Efficacy of Low-Frequency, High-Intensity Ultrasound for Reduction in Subdermal Adipose Layers

Device Investigated: Ultimate Contour Body Sculpting Device

Indication Studied: Application of ultrasound for non-invasive waist circumference reduction.

A randomized, blinded comparison of waist circumference reduction of an active test group vs. a placebo control in adults.

Sponsor: CAO Group, Inc. Protocol ID: 005-00036-3
Development Phase: Performance Validation

Initiation Date: 3 November 2017 Completion Date: 13 November 2017

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SYNOPSIS

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Study Title: Efficacy of Low-Frequency, High-Intensity Ultrasound for Reduction in Subdermal Adipose Layers
Investigator: Thomas L. Sutton, MD (no affiliation with the Sponsor), John O. Meadors
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Objectives
The purpose of this study wass to evaluate principally the effectiveness, and secondarily the safety, of external application of lower frequency ultrasound to the waist/abdominal region of adults to achieve a reduction of adipose cells/tissues in the subcutaneous region. The application of higher frequency (200kHz to 3MHz) ultrasound for this purpose has previously been demonstrated and such devices have received clearance for treatment in the United States. The question remained whether application of ultrasound at a lower frequency (35kHz to 45kHz) could achieve comparable results without introducing any new or elevated risks to the patient. This study sought to answer this question.

Methodology
Samples of the test device (Ultimate Contour Mini by CAO Group, West Jordan, Utah, U.S.A.) were provided for the test. The devices consist of a touch screen interface whereby the operator may select the intensity of the delivered energy and the duration of treatment. The device features a single output cable to which is attached the ultrasound handpiece assembly. For the purposes of this test, the duration of treatment was set at 30 minutes, and the intensity set at Level 4 (the maximum the device is capable of).

Application of the ultrasound energy consists of applying a treatment gel or liquid to the patient's skin (to eliminate air gaps between the applicator and the skin) and gently kneading the skin in circular motions, slowly progressing across the surface of the treatment area, making methodical passes until the entire treatment area has been exposed, then returning to the origin point and repeating this application approach.

Eligible patients were randomly assigned to either a test group or a placebo control group. For those assigned to the test group, the application of the overall treatment as just described was performed. For those assigned to the control group, the device setting and application method as described above were employed. The only difference in treatment was that the device's energy emissions were not activated, thus no energy output occurred from the handpiece. The application time, contact treatment approach, and all other aspects of the application and treatment sessions were consistent with the those of the test group.

Following treatment, the patient was asked regarding the extent of discomfort experienced during the ultrasound application, and assessment was made by a blinded, independent evaluator whether a number of visible skin conditions are observed or experienced by the patient.

Prior to the first treatment, the patient's weight and height were measured by the blinded, independent evaluator, and the patient's waist circumference measured using a constant-tension flexible tape

measure. At the prior to and at the conclusion of each treatment session, the patient's waist circumference was measured. Each patient was treated a total of three (3) times, with a gap of 2-4 days between each treatment. Prior to each treatment, the patient was weighed. At 2-4 days after the final treatment, the patient was given a final assessment of weight and another circumference measurement made of the patient.

Inclusion/Exclusion Criteria

Inclusion in the study consists of the following criteria:

- Age equal to or above 18.
- Body Mass Index ≥ 20.

Exclusion from the study consists of the following criteria:

- Age equal to or below 17.
- Body Mass Index < 20.
- Open sores, wounds, or otherwise compromised skin in the treatment area
- Known or suspected pregnancy, or active nursing.
- General systemic conditions of arteriosclerosis or hypertension.
- Existing bacterial or viral infections (influenza, rhinovirus, hepatits, pneumonia, tuberculosis, and the like)
- Presence of acne vulgaris, herpes zoster, psoriasis vulgaris, or similar skin conditions in the treatment area.
- Implanted active medical device anywhere in the subject, or metallic or polymeric implants in the vicinity of the treatment area.
- Failure to complete the study as outlined.

Statistical Methods

Single factor ANOVA analysis was used to determine if the extent of circumference reduction in the test group is statistically significant over changes in the control group. Additional correlation assessment was performed to identify any potential relationships between patient data sets, and single-factor ANOVA assessment applied to those correlations as applicable.

Recruitment

Recruiting consisted of a minimum of 60 patients, with a target of at least 40 patients completing the study (20 each in the test and placebo groups). Should patients drop out of the protocol such that 20 test patients and 20 placebo patients are not achieved at the end of the study, additional patients shall be recruited to achieve the target number.

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LIST OF ABBREVIATIONS AND TERMS

BMI - Body Mass Index: A calculation incorporating a patient's height and weight to provide a comparative value on the extent of obesity of the patient.

RF - Radio Frequency. In the context of this device, this is radio frequency emissions intended by the product. This feature of the device will not be included in this study.

US - Ultrasound

INVESTIGATORS AND ENVIRONMENT OF TREATMENT

All testing conducted under this investigation was performed at a single site, a private residence located in Highland, Utah. This setting is representative of the medical office environment under which the device would be used in the market. Consistent with this setting, patients were scheduled for treatment and upon arrival have the procedure performed, along with appropriate pre-treatment and post-treatment assessment and instructions, and then allowed to depart. The principal investigator for this study was Dr. Thomas L. Sutton, MD. Dr. Sutton has no contractual or financial relationship with the sponsor or with the specification developer. A secondary researcher, John O. Meadors (a former Doctor of Chiropractic), assisted with the performance of this study. Mr. Meadors does have a relationship with the sponsor in that he is the specification developer for this product. Assessment and measurements activities were conducted in a separate room from where the treatment took place.

INTRODUCTION

The purpose of this study was to evaluate principally the effectiveness, and secondarily the safety, of external application of lower frequency ultrasound to the waist/abdominal region of overweight adults to achieve a reduction of adipose cells/tissues in the subcutaneous region. The application of higher frequency (200kHz to 3MHz) ultrasound for this purpose has been previously demonstrated and such devices have received clearance for treatment. The question remains whether application of ultrasound at a lower frequency (35kHz to 45kHz) can achieve comparable results without introducing any new or elevated risks to the patient. This study sought to answer this question. Some studies have been published that touch on this question to some extent, but these studies do not take into account variables such as instructions for use, or the operation of a device at the intensity levels designed into the Ultimate Contour device.[1-5]

The proposed clinical mechanism of operation for this device is as follows: High intensity ultrasound energy is applied externally to the outside skin surface. A sonically conductive medium such as an ultrasound-conducting gel or fluid is applied to the skin surface to help avoid air pockets or gaps between the transducer surface and the skin. The ultrasound energy passes through the skin and into the subcutaneous adipose layer, where sonic cavitation occurs. This cavitation disrupts and ruptures cell membranes of the adipose cells. The liberated contents of the adipose cells are then cleared away naturally via the lymphatic system. It should be noted that the purpose of this study is not to verify this mechanism of action, but to validate overall results via assessment of factors that may occur as a result of this theory.

The device in question, presently branded as the Ultimate Contour Mini, is at the stage of development where functional demonstration devices have been constructed and assembled. The design at present is representative of the final released configuration to the extent that third-party safety testing and certification has been conducted on the device and the device demonstrated to be safe relative to the design and constructional requirements of IEC 60601-1 (3rd Edition) for safety of electrical and electronic medical devices and systems, as well as IEC 60601-1-2 (3rd Edition) for electromagnetic compliance safety and performance of electrical and electronic medical devices and systems.

The study has a fixed endpoint of three (3) treatment sessions per patient, with an additional subsequent follow-up visit, to the extent that a sufficient quantity of patients have completed the study. Given that a minimum of two days gap is proscribed between treatments, and the follow-up visit to occur a minimum of two days after the final treatment, and with the scheduling of patients staggered to best utilize investigator and equipment resources, the overall course of the study is not expected to exceed 2 weeks of total study time. Once patient treatments was completed, analysis of the data was performed by the sponsor to determine the extent of success in achieving the primary and secondary objectives.

