Basic Information

1. * **Title of study:**

   Impact of Theraworx Foam on Pain and Motion and Patient-Reported Outcomes in Thumb Arthritis

2. * **Short title:**

   Theraworx Foam

3. * **Brief description:**

   Thumb carpometacarpal osteoarthritis (CMC OA) affects up to 33% of people over the age of 40, which leads to inflammation, pain, and weakness of the CMC joint. Treatment modalities are both conservative and surgical with surgical options including osteotomy,
   bone excision, ligament reconstruction, and various prosthetic implants. The conservative treatment options, however, are limited to NSAIDs and bracing or steroid injections.

   Advances in topical therapies have the potential to deliver focused treatment to the CMC joint. Novel treatment of inflammation can potentially reduce inflammation and pain associated with progressing osteoarthritis. Theraworx Relief is an FDA registered foam that has theoretical impact on inflammation reduction in human subjects treated with the topical foam.

   This pilot study seeks to investigate potential benefit in the use of Theraworx Foam in patients diagnosed with thumb CMC OA. Patients presenting to our upper extremity orthopedic surgery clinic for thumb/hand/wrist pain will be diagnosed by a Board Certified Hand
   Surgeon as per standard protocols. Patients who are recommended to follow a conservative treatment modality and are interested in participating in this study will be randomized into treatment or control groups. Both groups will undergo symptom assessment, strength testing, and range of motion testing prior to starting the

standard
conservative treatment of bracing. The treatment group will use the TheraWorx topical foam and the compression wrap nightly for 2 weeks for at least 6 hours per night. Control group will use a compression wrap for the same time period. Both groups will return at 1 and 2 weeks for repeat strength and range of motion testing and symptom assessment.

4. * **Principal investigator:**
John Fowler

5. * **Does the investigator have a financial interest related to this research?**
○ Yes ● **No**

6. * **Will an external IRB act as the IRB of record for this study?**
○ Yes ● **No**

7. * **What kind of study is this?**
Single-site study

8. **Attach the protocol:**
   - Sponsor/Multicenter protocol
   - Investigator-initiated protocol
   - Emergency Use Consent/ Protocol/ FDA Form 3926
   - Exempt Application form

Document	Category	Date Modified	Document History
There are no items to display			

Study Aims

1. * **Describe the purpose, specific aims, or objectives and state the hypotheses to be tested:**
The purpose of this study is to assess the efficacy of Theraworx foam in reduction of inflammation and pain as measured by subjective pain/disability scales, motion, and strength testing.

Specific Aim 1: To assess the efficacy of Theraworx foam in reduction of pain on subjective pain/disability scales for thumb CMC arthritis.

- Hypothesis 1a: Patients given the Theraworx foam and compression wrap will see significant improvements in reported Numeric Pain Rating Scale (NPRS) compared to patients who are given the placebo foam and compression wrap and Theraworx foam alone.

- Hypothesis 1b: Patients given the Theraworx foam and compression wrap will see significant improvements in score on the Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire compared to patients who are given the placebo foam and compression wrap and Theraworx foam alone.

Specific Aim 2: To assess the efficacy of Theraworx foam to improve function and patient reported outcomes for thumb CMC arthritis.

- Hypothesis 2a: Patients given the Theraworx foam and compression wrap will see significant improvements wrist range of motion compared to patients who are given the placebo foam and compression wrap and Theraworx foam alone.

-Hypothesis 2b: Patients given the Theraworx foam and compression wrap will see significant improvements in grip and pinch strength compared to patients who are given the placebo foam and compression wrap and Theraworx foam alone.

2. * **Describe the relevant prior experience and gaps in current knowledge including preliminary data. Provide for the scientific or scholarly background for, rationale for, and significance of the research based on existing literature and how it will add to existing knowledge:**
Recent research surrounding the structure and function of the outermost layers of

skin have provided insights into potential avenues for improved health. The skin, primarily the stratum corneum was conventionally described as a biologically inert layer, comprised of keratin and dead epidermal cells. The scientific understanding of the stratum corneum has evolved to see a more dynamic and critical structure to skin health. This barrier has a major
role in inflammatory regulation of underlying skin, barrier protection from infection and maintenance of superficial pH that modulates bacterial flora growth and sweat loss.(5,6) Stratum corneum health allows for a multitude of protective functions. The stratum corneum maintains skin pH at approximately 5.0, which allows for healthy flora to exist and
deters pathogenic flora colonization. Exogenous rise in skin pH or psychological stress, impacts the skin function, including inflammatory cascade modulation.(7) This is where investigation of agents that maintain stratum corneum integrity can impact the health and physiologic functions of the skin in patients with inflammatory disease.

