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**Bioelectrical Stimulation for Breast Augmentation:
A Prospective Pilot Study**

Introduction:

Breast augmentation is the most common cosmetic surgical procedure in the United States, with nearly 300,000 procedures performed annually (1). The problem of small breast size may be due to several factors including hereditary, due to weight loss, post-partum, or due to lean body habitus. Most women interested in breast augmentation are seeking improvement in self-image and self-confidence (2).

The surgical approach has a number of limitations including the need for at least one surgical procedure under general anesthesia, and has a significant incidence of local complications, and a relatively high rate of reoperation. The most common overall indication for reoperation is capsular contracture (3).

The use of micro-current Bioelectric Stimulation (BES) is a new science-based, and non-invasive approach that involves the use of precise micro-current signals delivered to the skin of the breast via two electrodes placed on the surface of the skin and connected to a stimulator. The micro-current delivered is totally painless and generates an increase the local tissue expression of a number of specific pro-regenerative proteins or substances that are normally present in the breast tissue, that can stimulate native tissue, specifically the glandular tissue. This stimulation works by attracting stem cells, enhancing blood flow, and helping to enhance normal tissue growth as well as collagen for tissue support.

The benefit of this non-invasive approach was demonstrated in an animal study in sheep which demonstrated a 30% increase in breast size after every other day stimulation for one hour for only one month. Ultrasound examination of the treated breast was interpreted as showing normal tissue appearance, with size increase due primarily to increased normal glandular

tissue, with no changes found in the non-stimulated breast. There were no signs of discomfort in the animal during stimulation, who often slept through treatments.

A second study has been conducted in three different species of cows to assess a possible increase in milk production using BES to two teats on one side of the cow utter. These studies showed an average of 15% increase in milk production after two weeks of daily stimulation of the cow utter for 40 minutes/day. These animals also did not exhibit any signs of discomfort during stimulation. Clinical examination of the teats revealed no evidence of inflammation or irritation. Ultrasound examination also showed an increase in glandular tissue as the presumed mechanism of increased milk production, and histologic examination of the utter showed no signs of inflammation or pathologic changes.

Importantly, the increase in milk production persisted for two months after the stimulation was discontinued, suggesting sustained effect on breast enlargement.

The stimulators to be used are the Mettler model 740, and the Ventura Axion, which both have FDA approval for use to improve blood flow. The stimulators reach different local tissue proteins and will be used on an alternate basis at each treatment session. The stimulator will be connected to surface patch electrodes placed on either side of each breast. The stimulator will be initiated at the lowest current and increased to the individual patient's level of comfort, which will be used for each treatment.

The safety of this treatment was previously evaluated by ultrasound before and after the end of treatment in the initial pilot study in 10 women treated for 8 weeks. The study demonstrated no changes before and after treatment, and no reports of any adverse events or side effects, including no pain.

Study Duration: 8 weeks

Treatment Frequency: 4 x's/ week

Treatment Duration: 60 mins/treatment

Treatment Locations:

All treatments will take place in a clinic conducting this Registry Pilot study, under the supervision of the lead Site Investigator or their designated staff trained in operation of the stimulator

Objectives:

To evaluate the effectiveness of BES to safely achieve breast augmentation.

Primary End Point: Increase in breast size

Secondary End Point: Incidence of any adverse effects related to the treatment

Assessment Methods:

1. Direct measurement of breast size by tape measure by the Principal Investigator or designated staff at each site conducting the Registry.
2. De-identified frontal and lateral photos of each breast with face not included, taken before and after treatment from a uniform distance which will be graded by a breast surgeon not involved with the study.
3. Validated questionnaire using the Rosenberg Self-Esteem Scale, Body Dysmorphic Disorder Examination —Self Report (modified so that each item specifically assesses breast size dissatisfaction).
4. <https://www.herroom.com/bra-fitting-center,954,30.html>
5. Each of the first 10 subjects will have an ultrasound done of each breast before and after the full 8 weeks of treatment to confirm the safety of the treatment.

Inclusion criteria:

1. Age: 21-50 yrs, female
2. Agree to be present for each of the treatments outlined in the protocol.
3. Agree to have completely de-identified measurements and photos taken of both breasts before and after treatment, and at 3 month follow up to assess benefit.
4. Good general health and taking no medications for a chronic disease
5. Non-smoker for past month
6. Agree to use an approved form of birth control throughout the treatment period.

Exclusion criteria:

1. Subjects who are pregnant, nursing, planning to become pregnant, and/or not using a reliable form of birth control.
2. Subjects who have had prior breast surgery or any therapy for breast augmentation.
3. History of breast cancer and treatment with radiation and/or surgery.
4. Renal replacement therapy
5. Patients who have implantable pacemaker, automatic implantable defibrillator (AICD), or any other implantable electric device.

Study Duration: 8 weeks

Treatment Frequency: every other day or 4 x's/ week

Treatment Duration: 60 mins/treatment

Treatment Location:

All treatments will only take place in a clinic conducting this Registry Pilot study, under the supervision of the lead Site Investigator or their designated staff trained in operation of the stimulator.

Enrollment Criteria:

All patients who meet all of the Inclusion and none of the Exclusion criteria and sign the Informed Consent will be enrolled in the study.