STUDY OBJECTIVES

PRIMARY - The primary objective of this study was to determine if the application of lower frequency (35kHz to 45kHz) ultrasound energy to the waist/abdominal region of the human body is capable of effecting a reduction in the amount of subcutaneous adipose cells and/or tissue to a statistically significant level. Determination of the reduction in this adipose tissue is achieved via measurement of the body circumference that includes the abdominal area that was treated, and comparing measurements prior to the initial treatment with measurements after the entire treatment regime is concluded.

SECONDARY - The secondary objective of this study was to assess the safety of this device. Assessment was made by having the patient rate the treatment experience and report any symptoms, side effects, or associated abnormal conditions. Additional assessment was made by a blinded investigator to qualitatively confirm if visually detectable abnormal conditions (example: edema) were presented following the treatment. Success was determined by whether the patients indicated any discomfort experienced during the treatment, and following the treatment, that are directly attributable to the treatment, along with an absence of side-effects or abnormal conditions directly attributable to the treatment, creating a risk/benefit condition where the benefit of treatment is regarded to outweigh the risks and temporary discomfort. Quantitatively, the benefit was regarded to outweigh the risk when: 1) No patients report a pain rating of 4 or higher on the Stanford Pain Scale, 2) No patients exhibit any side effects or abnormal conditions at the post-treatment follow-up, and 3) No patient who was included in the Test group reports that the treatment regimen was unsuccessful.

INVESTIGATIONAL PLAN

Device description and settings

The Ultimate Contour device is a portable device that consists of a single central unit which houses all of the device electronics. The device features a fold up touchscreen that shows the device's operating condition and allows the operator to select the device's functional parameters. A single external, detachable power cord connects the device to an ordinary electrical outlet. The device contains an internal power supply that is auto switching to the input voltage and input frequency (100-240VAC, 50-60Hz). The device include a single, permanently attached output cable. The operator attaches the ultrasound treatment handpiece to the end of the output cable. The device is designed to allow application of RF energy via separate specifically designed handpieces, but the application of RF energy is not within the scope of this study. The device is capable of sensing if a handpiece is attached and to identify which handpiece is attached, in order to prevent any inappropriate power from reaching the handpiece or prevent the device from being configured in an inappropriate manner.

After attachment of the handpiece, the operator selects which treatment type (US or RF) is to be done. The device then presents only two parameters for operator to adjust: the duration of the treatment, and the relative intensity of the applied energy. The duration can be selected from 10, 20, 30, or 40 minutes duration. The intensity is selected from a comparative rating Level of "1, 2, 3, or 4", with Level 4 being the maximum energy level the device can output and Levels 1 through 3 being at staggered levels less than the maximum. Once the settings are selected, the operator places the device into a Ready state. At this point, the handpiece is placed in contact with the skin and the operator presses a button on the screen to Activate the handpiece. The unit applies energy to the handpiece at the selected intensity Level and the unit begins to count down from the selected time duration. Generally, the operator allows the device to operate until the selected time elapses, at which point the device automatically returns to the Ready state and beeps to inform the operator the cycle is complete. The operator may also stop the treatment at any time, either by pressing the stop button on the screen or activating a separate emergency stop button located on the device. During treatment, the device monitors the temperature of the handpiece (and by contact, the temperature of the skin) via temperature sensors located in the handpiece and in direct contact with external metal surfaces of the handpiece that contact the skin. If excessive temperature is measured, the device halts operation of the handpiece.

For the purposes of this study, the device will be set at a treatment time of 30 minutes and an intensity level of 4. For patients in the control group, the device will be set at these same levels, however the clinician will not activate the handpiece. The clinician will manually keep track of the elapsed time (watch the clock) to ensure that 30 minutes of application of the handpiece occurs.

Adjunctive activities associated with the treatment will also be performed. These included conversation with the patient about what to expect during the individual treatments and overall outcomes of the entire regimen, as well as instructions to the patient regarding care and proper lifestyle habits both immediately after the treatment as well as in-between sessions. All of these adjunctive activities are described in the operator's manual for the device, and the clinicians will be instructed on the presence of these consultative activities in the manual and the execution of these activities for the purposes of this study.

Patient population

The population for this study consisted of adults age 18 and over. Recruiting efforts focused on obtaining a reasonably even number of male and female patients, obtaining some representation from different ethnicities or skin types, and to include patients exhibiting a body mass index (BMI) of 20 or

higher. Patients were evaluated relative to the inclusion and exclusion criteria indicated below. A recruitment target of a total of 60 patients was established, with an even assignment of patients to either the Test group or the Control group, such that basically there were the same number of participants in each group. During recruitment, each candidate was assigned a test subject number for identification purposes.

Level of blinding, discussion on application and control of blinding
Blinding occurred at the patient level, where the patient was not made aware of their assignment to either the Test or the Control groups. Once the recruitment activity was finished, eligible recruits were listed only by patient ID number and by gender. The listed patients were then randomly assigned to either the Test or Control group, with the only constraint that the number of patients were reasonably evenly distributed between the two groups.

During the patient visit, only the treating clinician was provided with information as to which group the patient is assigned. The assessing clinician was blinded for the purposes of this study. The assessing clinician was provided with a patient treatment record that indicated only the patient's identification number. The assessing clinician was not informed regarding which group the patient is assigned to. The patient was not shown the treatment record or otherwise informed at any time which group they are assigned to. The assessment clinician performed the same pre and post-treatment assessments and measurements regardless of which group the patient was assigned. As discussed previously, the device handpiece was not activated for those patients assigned to the Control group, while for those in the Test group the handpiece was activated. Post-treatment instructions to the patient were provided and were identical, regardless of the group. These instructions consisted of having the patient maintain their existing lifestyle of eating, physical activity, and so forth without any special adjustment due to participation in this study.

Only one patient was permitted in the treatment area at a time, to prevent an occurrence where a Test patient and a Control patient may be treated simultaneously and whether through observation or discussion discover that one or the other is in the Test or Control group. The clinicians did not exchange information between themselves in order to maintain blinding. Records of treatment were transmitted directly to the sponsor for data analysis.

Kind of control (placebo concurrent)
The Control group for this study consisted of randomly assigned patients who are administered a placebo or sham treatment. This approach was taken to help reduce subconscious or psychological influences that may skew the resultant data. By proceeding with the treatment regimen, observing the device set up, and experiencing the application of the device handpiece (although not electrically activated), this approach was believed to equally incorporate any sort of psychological contributions that may exist relative to undergoing this treatment and thus demonstrate the true contribution that the device in and of itself is providing. Patients in the control group were scheduled and treated concurrently with those of the Test group, although only one patient was permitted in the treatment area at a given time.

Study configuration (parallel, cross-over, etc.)
This study was designed as a parallel (non cross-over) study. Once a patient was assigned to a group, that patient was subject only and exclusively to the conditions of that group. This approach was taken primarily in that if a cross-over study were to be undertaken, those patients who first were subjected to the Test treatment would immediately determine that the second round of treatment was the Control

treatment, this knowledge could skew the overall results. Further, a cross-over study could obscure the contribution and impact of the actual treatment, particularly the lasting effects as determined in the follow-up visit.

Method of assignment

Once recruitment was completed, eligible patients were listed on a spreadsheet only by patient ID number. Each patient was identified with a number supplied by a random number generator. The patients were sorted according to the random number, and half were assigned to the Test group while the other half were assigned to the Control group. In this process, all other patient information (particularly the age and body mass index) will not be visible to those performing the assignment, to further ensure that no subconscious bias is made to assign to the Test group those individuals who may be more susceptible to a dramatic or statistically significant outcome.

