-Q Satisfaction of Lips (depending on the area treated with filler)

SATISFACTION QUESTIONNAIRES – FOLLOW-UP

The following surveys/questionnaires will be administered at the final study visit:

- FACE-Q Aging Appraisal
- FACE-Q Patient-Perceived Age VAS
- FACE-Q Satisfaction with Facial Appearance
- FACE-Q Satisfaction with Outcome
- FACE-Q Social Function
- FACE-Q Psychological Function
- FACE-Q Appraisal of Lines: Overall
- FACE-Q Appraisal of Lines: Between Eyebrows
- FACE-Q Appraisal of Lines: Forehead
- FACE-Q Appraisal of Lines: Crow's Feet
- FACE-Q Satisfaction with Cheeks
- FACE-Q Appraisal of Lines: Lips *and/or* FACE-Q Satisfaction of Lips (depending on the area treated with filler)
- Exit Questionnaire

PHOTOGRAPHY

Standardized photographs of the face will be taken in 3 views – full frontal, left lateral, and right lateral – with a digital single-lens reflex (DSLR) camera. Additional photographs will be taken using

the VECTRA H2 3D camera (Canfield Scientific, Parsippany, NJ) and VISIA Complexion Analysis System (Canfield Scientific, Parsippany, NJ) for documentation purposes.

CLINICAL EVALUATION

A blinded evaluator will provide a score on the Global Aesthetic Improvement Scale (GAIS) to assess overall cosmetic results based on photographs obtained at the final study visit as compared to baseline.

Score	State
3	Exceptionally improved
2	Much improved
1	Improved
0	No change
-1	Worse

SAFETY AND TOLERABILITY

Throughout the study, participants will be monitored for the occurrence of AEs. Participants will be asked to document any AEs in a diary and to notify the research team of any treatment-emergent concerns. All AEs, serious AEs (SAEs), and unanticipated problems will be documented in the appropriate case report form and reported to the safety monitor and Allergan as specified in the section “Data and Safety Monitoring.”

An AE is any untoward medical occurrence in a subject administered a study intervention and which does not necessarily have a causal relationship with the study intervention. At each study visit, the subject will be assessed for the occurrence of new and ongoing AEs. Dermal safety and tolerability assessments that result in the subject requiring concomitant therapy or discontinuation from the study will be reported as an AE. The following data will be collected on all AEs and recorded on the appropriate case report form:

- Event description

- Date of onset
- Date of resolution
- Serious or non-serious
- Maximum severity: mild, moderate, or severe
- Relationship to the study intervention: not related, unlikely, potentially, probably, or definitely
- Treatment, if initiated
- Action taken with the study intervention: none, temporarily interrupted, or permanently withdrawn
- Outcome: resolved without sequelae, resolved with sequelae, resolving, or ongoing

FOLLOW-UP

Follow-up study visits occur at approximately 2 weeks (for the optional touch-up treatment) and 2 months (for the final study visit). Study participants will be contacted by telephone within 24 hours following each procedural visit to assess for the occurrence of any AEs or concerns.

At the end of the study, if a study participant is dissatisfied with the outcomes of the treatment, they will be offered a complimentary consultation visit with the principal investigator to discuss their aesthetic results and options for cosmetic treatment. Any treatments or procedures that the participant wishes to pursue will be outside of the scope of this research study. The optional 2 week touch-up visit is offered to assess the results and administer additional injections, as requested by the participant or recommended by the clinician, to achieve the desired aesthetic outcomes. No additional touch-up treatments will be administered as part of the research study. Participants who wish to receive facial cosmetic treatments or procedures following the conclusion of the study will be allowed to do so at their own expense, at the facility or provider of their choosing.

DURATION OF STUDY

Study duration is approximately 2 months from the baseline visit to the final follow-up study visit.

HUMAN RESEARCH CONSIDERATIONS

RECRUITMENT PROCEDURES

Potential study participants may be recruited through the following methods:

- IRB-approved flyers at SUNY Downstate Medical Center
- Websites: SUNY Downstate Department of Dermatology, SUNY Downstate Clinical and Translational Science Center, StudyPages.com
- Social media

Recruitment materials will be distributed or made available to the general public. Potential participants may inquire about the study by contacting the research team directly.