PROTOCOL:**Pre-treatment Questionnaire:**

Each patient will complete a questionnaire at baseline before treatment to assess the reason for seeking breast enlargement and any underlying health issues that might impact the response to this treatment, as well as at the end of the study and again at the follow up examination at 3 months to see how long the benefit lasts without ongoing treatment.

Pre-Treatment Ultrasound of the Breast:

Each of the first 10 enrolled subjects will have a baseline ultrasound to confirm the absence of any abnormal tissue in both breasts, which will be repeated at the completion of the study.

Electrode Placement:

Two adhesive hydrogel patch electrodes, which will be provided by the sponsor, will be applied to both sides of each breast (4 total), and then connected to the stimulator provided by the sponsor, either Mettler or Ventura Axion. The stimulator used will be alternated at each treatment.

Stimulators to be used: The 510 K Mettler stimulator model 740 and the Ventura Axion stimulator, both of which have been approved by the FDA (510K), will be alternated between each treatment to take advantage of the different pro-regenerative signals reached by each stimulator. The patient and clinic will maintain a record of the type of stimulator used with each treatment to assure accuracy of this rotation for the 8 weeks of treatment.

Screening Stimulator Evaluation:

Each woman will have a screening pre-treatment test of their pain sensitivity to BES. The patient will have surface electrodes applied as will be used during the study, and the micro-current strength of each stimulator will be tested separately for 15 minutes each. The current of the stimulator will be increased to a level identified by the patient as their preferred level of comfort before starting the study. This current will be the one used for that patient for each stimulator for each treatment during the study. Patients who are unable to tolerate the minimum current strength with either stimulator will not be included in the study.

Signals to be used in the Stimulation protocol:

Each stimulator will deliver a series of very precise signals targeted to increase the local expression or quantity of specific proteins (genes) present in the breast, that have been shown to have significant pro-regenerative effects. The series of signals will be delivered sequentially for a total of 60 minutes, with a period of 5-15 minutes duration for each signal to be used. These signals are collectively designed to stimulate stem cell recruitment to the breast, increase blood supply, and improve tissue turgor and collagen content leading to breast enlargement.

Protocol:

Each subject will have the surface electrodes applied to either side of the breast inside their own bra to be worn during the entire treatment period. The two sets of electrodes will then be connected to one of the stimulators to be used on an alternate treatment basis. The current will be turned on the increased to the level selected by each patient during the screening test for each stimulator and continue for the 60 minute treatment. The subject may remain quiet or engage in any activity that will not risk loss of the adhesion of the electrodes to the breast. The specific stimulator to be used will be alternated after each treatment.

Adverse Events:

Patients will have direct assessment of any possible adverse effects of the bioelectric stimulation at each of the treatment sessions to include pain in any area of the breast including nipples, skin irritation over the breast, or at the site of the stimulation electrodes, lactation or drainage from the nipple, or any constitutional symptoms.

Stopping Rules:

Each patient may elect to stop any treatment session at any time for discomfort or other adverse symptoms, or elect to withdraw from the study at any time. The study will be paused if three subjects report adverse symptoms sufficient to request to stop the treatment, and will be resumed only when an assessment of potential cause of the symptom has been made and an action plan implemented.

De-identified Photographs:

Each patient will sign a consent form in advance of starting treatment to grant permission of a photo taken from a frontal and side view of each breast at both the start and end of treatment. Each consented patient will then be assigned a study enrollment number which will be the only identification ever used to report the results of the photos obtained.

Data Analysis:

All pre and post treatment de-identified photos will be reviewed by an experienced breast surgeon not involved in the study. Results will be collated and reported as average enlargement as well as median and range change. The outcome will be assessed on both individual results, and the average percentage enlargement of all patients treated.

Data Release: Each enrolled subject will sign a release acknowledging their permission to have the collated data and potential individual de-identified

breast images used for potential scientific publication or investor presentation.

QUESTIONNAIRE: Rosenberg's Self-Esteem Scale

	STATEMENT	Strongly Agree	Agree	Disagree	Strongly Disagree
1.	I feel that I am a person of worth, at least on an equal plane with others.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2.	I feel that I have a number of good qualities..	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3.	All in all, I am inclined to feel that I am a failure.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4.	I am able to do things as well as most other people.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5.	I feel I do not have much to be proud of.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
6.	I take a positive attitude toward myself.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7.	On the whole, I am satisfied with myself.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8.	I wish I could have more respect for myself.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9.	I certainly feel useless at times.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10.	At times I think I am no good at all.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Your score on the Rosenberg self-esteem scale is: .

Scores are calculated as follows:

- For items 1, 2, 4, 6, and 7

Strongly agree = 3

Agree = 2

Disagree = 1

Strongly disagree = 0

For items 3, 5, and 8

Strongly agree = 0

Agree = 1

Disagree = 2

Strongly disagree = 3

The scale ranges from 0-30. Scores between 15 and 25 are within normal range; scores below 15 suggest low self-esteem.

Patient Satisfaction Survey:

My satisfaction with the amount of breast enlargement I have gained following this treatment is:

Very Satisfied: _____

Satisfied: _____

Not Satisfied: _____

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BIOELECTRIC STIMULATION

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