Sequence and duration of study period

Patients were scheduled according to each one's availability for the first of three treatment sessions, without regard to which study group (Test or Control) the patients belonged to. After each particular treatment, the patient was scheduled for the next visit, with it being preferred that subsequent treatments occurring no sooner than 2 days into the future of the present treatment, and the post-treatment follow-up occurring no sooner than 2 days into the future of the last treatment session. Each patient received 3 treatment sessions, with each session featuring the same device settings and conditions of application relative to which study group the patient is assigned to.

Measurement tools and methods

CIRCUMEFERENCE

The patient's circumference was measured via use of a Gulick II (Model: 67020) tape measure with a constant-tension feature that is factory-calibrated by the manufacturer. The process of obtaining a measurement proceeds as follows:

1. The area of the body is exposed (in this case lifting up the shirt to expose the abdominal region).
2. The patient is informed to stand straight and to breathe normally, but to focus on steady shallow breaths.
3. The clinician applies the tape measure by locating the top of the hip bone (iliac crest) and positioning the tape just above this bony landmark, just where one finger can fit between the iliac crest and the lowest rib.
4. The clinician ensures that the tape measure is positioned horizontally, parallel to the floor.
5. Measurement is taken at the end of normal expiration.
6. At a signal from the clinician the patient is to pause at the conclusion of an exhale, at which point the clinician pulls the tape until the constant-tension feature is enabled. The clinician then observes the measurement value and documents this value in the treatment record.

Inclusion/Exclusion with discussion of rationale; address both sexes and race allowance vs. availability

Inclusion in the study consisted of the following criteria:

- Age equal to or above 18.
- Body Mass Index ≥ 20.

Exclusion from the study consisted of the following criteria:

- Age equal to or below 17.
- Body Mass Index < 20.
- Open sores, wounds, or otherwise compromised skin in the treatment area
- Known or suspected pregnancy, or active nursing.
- General systemic conditions of arteriosclerosis or hypertension.
- Existing bacterial or viral infections (influenza, rhinovirus, hepatits, pneumonia, tuberculosis, and the like)
- Presence of acne vulgaris, herpes zoster, psoriasis vulgaris, or similar skin conditions in the treatment area.
- Implanted active medical device anywhere in the subject, or metallic or polymeric implants in the vicinity of the treatment area.
- Failure to complete the study as outlined.

The primary rationale for the exclusion criteria that were identified is to ensure that any existing health conditions that may be adversely impacted by the use of this device are not aggravated or made worse. Additionally, exclusion of women who are pregnant or nursing is viewed as an appropriate precaution to prevent any possible complications to the fetus or nursing child that cannot presently be anticipated. A secondary rationale for these exclusions is that the conditions and situations listed in the exclusions may contribute to a change in weight, skin condition, or the patient's response to the ultrasound energy which may obscure the resultant data and make it more difficult to objectively assess if the study objectives have been met. The exclusion of persons age 17 and under primarily is a matter of responsible consent and the prospective patient being capable of making an informed and rationale decision regarding the possible risks and benefits of the treatment, as well as being in a legally permissible status to elect a medical procedure on their own behalf.

The study was conducted at a private residence location in Highland, Utah, U.S.A. with recruiting efforts being made in the immediate vicinity of this location. The ethnic demographics of this location are overwhelmingly Caucasian, and thus a reasonable cross-section of all major ethnicities was not reasonably expected. Recruit of ethnicities other than Caucasian was encouraged, but no thresholds or limits were enforced.

During selection, the patient's gender, age, height, and ethnicity were documented.

Details of the treatment
At the appointed date and time, the patient was admitted to the assessment area.
Prior to the Treatment:

- The date of the treatment and the time of arrival was documented in the treatment session record. The time that the patient last ate a meal was also documented.
- Prior to Treatment #1 only, the patient was provided with and asked to sign the informed consent, and provided with information regarding the treatment and the risks and benefits associated with the treatment.
- The patient had their waist circumference and weight measured and documented, with these measurements being made by the blinded assessment clinician.
- Prior to Treatments 2 and at the Follow-Up visit, the patient was asked about any abnormal body functions or observations that may be relevant to the treatment. If any are indicated, these will be documented.
- The patient was moved to the treatment area.

- The treatment clinician prepared the patient for treatment by displacing clothing from the treatment area.
- The patient was asked to lie down on their back on the treatment table.
- The treatment clinician turned on the Ultimate Contour Mini device and set it to the indicated parameters for this study.
- The treatment oil/fluid was applied to the patient's skin over the area intended for exposure.

Application of the Treatment:

- The treatment clinician applied the treatment handpiece to the patient's skin in the intended treatment area.
- The clinician measured the surface skin temperature for monitoring purposes only within the abdominal region using a Ryobi Laser Model GS17054d129357 thermometer. This was documented in the treatment session record.
- **Test Group Only -** The treatment clinician pressed the Activation button on the Ultimate Contour screen to begin energy emissions from the handpiece.
- **Control Group Only -** The treatment clinician pressed a spot on the Ultimate Contour screen adjacent to the Activation button to give the illusion the device was activated, but ensured that energy emissions from the handpiece were not occurring. This is confirmed by the device remaining in the Ready state, the Stop button not present on the screen, and the Timer is not counting down.
- The treatment clinician moved the handpiece along the skin with slight pressure to maintain contact, moving in a circular motion and progressively advancing in a linear direction from one edge of the treatment zone to the other in an overall back-and-forth approach.
- At the 10 minute and 20 minute marks, the treatment clinician again measured the skin temperature at approximately the same location as previously and documented this in the treatment session record.
- The treatment clinician continued application of the handpiece until either the proscribed 30 minutes had expired, or the patient indicated to halt the treatment due to discomfort.
- Once energy emissions ceased, the handpiece was removed from the skin, and a final temperature measurement made.
- The clinician the cleaned off the treatment oil/gel.
- The patient replaced clothing and moved back to the assessment room.

Post-Treatment Assessment:

- The assessment clinician observed the treated area for any redness, edema, or swelling. The patient was also asked if they felt any of these symptoms, or any sensations of high heat or of a "pins and needles" tingling effect in the tissue. If such were indicated, they were documented in the treatment session record.
- The patient was presented with the Stanford Pain Scale chart and asked to rate their overall pain and discomfort during the treatment. This was documented in the treatment session record.
- A measurement of the abdominal region was made using the constant-tension tape measure.
- The patient was advised to continue their usual lifestyle and routine without any special adjustments due to participation in this study.
- The patient was then excused.

Follow-Up Visit (conducted by the assessment clinician):

- The date of the visit and the time of arrival were documented in the treatment session record.
- The patient was weighed and a measurement of the abdominal circumference made via the constant-tension tape measure. These were documented in the treatment session record.
- The patient was asked about any abnormal body functions or observations that may be relevant to the treatment. If any were indicated, these were documented. Any other comments the patient wished to make were also recorded in the visit record.

Efficacy & Safety variables, including collection of adverse event data and anticipated adverse reactions

EFFICACY

Input variables related to the determination of efficacy include the patient's age, gender, ethnicity, height, and weight (to determine the relative extent of obesity). Other input variables include any existing illness or condition the patient might have which could also impact the change in weight or body dimensions of the patient. Study output variables collected during this trial included the change in patient waist circumference as a primary indicator. Secondary, but non-essential indicators were patient weight changes and skin temperature during treatment.

SAFETY

Input variables related to safety are reflected in the exclusion criteria. Primary among these is the effect the ultrasound treatment has on existing illnesses or conditions. There is concern that the delivered energy could adversely affect these conditions, making the patient's overall status worse. Other input variables for safety include the effect on localized tissue directly exposed to the ultrasound, as well as possible systemic effects that may occur.

Output data collected for safety included the patient's assessment of pain or discomfort experienced during or following the treatment, and questioning regarding any observations about systemic health that the patient may make during the overall trial. Any such comments or concerns from the patient were documented in the patient treatment records. Additionally, observations by the clinician about localized tissue response and patient general behavior were collected if any occurred and made part of the patient record.