At the initial screening visit, the research team will explain the study, provide relevant literature and information, and answer all questions. Written informed consent will be obtained prior to any study-related procedures or interventions. We will indicate that the subjects will receive the same standard of clinical care options regardless of whether they decide to participate in the study. Subjects will be informed that participation is voluntary, allowing them to withdraw from the study at any time.

RISKS/DISCOMFORTS

The potential risks associated with participation in the research study can be categorized as follows:

Physical Risks

Procedure-related potential side effects	<ul style="list-style-type: none">• Injection site ecchymoses• Injection site discomfort• Injection site erythema• Edema
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		<ul style="list-style-type: none"> • Post-inflammatory hypopigmentation and/or hyperpigmentation
Product-related potential side effects	General	<ul style="list-style-type: none"> • Pruritus • Burning • Irritation • Erythema • Rash • Injection site induration • Injection site granuloma • Edema
	Botox Cosmetic	<ul style="list-style-type: none"> • Facial pain • Eyelid ptosis • Eyelid edema • Brow ptosis • Vision changes • Eye discomfort or irritation • Muscle weakness • Headache • Neck pain • Skin tightness
	Juvéderm Volbella XC	<ul style="list-style-type: none"> • Injection site nodules • Allergic reaction • Discoloration • Hardening of the skin • Headache • Swelling of the side of the nose • Lip numbness • Lip dryness • Mild herpes simplex virus • Moderate cold sores • Rare but serious adverse events associated with intravascular injection of soft tissue fillers in the face have been reported and include temporary or permanent vision impairment (including blindness) and

		<p>cerebral ischemia or hemorrhage.</p> <p>Intravascular injection can lead to stroke, skin necrosis, and damage to underlying facial structures.</p>
	<p>Juvéderm</p> <p>Voluma XC</p>	<ul style="list-style-type: none"> • Injection site nodules • Rare but serious adverse events associated with intravascular injection of soft tissue fillers in the face have been reported and include temporary or permanent vision impairment (including blindness) and cerebral ischemia or hemorrhage. <p>Intravascular injection can lead to stroke, skin necrosis, and damage to underlying facial structures.</p>
<p>Hyaluronidase (reversal agent)</p>		<ul style="list-style-type: none"> • Injection site reactions such as erythema (redness) and pain • Edema (swelling) • Hyaluronidase has been reported to enhance the adverse reactions associated with co-administered drug products

Social/Psychological Risks

- Dissatisfaction with outcomes of the facial aesthetic treatment
- Boredom during study visits
- Discomfort answering satisfaction questionnaires

Confidentiality Risks

- Breach of privacy (e.g., protected health information)

Economic Risks

- Loss of time and potential income by attending study visits

POTENTIAL BENEFITS

There are no direct benefits from participating in this research study. Potential benefits associated with participation in this study may include:

- Satisfaction with aesthetic results
- Improvement in self-esteem and confidence
- Improvement in quality of life

PARTICIPANT REIMBURSEMENT AND PAYMENTS

Subjects will be compensated for study participation. Up to \$150 will be given in the form of check(s) distributed by the SUNY Downstate Research Foundation. Participants will receive \$50 for the baseline visit and \$100 for the final follow-up visit, for a maximum total amount of \$150 for completing the entire study.

INFORMED CONSENT

A consent form describing the study intervention, study procedures, and risks will be given to the potential participant at the screening visit. All subjects must provide written informed consent will before any study related procedures are performed.

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Consent forms will be IRB-approved and the participant will be asked to read and review the document. The investigator will explain the research study to the participant and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. Participants will

be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the participants for their records. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the participant undergoes any study-specific procedures. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

CONFIDENTIALITY

Participant confidentiality and privacy is strictly held in trust by the investigators, key study personnel, and the research grant provider. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party.

All research activities will be conducted in as private a setting as possible. The study subject's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the IRB, SUNY Downstate institutional policies, or research grant provider requirements.