ADVERSE INTERACTIONS

Anticipated adverse responses include:

- Localized inflammation, edema, and elevated temperature of the treatment area: Based on the proposed mechanism of action, the application of ultrasound and the disruption of cells could result in a localized increase in tissue temperature, accompanied by increased blood circulation through the insulted tissue.
- Localized pain or discomfort: The action of ultrasound of this frequency and intensity on nerve cells is not well understood. The same mechanism of action could trigger nervous cell responses interpreted by the brain as a pain response. The disruption and cavitation of adjacent adipose cells could also trigger a pain response.
- Possible system disruption: The applied ultrasound energy is intended to provide localized energy at the typical depth of tissue where sub-dermal adipose cells are found. The ultrasound energy could continue to propagate further into the body, reaching gastro-intestinal organs beneath the treated area. In generalized terms, there could be disruptions to digestive processes resulting from exposure to the ultrasound energy.

- Possible elevation of blood glucose levels: The disruption and lysis of adipose cells may release an increased amount of glycogen into the blood stream. Patients who present with diabetes or pre-diabetes or who are susceptible to variations in blood glucose levels may experience side-effects consistent with elevated glucose levels wherein they are unable to metabolize and/or process the glucose products adequately.

If any adverse events occur, such will be immediately reported to the study sponsor who will assess the events and make determinations about whether the study should be halted or modified.

Data quality assurance

Patient and study data were documented on physical, printed patient treatment session sheets. The completed sheets were provided to the sponsor, who had the responsibility of uploading the data into electronic files for statistical analysis and processing. Calculations made from the data were conducted in the electronic files, and the accuracy of calculations provided by the electronic spreadsheets were relied on. The clinicians and those who participate in the data collection did not have access to the electronic files, calculations, or analyses. Electronic data management tools were also employed to perform the statistical analysis of the key data.

The tape measurement device used for this study was purchased brand new and had not been utilized for any other purpose prior to or during the course of this study. The tape measure selected incorporates a constant-tension feature to ensure that the tape is not pulled excessively taut or left overly slack when conducting the measurement. The tape measure was calibrated at the manufacturer to ensure consistent tension.

Where patients discontinue participation in the study, or key data is not documented properly on the treatment sheets, data from such patients was not incorporated in the statistical analysis of the data.

Statistical methods planned, including handling data exclusion, analysis of sub-groups if any

Any patient that did not conclude all three treatments and the follow-up was excluded from the analysis. If there are fewer than 40 patients remaining after the study concludes and exclusions are applied, than no analysis shall take place and additional study subject enrolled until a minimum of 40 completed participants exist.

Primary analysis consisted of applying the Anova single-factor acceptance test evaluating which group the participants were in (Test or Control) and the overall change in waist circumference based on the data collected by the tape measure. A confidence of P=0.05 was applied. The results of this analysis were directly applied to determining if the primary objective of the study had been met.

A correlation analysis was applied to all variable data recorded, as well as key calculations from the data, to identify any potential two-way connections or relationships between sets of data. Any correlations scoring a magnitude of 0.85 or greater shall be discussed and if appropriate, Anova single-factor analysis applied to determine if there is statistical significance to the relationship and any statements that might be supported by the data. Of primary interest is any impact the starting BMI might have had on the amount of change, and any impact that gender may impart to the outcome.

Sample size

A total sample size of a minimum of 40 patients was established for this study. This number is based on

$$n = \frac{(Z_\alpha + Z_\beta)^2 \cdot \sigma^2}{d^2}$$

where:

Z_α = 1.96, based on a confidence of P=0.05 (false rejecting of a true null hypothesis),

Z_β = 0.84, based on a power of 80% (failure to reject a false null hypothesis),

d = 1.0 inch reduction in waist circumference as a meaningful/successful change in measurement,

σ = 1.50 inches, based on the evidence presented by a published study[5] under similar treatment parameters and conditions reporting a typical response of 0.75 inches through the umbilical region and assuming some of the population may not respond at all.

The resulting calculation gives a population size of 18. Accounting for possible attrition and adding a generous margin of safety, a minimum sample size of 40 individuals is arrived at.

STUDY PATIENTS

A total of 60 candidates were reviewed and selected to participate in the study. A total of 20 men and 40 women were selected, and each of the Test and Control groups received 30 participants. The distribution of men to women among the groups was not exactly even as assigned by the random number generator: 13 men and 17 women in the Control group, and 7 men and 23 women in the Test group. Of the 60 participants, 3 of the patients were ultimately excluded from the study because the collected data was incomplete or contained discrepancies. Two of these individuals were men in the Test group and one was a man in the Control group.

Analysis of each group shows that the mean BMI of the Control group was 30.78, and the mean BMI of the Test group was 31.56. Thus on average, both sample groups were considered to be obese (according to common BMI classifications). The mean age of the Control group was 44.4 years and the mean age of the test group was 39.9 years. Owing to the demographics of the geographical location where this study occurred, there was very little variety of ethnic backgrounds reflected in the study: 3 individuals of Hispanic origin, 3 individuals of Polynesian origin, and the remaining of Caucasian origin.

EFFICACY EVALUATION

Application of Anova single-factor analysis on the following suppositions is now presented based on the relevant included data:

Supposition	Anova analysis
PRIMARY OBJECTIVE Application of the Ultimate Contour device's ultrasound at a setting of level 4 for 30 minutes per treatment, with a total of 3 treatments, achieves a reduction in waist circumference.	Statistically significant results
Application of the Ultimate Contour device's ultrasound at a setting of level 4 for 30 minutes per treatment, with a total of 3 treatments, achieves different waist circumference results in men vs. women.	Statistically significant results
The ultrasound treatment produces greater circumference reduction the more overweight the patient is.	Statistically significant results

The ultrasound treatment produces greater circumference reduction in older patients.	Statistically significant results

The primary objective of this study is a reduction in the waist circumference. The data collected via the flexible tape measure supports this hypothesis.

Review of the correlation data did not reveal any other significant relationships in the data. Some relationships exist between the weight and circumference measurements between the treatment dates, but this is expected and supports that the same patient was coming back in for each of the successive treatments for each listed patient ID.

Mean results and outcome are now presented:

	Test Group	Control Group
Circumference Reduction	3.12 inches	0.01 inches
Weight Loss	0.47 pounds	0.02 pounds

SAFETY EVALUATION

The secondary objective of this study was to identify any concerns over health or safety over the use of this device. Not a single patient indicated any pain, any discomfort, nor did anyone present with any adverse reaction or visible skin responses following any of the treatments. No systemic health observations or concerns were reported.

Measurement was made of the patient's surface skin temperature during the treatment. This was done primarily for informational purposes. Anova single-factor analysis of the temperature data supports that the ultrasound was having an actual effect on the tissue, and demonstrates that the tissue temperature did not reach any levels that would engender discomfort or actual tissue damage from thermal effects. The maximum skin temperature recorded for any patient at any time was 39.8°C.

DISCUSSION

The results of this study point positively towards a finding that application of ultrasound energy at 37kHz achieves a measureable and significant reduction in the patient's waist circumference. Substantial change in circumference is even observed within the context of a single treatment. Evaluation of the change in circumference among the Test patients from the commencement of one visit to the commencement of the next visit does some diminishing returns, with the first treatment achieving the most drastic reduction in circumference.

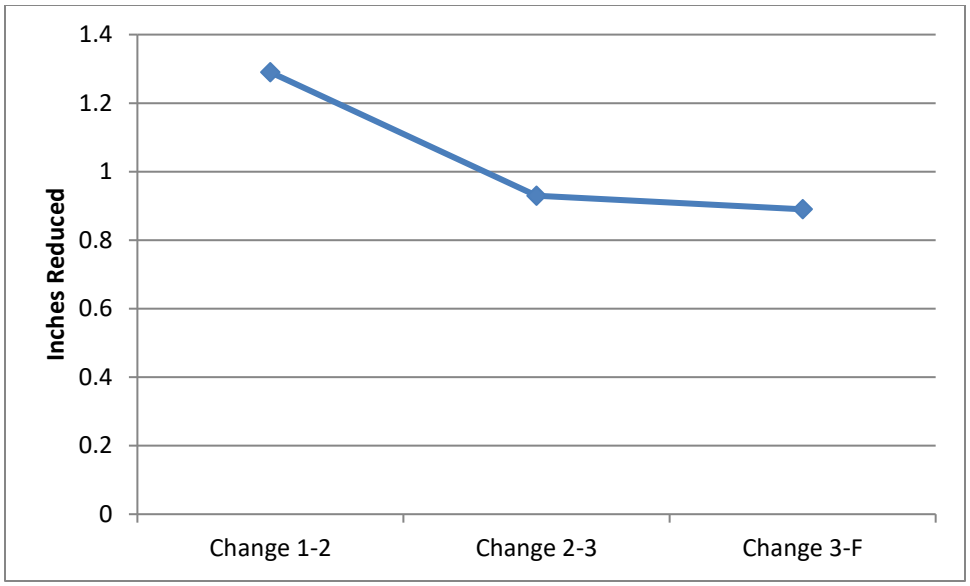

Figure 1. Reduction in circumference between treatments

Although the data statistically indicated a difference in waist reduction between the men and women in the Test group, since there was a small representation of men in the Test group compared to the women, further study is encouraged to verify if this phenomenon is verifiable. Reasons for the increased performance among older patients cannot immediately be explained and should be investigated further. The improved performance relative the BMI of the patient is plausible since the higher BMI generally reflects a greater extent of obesity in the patient, who is more likely to have a greater amounts of subcutaneous fat for the ultrasound to act upon. However, since this relationship was not expressly looked for in this study, further examination and testing is recommended relative to this relationship.

CONCLUSION

The results of this study indicate that the application of ultrasound energy in the 35-45kHz range is effective for reducing the circumference of the waist, when applied directly to the waist area of the patient. This is accomplished without any significant effects or adverse reactions to the patient and no reported pain or discomfort. Test data demonstrate an average of 3.12 inches of waist reduction after 3 treatments, whereas the control group saw essentially 0 change in waist reduction.

REFERENCES

1. Atluri, P. , et al. "Clinical effects of noninvasive ultrasound therapy for circumferential reduction." *Am J Cosmetic Surg,* **Vol. 29 No. 2 (Jun 2012),** pp. 114-120.

2. ELdesoky, M.T.M., Abutaleb, E.E.M., and Mousa, G. S. M. "Ultrasound cavitation versus cryolipolysis for non-invasive body contouring." *Australasian J Dermat,* **Vol. 57, No. 4 (Nov 2016),** pp. 288-293.

3. Mohammadzadeh, M., et al. "Reduction in measures of adiposity using a combination of radio frequency and ultrasound cavitation methods." *Eur J Integrative Med,* **Vol. 8, No. 3 (Jun 2016),** pp. 313-316.

4. Pugliese, D., Maiorano, E., and Pascone, M. "Histopathological features of tissue alterations induced by low frequency ultrasound with cavitation effects on human adipose tissue." *Intl J Immunopath and Pharmac,* **Vol. 26 No. 2 (Apr 2013),** pp. 541-547.

5. Tonucci, L. B., Mourão, D. M., Ribeiro, A. Q., and Bressan, J. " Noninvasive body contouring: Biological and aesthetic effects of low-frequency, low-intensity ultrasound device." *Aesth Plast Surg,* **Vol. 38, No. 5 (Oct 2014),** pp. 959-967.

APPENDIX A - CONSENT AND TREATMENT FORMS

INFORMED CONSENT TO PARTICIPATE IN MEDICAL PRODUCT EVALUATION

Study Sponser :
CAO Group, Inc.
4628 West Skyhawk Drive
West Jordan, Utah 84084
Phone: 801 256 9282

Principal Investigator:
Name: _____
Address _____
_____
Phone# _____

Participant: Name: _____
Address _____
Phone # _____

TERMS OF CONSENT

1. BACKGROUND: Participant has been asked to participate in an evaluation of the efficacy of a new medical/dental product designed by the CAO Group, Inc. ("CAO Group"). The Principal Investigator will be available to answer any of your questions during and after the study. You can refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled. You can stop your participation at any time and your refusal will not impact current or future relationships with the CAO Group. To do so, simply tell the Principal Investigator you wish to stop participation.

2. PURPOSE: The purpose of this study is to assess the efficacy of a product referred to as "Ultimate Contour" which is designed to perform the function of reduction of waist circumference via ultrasound cavitation (the "Product").
The portions of this study that are experimental are the use of ultrasound at a lower frequency of 35-45 kHz and lower intensity of 1 W/cm².

3. ROLE: If you agree to participate in this study, you will be asked to participate in treatments involving the use the Product according to its instruction and to report to the Principal Investigator the effectiveness of the product as well as any discomfort or side effects.

4. TIME COMMITMENT: If you participate in this study, your estimated time commitment will be: approximately 1 hour per treatment, 1 treatment every 5-6 days for three total treatments, plus 30 minutes for a follow-up visit about 5-7 days after the last treatment.

5. ALTERNATIVES: Some medically acceptable alternatives that may achieve comparable results are currently available. They are a reduced calorie diet, and/or moderate frequent exercise.

6. BENEFITS & RISKS:
Anticipated benefits from this procedure are a rapid and lasting reduction in the circumference of the waist region where the treatment is applied, and an associative reduction in body weight.
The Product and its use may involve risks, some of which may be unforeseeable. Some risks may include: swelling or tenderness of the treatment site; texture, wrinkling, or puckering of the skin at the treatment site due to collapsed/cavitated underlying tissues; inflammation or tenderness of internal organs; increased blood sugar level due to metabolized products of cell cavitation. If you notice any discomfort or other symptoms, please contact the Study Director immediately.

7. COMPENSATION: You will not be compensated for participating in the study. You will, however, receive free treatment utilizing the Product for the duration of the study.

8. CONFIDENTIALITY: The data resulting from your participation in the study may be made available to regulatory agencies, other researchers, or commercial entities interested in the Product. In these cases, the data will contain no identifying information that could associate you with the data. The CAO Group will protect confidentiality of records which contain your medical information. Any publications will exclude any information that will make it possible to identify you as a subject.

STATEMENT OF CONSENT:

I have read the above information and have sufficient information to make a decision about participating in this study. I consent to participate in the study.

Participant Signature:_____ Date: _____

Signature of Study Director: _____ Date: _____

Patient Information Form

Patient ID # _____

Name _____

Address _____

_____

Phone # _____

Age _____ Height _____

Gender _____ Ethnicity _____

Existing _____

Health _____

Concerns _____

Visit # 1 Date _____

Patient Signature _____

Visit # 2 Date _____

Patient Signature _____

Visit # 3 Date _____

Patient Signature _____

Follow-up Visit Date _____

Patient Signature _____

Patient Treatment Form

Patient ID # _____

Visit # _____

Date _____ Time _____

Weight _____ Time of last meal _____

Ultrasound Time 30 Power 4

Room Temperature _____

Site Temperature 0 min _____ 10 min _____

20 min _____ 30 min _____

Pain - Ultrasound (circle)

0 1 2 3 4 5 6 7 8 9 10

None Excruciating

Post-treatment observations-
(circle if appropriate) swelling edema redness heat/burning

Patient Comments:

_____

_____

Post-treatment instructions-

Drink Fluids: ☐ Exercise: ☐

Reduced calorie diet: ☐

APPENDIX B - Resume or CV of the investigators

DR. JOHN MEADORS

12458 Timberline Drive, Highland, UT 84003 | (H) 8013699448 | (C) 8013699448 |

johnomeadors@yahoo.com

PROFESSIONAL SUMMARY

I have been self employed for 24 years as A Doctor of Chiropractic. As The formost Doctor of Chiropractic in the country I have a vast knowledge of running a clinic. I have advanced certifications in numerous treatments. I have done consulting for hundreds of doctors on treatment procedures and office management.