The study monitor, representatives of the IRB, or regulatory agencies may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

Study subject research data, which is for purposes of statistical analysis and scientific reporting, will be managed and protected in accordance with SUNY Downstate Medical Center Human Research Protections Program. This will not include any participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. Written individual or aggregate data from the study will be secured in a locked cabinet in a locked room. Computerized data will be stored on the HIPAA-compliant SUNY Downstate Department of Dermatology desktop computers that are connected to the SUNY Downstate Medical Center's secure network behind a firewall, complete with 128-bit data

encryption. Storage of any PHI on a laptop or portable device (e.g., external drive, flash drive, CD/DVD, USB drive or similar) will be encrypted and used only for temporary storage. In addition to being encrypted, removable storage devices will be stored in a locked cabinet or drawer when not in use.

DATA AND SAFETY MONITORING

The safety of research participants will be monitored according to standard clinical practice for outpatient cosmetic procedures involving facial injectables. The products in this study (Botox Cosmetic, Juvéderm Voluma XC, and Juvéderm Volbella XC) will be used in accordance to their FDA-approved indications. All AEs, SAEs, and unanticipated problems will be recorded in the appropriate case report forms and reported to the safety monitor (Dr. Edward Heilman) within 24 hours of the occurrence. The safety monitor is not a member of the research team and has no relevant conflicts of interest.

The research team will reported to Allergan Medical Affairs all SAEs within 24 hours after its first knowledge of the SAE in accordance with the SAE Report Form by emailing aus-psreporting@allergan.com or DL-AUS-PS1stLine@allergan.com and calling 1-800-678-1605. The SAE Report Form shall include an assessment of the causal relationship between the Allergan products and the SAE.

DISCONTINUATION OF RESEARCH PARTICIPANTS/WITHDRAWAL

Participation in the study is voluntary. A subject has the right to withdraw from the study at any time for any reason, without prejudice, and is under no obligation to disclose the reason.

The research team may consider discontinuing a subject from the study for the following reasons:

- Major protocol violation or deviation (e.g., significant non-compliance with the study procedures)
- Any clinical AE or other medical condition or situation occurs such that continued participation in the study would not be in the subject's best interest
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation
- Unforeseen serious AE occurs

The reason for a subject's discontinuation or withdrawal from the study will be recorded on the appropriate case report form, if applicable.

AEs, SAEs, and unanticipated problems will be monitored, and the trial will be halted early if necessary, to protect subjects. Any life-threatening events and/or deaths attributable to the study protocol will result in halting the study.

RECORD RETENTION

Study documents will be securely maintained to protect confidentiality and privacy in accordance with SUNY Downstate policies. According to the minimum retention periods required by Downstate, research records collected by investigators will be maintained for at least three years, and up to 10 years as practicable, after completion of the research. Study participants' signed HIPAA Research Authorization forms will be kept for a minimum of six years after such authorization last was in effect. Research records will not be destroyed unless in conformity with Downstate policies and requirements of the research grant provider.

CONFLICT OF INTEREST

The principal investigator has no relevant conflicts of interest to disclose.

REPORTABLE EVENTS

As required by Policy IRB-01, all reportable events will be reported to the IRB within the specified deadlines. Additional information is provided in the IRB Guidance on "Reportable Events." Events are defined in the IRB Guidance on "Acronyms and Definitions." For additional information see: <http://research.downstate.edu/irb/irb-policies.html>

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TABLE 1. SCHEDULE OF ASSESSMENTS

	Screening[†]	Baseline Visit[†] (Procedure)	2 Week Touch-Up Visit (optional)	2 Month Follow-Up Visit (End of Study)
Informed consent	X			
Inclusion/exclusion	X			
Demographics	X			
Medical history	X			
Concomitant medications	X	X	X	X
Facial aesthetic treatment		X	X	
Photography		X	X	X
Clinical evaluation		X		X
Satisfaction questionnaires		X		X
Safety and tolerability		X	X	X
Adverse events		X	X	X
Exit survey				X

[†] The screening visit and the baseline visit may occur on the same day, depending on the preferences of the participant and scheduling considerations by the research team.