SKILLS

- Budgeting and finance
- Project management
- Team liaison
- Self-motivated
- Strong verbal communication
- Conflict resolution
- Powerful negotiator
- Extremely organized
- Team leadership
- Staff development

WORK HISTORY

SEPTEMBER 1990-JUNE 1992

Associate Doctor of Chiropractic | Pacific Chiropractic | Escondido, California

NOVEMBER 1992-NOVEMBER 2003

Owner Meadors Chiropractic | self | Escondido, California

JANUARY 2003-NOVEMBER 2003

Owner of Escondido Pain Management and Surgical Center | self | Escondido, California

JANUARY 1992-MARCH 2014

Owner Dynamic Consulting | self | Escondido, California

OCTOBER 2006-MARCH 2014

Owner Utah Spine and Disc | self | Murray , Utah

EDUCATION

1990

Doctor Of Chiropractic: Chiropractic

Los Angels College of Chiropractic Whittier California

1988

Bachelor of Science: Science

Los Angeles Chiropractic College Whittier California

1980

High School Diploma:

Ft Walton High School Ft Walton Beach Florida

Curriculum Vitae

PERSONAL DATA

Name: Thomas L. Sutton

Birth Place: St. Louis, MO

Citizenship: United States

EDUCATION

Years	Degree	Institution (Area of Study)
1991 - 1995	B.S.	Brigham Young University Provo, Utah
1995 - 1999	M.D.	Medical College of Virginia, Virginia Commonwealth University (Medicine) Richmond, VA
1999 - 2002	Resident	Madigan Army Medical Center (Pediatrics) Ft. Lewis, Washington
2003 - 2006	Fellow	Walter Reed Army Medical Center (Pediatric Gastroenterology and Nutrition) Washington, D.C.

BOARD CERTIFICATIONS

01/01/2002	American Board of Pediatrics (Pediatrics), Certified
01/01/2008	American Board of Pediatrics (Sub: Ped Gastroenterology), Certified

CURRENT LICENSES/CERTIFICATIONS

2001– Present	State of Utah Medical License

ACADEMIC HISTORY

Pediatrics (Pediatric Gastroenterology)

2006 - 2010	Assistant Professor (Clinical), F. Edward Hebert School of Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD.
2010 – Present	Assistant Professor (Clinical), University of Utah School of Medicine

PROFESSIONAL EXPERIENCE

Full Time Positions

2006 - 2010	Staff, Walter Reed Army Medical Center,Pediatric Gastroenterology Division, Department of Pediatrics, Washington, D.C.-+
2009 - 2010	Chief, Walter Reed Army Medical Center, Pediatric Gastroenterology Division, Department of Pediatrics, Washington, D.C.
2010 – Present	Staff, Pediatric Gastroenterologist, Intermountain Rock Canyon Pediatric Specialists, Utah Valley Regional Medical Center, Provo, UT.
2010 – Present	Staff, Pediatric Gastroenterologist, Primary Children's Hospital, Salt Lake City, UT.

SCHOLASTIC HONORS

1995	Health Professions Scholarship Program
2001	Center for Excellence Customer Relations Award: Given for outstanding patient care
2002	Army Certificate of Achievement
2002	Winner Interdisciplinary Research Award at Madigan Army Medical Center Research Award for outstanding resident research. MAMC, Ft. Lewis, WA
2002	Winner for the Howard Johnson, Jr Research Award for outstanding research as a pediatric resident. 36th Uniformed Services Pediatric Section (AAP) Annual Meeting, San Diego, CA
2002	Physical Fitness Excellence
2002	Army Commendation Medal
2003	Iraqi Campaign Medal
2003	Army Commendation Medal
2004	Global War on Terrorism Service Ribbon
2004	Unit of Excellence Award (Walter Reed Army Medical Center)
2006	Finalist for Ogden Bruton Research Award for outstanding research as a fellow or staff pediatrician. 40th Uniformed Services Pediatric Section (AAP) Annual Meeting, Portsmouth, VA

2006	Finalist for the Walter Reed Army Medical Center Bailey K Ashford Laboratory Research Award for outstanding research as a graduating fellow. WRAMC, Washington, DC
2006	Army Commendation Medal
2007	Finalist for Ogden Bruton Research Award for outstanding research as a fellow or staff pediatrician. Uniformed Services Pediatric Section (AAP) 41st Annual Meeting, Washington, D.C.
2007	Semi-Finalist for Ogden Bruton Research Award for outstanding research as a fellow or staff pediatrician. Uniformed Services Pediatric Section (AAP) 41st Annual Meeting, Washington, D.C.
2008	Iraqi Campaign Medal
2008	Army Commendation Medal
2010	Meritorious Service Medal

ADMINISTRATIVE EXPERIENCE

Administrative Duties

2002 - 2003	Battalion Flight Surgeon, 2nd Battalion, 3rd Brigade, 1 AD; Hanau, Germany
2002 - 2003	Field sanitation supervisor, Hanau, Germany
2002 - 2003	Hearing conservation program supervisor, Hanau, Germany
2002 - 2003	Aviation Life Support Equipment (ALSE) shop supervisor, Hanau, Germany
2003	Battalion Flight Surgeon, 2nd Battalion, 3rd Brigade, 1 AD; Baghdad, Iraq
2006 - 2010	Staff, Pediatric Gastroenterology Division, Department of Pediatrics, Walter Reed Army Medical Center, Washington, D.C.
2007 - 2008	Brigade Medical Officer, 1st Combat Aviation Brigade Suicide Prevention Committee, Camp Speicher, Iraq
2007 - 2008	Battalion Flight Surgeon, 601st ASB, CAB, 1 ID; Camp Speicher, Iraq
2007 - 2008	Officer in Charge, Combined Aviation Aid Station; Camp Speicher, Iraq
2008 - 2010	Chief, Pediatric Gastroenterology Division, Department of Pediatrics, Walter Reed Army Medical Center, Washington, D.C.

Professional Organization & Scientific Activities

2010 - 2012 Member, North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition Endoscopy Committee

Grant Review Committee/Study Section

Symposium/Meeting Chair/Coordinator

CURRENT MEMBERSHIPS IN PROFESSIONAL SOCIETIES

Society of US Army Flight Surgeons

North American Society for Pediatric Gastroenterology, Hepatology and Nutrition

American Gastroenterological Association

American Society for Gastrointestinal Endoscopy

TEACHING RESPONSIBILITIES/ASSIGNMENTS

Education Administration

Course and Curriculum Development

2007 Designed 3 year Pediatric resident curriculum pertaining to Pediatric Gastroenterology

2008 - 2010 Overseer of Pediatric Gastroenterology curriculum and related morning report lectures. National Capital Consortium Pediatrics Training program.

Courses Directed

Course Lectures

2005 Intestinal Malabsorption. Adult and Pediatric Gastroenterology Continuing Education Course, Walter Reed Army Medical Center, Washington, D.C.

2006 Gut Embryogenesis and Congenital Malformations, Adult and Pediatric Gastroenterology Continuing Education Course, Walter Reed Army Medical Center, Washington, D.C.

2010 Obesity. Pediatric Gastroenterology and Nutrition Rounds. Walter Reed Army Medical Center, Washington, D.C.

2010 Foreign Body Ingestion. Family Medicine Residency Noon Lecture Series. Utah Valley Regional Medical Center, Provo, UT.

2012 Pediatric Chronic Abdominal Pain. Family Medicine Residency Noon Lecture Series. Utah Valley Regional Medical Center, Provo, UT.

Clinical Teaching

2000 - 2002 Family Practice, OB/GYN, Transitional and Pediatric interns during their NICU, Pediatric inpatient and clinic rotations at Madigan Army Medical Center, Ft. Lewis, WA.

2006 – Present Bedside teaching of pediatric and family practice residents as well as pediatric gastroenterology fellows during outpatient clinics and inpatient rotations

Laboratory Teaching

1992 Undergraduate Human Anatomy lab instructor, Brigham Young University.

1992 - 1995 Undergraduate Kinesiology lab instructor, Brigham Young University.

2006 – Present Teaching endoscopy techniques to pediatric gastroenterology fellows, to include diagnostic upper endoscopy, colonoscopy, polyp removal, gastrointestinal bleeding interventions, dilation, PEG tube placement, etc.

Small Group Teaching

2003 - 2006 Pediatric Gastroenterology Fellow: responsible for teaching pediatric residents rotating on the gastroenterology service.

2006 - Present Pediatric Gastroenterology Attending: Responsible for teaching pediatric gastroenterology fellows and pediatric or family practice residents through group discussion during outpatient or inpatient rounds and informal or formal lectures.

Prepared lectures include:

Foreign Body Ingestion

Chronic Abdominal Pain

Celiac Disease

Constipation Basics

Evaluation of Non-Infectious Hepatitis

Trainee Supervision

MD, PhD

2007 - 2008 Supervisor, Combined Aviation Aid Station. Officer in Charge. Responsible for continuing education of 3 medical providers and 12 enlisted army medics.

Educational Lectures

Didactic Lectures

2000 - 2002 Monthly didactic lectures to USUHS, HPSP and University of Washington third and fourth year medical students during their pediatric rotation

2001 - 2002 Didactic lectures at the Critical Care Nursing Course at Madigan Army Medical Center

Other Educational Activities

2000 - 2011 Active Pediatric Advanced Life Support Instructor

BOOKS or BOOK CHAPTERS

Chapter: Gastric Foreign Bodies. Pediatric Gastroenterology, Pohl J, Gelfon D, and Jolley C. CRC Press. 2014.

PEER-REVIEWED JOURNAL ARTICLES

1. **Sutton TL**, Martinko T, Hale S, Fairchok MP. (2003). Prevalence and high rate of asymptomatic infection of Chlamydia trachomatis in male college Reserve Officer Training Corps cadets. *Sex Transm Dis*, *30*(12), 901-4.

2. **Sutton TL**, Zhao A, Madden KB, Elfrey JE, Tuft BA, Sullivan CA, Urban JF Jr, Shea-Donohue T. (2008). Anti-Inflammatory mechanisms of enteric Heligmosomoides polygyrus infection against trinitrobenzene sulfonic acid-induced colitis in a murine model. *Infect Immun*, *76*(10), 4772-82.

NON PEER-REVIEWED JOURNAL ARTICLES

1. **Sutton TL**. (2006). Index of Suspicion in the Nursery (Small Left Colon Syndrome). *Neoreviews*, e269-e271.

2. **Sutton TL.** (2011). Unusual cause of chronic abdominal pain. *Contemporary Pediatrics,* 2011 Feb 1.

OTHER (Commentary/Letters/Editorials/Case Reports/Video/Film)

Case Reports

1. **Sutton TL**, Foster RL, Liner SR. (2002). Acute methanol ingestion. *Pediatr Emerg Care*, *18*(5), 360-3.

Other

1. **Sutton TL**. (2001 - 2003). Pediatric Intern Orientation Packet. Madigan Army Medical Center.

2. **Sutton TL**. (2001-2002). Pediatric Pearl Book. *General reference book for Pediatric residents and staff*. Madigan Army Medical Center.

UNPUBLISHED POSTER PRESENTATIONS

1. **Sutton TL**, Martinko T, Hale S, Fairchok M. (2002). *Prevalence of Chlamydia trachomatis in the male college ROTC cadet.* Poster session presented at 40th Annual Meeting of the Infectious Disease Society of America, Chicago.

2. Madden KB, **Sutton TL**, Elfrey J, Zhao A, Morimoto M, Katona I, Weinstock JV, Urban JF, Shea-Donohue T. (2005). *Colitis-induced changes in epithelial cell responses are attenuated by helminth-induced upregulation of Th2 cytokines.* Poster session presented at AGA – 106th Annual DDW, Chicago.

3. **Sutton TL**, Zhao A, Elfrey J, Tuft B, Morimoto M, Sullivan C, Weinstock JV, Madden KB, Urban JF, Shea-Donohue T. (2005). *Impact of upregulation of Th2 cytokines on colitis-induced changes in epithelial cell responses to PAR activation.* Poster session presented at AGA – 106th Annual DDW, Chicago.

4. Madden KB, **Sutton TL**, Elfrey J, Zhao A, Morimoto M, Katona I, Weinstock JV, Urban JF, Shea-Donohue T. (2005). *Upregulation of Th2 cytokines by helminth infection alters colitis-induced changes in colonic epithelial cell function.* Poster session presented at Uniformed Services University of Health Sciences Research Day, Bethesda.

5. **Sutton TL**, Zhao A, Elfrey J, Tuft B, Morimoto M, Sullivan C, Weinstock JV, Madden KB, Urban JF, Shea-Donohue. (2005). *Impact of helminth infection on Th2 cytokines and colitis-induced changes to PAR activation in colonic mucosa.* Poster session presented at Mucosal Biology Research Center Conference, University of Maryland, Baltimore.

6. **Sutton TL**, Madden KB, Elfrey JE, Tuft BA, Sullivan CA, Zhao A, Urban JF, Shea-Donohue T. (2006). *Helminth-Induced Upregulation of Th2 Immune Response Prevents TNBS-Induced Colitic Changes in Colonic Mucosa and Smooth Muscle.* Poster session presented at Uniformed Services University of Health Sciences Research Day, Bethesda.

7. **Sutton TL**, Zhao A, Elfrey JE, Sullivan VA, Madden KB, Urban JF, Shea-Donohue T. (2006). *Upregulation of the Th1 immune response results in stereotypic changes in colonic smooth muscle and epithelial cell function.* Poster session presented at AGA – 107th Annual DDW, Los Angeles.

8. **Sutton TL**, Stiltz JA, Sun R, Riera DC, Madden KB, Sullivan CA, Smith A, Urban JF, Zhao A, Shea-Donohue T. (2007). *Prior enteric nematode infection impairs intestinal mucosal defense to bacteria.* Poster session presented at AGA – 108th Annual DDW, Washington D.C.

9. **Sutton TL**, Madden KB, Elfrey JE, Tuft BA, Sullivan CA, Zhao A, Urban JF, Shea-Donohue T. (2007). *Upregulation of the Th1 Immune Response Results in Stereotypic Changes in Colonic Smooth Muscle and Epithelial Cell Function.* Poster session presented at Uniformed Services Pediatric Section (AAP) 41st Annual Meeting, Washington, D.C.

10. Riera DC, Smith A, **Sutton TL**, Madden KB, Sun R, Stiltz, JA, Sullivan CA, Urbam JF, Zhao A, Shea-Donohue T. (2007). *Prior enteric nematode infection alters mucosal defense to infectious colitis.* Poster session presented at AGA – 108th Annual DDW, Washington, DC.

11. **Sutton TL**, Elfrey JE, Zhao A, Madden KB, Sun T, Sullivan CA, Smith A, Shea-Donohue T. (2007). *STAT4 Exhibits Contrasting Influences on the Immune and Physiologic Function in the Healthy and Inflamed Murine Colon.* Poster session presented at Uniformed Services University of Health Science's Annual Research Day, Washington, D.C.

12. **Sutton TL**, Madden KB, Elfrey JE, Tuft BA, Sullivan CA, Zhao A, Urban JF, Shea-Donohue T. (2007). *Th1 Cytokine Upregulation Results in Similar Changes to Colonic Smooth Muscle and Epithelial Cell Function Regardless of Etiology.* Poster session presented at Uniformed Services University of Health Science's Annual Research Day, Washington, D.C.

13. Darling MJ, **Sutton TL**. (2007). *Constipation and Crohn's disease.* Poster session presented at 20th Annual NASPGHAN Conference, Salt Lake City.

14. **Sutton TL**, Rogers PR. (2010). *Juvenile Polyposis Syndrome.* Poster session presented at NASPGHAN Annual Conference, New Orleans, LA.

15. **Sutton TL**. (2010). *Choledochal cysts - A rare cause of chronic abdominal pain.* Poster session presented at NASPGHAN Annual Conference, New Orleans, LA.

ORAL PRESENTATIONS

Keynote/Plenary Lectures

Meeting Presentations (Not Published Abstracts and Not Unpublished Posters)

International

2005 Upregulation of of Th2 cytokines improves colitis-induced changes in epithelial cell responses to protease activated receptor (PAR) agonists. International Congress of Mucosal Immunology. Boston, MA.

National

2002 The Prevalence and Rate of Asymptomatic Chlamydia Trachomatis Infection in College ROTC Cadets. Uniformed Services Pediatric Section (AAP) Annual Meeting, San Diego, CA.

2005 Anti-Inflammatory Mechanisms of Enteric Helminth Therapy in Murine Colitis.18th Annual NASPGHAN Conference, Salt Lake City, UT.

2006 Protective Immunodulatory Mechanisms and Resultant Functional Changes by Helminth Infection in TNBS-induced Murine Colitis. NASPGHAN 3rd Year Fellows Research Conference, Scottsdale, AZ.

2006 The Anti-Inflammatory Mechanisms of Intestinal Helminth Infection in a Murine Model of Colitis. Uniformed Services Pediatric Section (AAP) Annual Meeting, Portsmouth, VA.

2006 JE Elfrey, A Zhao, KB Madden, TL Sutton, JF Urban Jr, T Shea-Donohue. AGA – 107th Annual DDW. Los Angeles, CA.

2006 STAT4 Regulated Functional and Immune Responses in Murine Infectious Colitis, in vivo.19th Annual NASPGHAN Conference, Orlando, FL.

2007 The Contrasting Role of STAT4 in the Immune and Physiologic Function in the Healthy and Inflamed Murine Colon. Uniformed Services Pediatric Section (AAP) Annual Meeting, Washington, DC.

2007 Exogenous IL-25 exerts region-specific effects on gut epithelial cell function and promotes a Th2 environment. AGA – 108th Annual DDW. Washington, DC.

Invited/Visiting Professor Presentations

National

2007 Pediatric Foreign Body Ingestion, Pediatric GI concurrent group session at Uniformed Services Pediatric Section (AAP) 41st Annual Meeting, Washington, D.C.

Local/Regional

2002 E Coli and Hemolytic Uremic Syndrome. Regional Pediatric Conference: Madigan Army Medical Center Winter Pediatric Conference, Ft. Lewis, WA.

2006 Nematode Induced Mucosal Immunomodulation and Functional Changes in Type-1 Driven Colitis. Research Conference, Uniformed Services University of Health Sciences – National Capital Consortium, Bethesda, MD.

2006 IBD and Helminths: Modulation of the Mucosal Immune Response and Function in Murine Colitis with a Preceding Enteric Nematode Infection Intestinal Research Group, University of Maryland, Baltimore, MD

2007	STAT4 Regulates Functional and Immune Responses to Colic Bacterial Infection, *in vivo*. Research Conference at Uniformed Services University of Health Sciences – National Capital Consortium, Washington, DC.
2011	Chronic Abdominal Pain in Children. Primary Care Clinical Program: Clinical Learning Days, Murray, UT.
2011	Pediatric Obesity. Ashley Regional Medical Center Annual Conference 2012, Vernal, UT.
2011	Infant Formulas. Ashley Regional Medical Center Annual Conference 2012, Vernal, UT.
2012	Celiac Disease - An Update. Gluten Intolerance Groups of Utah – Utah Valley Chapter, Provo, UT.
2012	Chronic Abdominal Pain in Children. Pediatrics in the Wasatch 2012: A Clinical Skill Day, Intermountain Healthcare, Murray, UT.
2014	Food Protein Induced Enterocolitis Syndrome – Diagnosis, Treatment and Nutrition Intervention. Salt Lake City UT.
2014	Food Protein Induced Enterocolitis Syndrome – Diagnosis, Treatment and Nutrition Intervention. Colorado Springs, CO.
2014	Food Protein Induced Enterocolitis Syndrome – Diagnosis, Treatment and Nutrition Intervention. Denver, CO.
2014	Food Protein Induced Enterocolitis Syndrome – Diagnosis, Treatment and Nutrition Intervention. Oakland, CA.
2015	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. McKay-Dee Hospital. Ogden, UT.
2015	Gastroesophageal Reflux – An Update on Treatment of GER in Infants. Intermountain Healthcare North Region Clinical Learning Day. Ogden, UT.
2015	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. McKay-Dee Hospital. Provo, UT.
2015	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. Salt Lake City, UT.
2015	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. Sacramento, CA.

2015	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. Woodinville, WA.
2015	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. Santa Rosa, CA.
2015	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. Pleasanton, CA.
2015	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. Denver, CO.
2015	Food Protein Induced Enterocolitis Syndrome – Diagnosis, Treatment and Nutrition Intervention. Department of Women, Infant, Children. CME. Provo, UT.
2015	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. Richland, WA.
2015	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. Burbank, CA.
2015	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. Santa Monica, CA.
2016	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. Scottsdale, AZ.
2016	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. Chandler, AZ.
2016	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. Monterey, CA.
2016	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. Tacoma, WA.
2016	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. Portland, OR.
2016	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. San Jose, CA.
2016	Nutritional Interventions for Children At Risk for Malnutrition and/or Failure to Thrive. Redondo Beach, CA.
2016	Constipation – Emergency Essentials for Better Management. Intermountain Healthcare Central Region Clinical Learning Day. Murray, UT.

Grand Rounds Presentations

2006	Rebalancing the Inflammatory Scale: Intestinal Nematode Infection Effects on Colitis. Pediatric Grand Rounds, Uniformed Services University of Health Sciences, Bethesda, MD.
2007	The Contrasting Role of STAT4 in the Immune and Physiologic Function in the Healthy and Inflamed Murine Colon. Pediatric Grand Rounds, Uniformed Services University of Health Sciences, Bethesda, MD.
2010	Chronic Abdominal Pain – A Clinical Approach. Utah Valley Pediatrics and Utah Valley Regional Medical Center Grand Rounds, Provo, UT.
2013	Celiac Disease Update. Utah Valley Pediatrics and Utah Valley Regional Medical Center Grand Rounds, Provo, UT.
2014 (April)	Eosinophilic Esophagitis. Utah Valley Pediatrics and Utah Valley Regional Medical Center Grand Rounds, Provo, UT.
2014 (Sep)	Food Protein Induced Enterocolitis Syndrome – Diagnosis, Treatment and Nutrition Intervention. Utah Valley Pediatrics and Utah Valley Regional Center Grand Rounds. Provo, UT.
2015	Food Protein Induced Enterocolitis Syndrome – Diagnosis, Treatment and Nutrition Intervention. Brigham Young University Health Center. Provo, UT.
2016	Gastroesophageal Reflux – An Update on Treatment of GER in Infants. Utah Valley Pediatrics and Utah Valley Hospital Grand Rounds. Provo, UT.