The need for improved conservative treatment approaches to thumb CMC OA is increasing with increased population longevity and increased rates of OA in younger populations.(8) The Theraworx topical agent is an FDA-registered product and received approval for commercial labelling. The use of plant extracts in Thearworx, such as Aloe Vera, makes it a potent moisturizing agent, but the extracts in Theraworx also have antiinflammatory
and pain reducing effects. Allantoin, which has been used in cosmetic preparations for many years, moisturizes by increasing the water content and enhancing health of the upper layers of dead skin cells, helping improve wound healing and injuries of the skin. Beta-Glucan 1,3D is a complex carbohydrate that has been demonstrated to enhance the effectiveness of inflammatory responses within the skin and subcutaneous
tissue. These components have potential to impact acute inflammatory responses and promote more rapid healing than non-treatment. (5,6)
Previously completed studies on Theraworx foam have shown no allergic reaction at all in all patients as well as being a non-irritant for all patients. (9)

Significance: If the Theraworx foam and/or Theraworx foam with compression wrap can be shown to reduce pain and allow for improved functional measures, the product can be proposed as an option for conservative treatment of thumb CMC OA and reduce the reliance on oral pain medications, steroid injections, and surgery.

Study Design

1. **Total number of subjects to be enrolled at this site (enter -1 for chart reviews, banking, registries):**
   60

2. **Describe and explain the study design:**
   After informed consent, subjects will be randomized to one of three groups:
   1. Theraworx foam with compression wrap
   2. Placebo foam with compression wrap
   3. Theraworx foam alone

   Baseline testing will include Numeric Pain Rating Scale (NPRS). The Disabilities of the Arm, Shoulder, and Hand (DASH) will be administered to the participant by the study coordinator. Static range of motion will be tested with a wrist goniometer measuring flexion, extension, ulnar deviation, and radial deviation with the participant's elbow supported on a hand table. Strength testing will be performed with a hand dynamometer and pinch meter. These questionnaires/tests will be performed at baseline, 1 week, and 2 week visits. They should take approximately 10 minutes to complete.

   Subjects will be instructed to apply the foam every night (two pumps and rub into the base of the thumb). This will be demonstrated by the research coordinator (to be hired and added to this IRB application).

   Participants will be asked to apply the foam nightly for a minimum of 6 and maximum 10 of hours and avoid use of lotions, topical creams, or topical NSAIDs during the study period. Subjects will be advised to avoid other oral prescription or OTC pain relief medications during the 2-week study period. A study data sheet will be given at this time for the participant to document nightly compliance hours, daily Tylenol use, and daily pain rating. This sheet will be collected at the 2 week visit. This portion of the research visit should take approximately 5 minutes but will allow for time for questions.

   Randomization will occur via block randomization designed to randomize subjects into groups that result in equal sample sizes.

3. **Describe the primary and secondary study endpoints:**

All endpoints are primary:

1. Numeric Pain Rating Scale
2. Disabilities of the Arm, Shoulder, and Hand (DASH)
3. Pinch strength
4. Grip strength
5. Thumb range of motion

4. **Provide a description of the following study timelines:**

Duration of an individual subject's active participation:

2 weeks

Duration anticipated to enroll all subjects:

1 year

Estimated date for the investigator to complete this study (complete primary analyses):

9/30/2019

5. **List the inclusion criteria:**

Patients of John Fowler, the PI, with the following:

1. Thumb CMC arthritis
2. greater than or equal to age 18
3. Interested in non-operative treatment of thumb arthritis

6. **List the exclusion criteria:**

1. Recent corticosteroid injection into the thumb joint
2. Non-English speaking
3. skin lesions or rashes on the thumb
4. current use of topical anti-inflammatory medications
5. concomitant thumb/wrist diagnoses that would impact the results (as determined by the PI)
6. known allergy to magnesium

7. **Will children or any gender, racial or ethnic subgroups be explicitly excluded from participation?**

● **Yes** ○ No

* **Identify the subgroups and provide a justification:**

Children - arthritis of the thumb CMC joint does not typically exist in subjects less than the age of 18 and including a rare patient that might have CMC arthritis would bias our results.

8. **Describe the power analysis used and cite your method of statistical analysis. If a power analysis is not possible, thoroughly justify the sample size required for the study, including appropriate literature citation (alternatively provide page reference in attached protocol):**
The mean pain reported in subjects with CMC arthritis is 5 (out of 10) on the numeric pain rating scale. Assuming a clinical meaningful change in pain of 2 on this scale, an alpha of 0.05 and beta of 0.2, the power analysis demonstrates 16 subjects required per group. Assuming a drop out rate of 20%, we will enroll 20 subjects per group.

Research Activities

1. * **Provide a detailed description of all research activities (including screening and follow-up procedures) that will be performed for the purpose of this research study. This description of activities should be complete and of sufficient detail to permit an assessment of associated risks.**
Screening and Enrollment: Patients diagnosed with thumb CMC OA by the PI and recommended for participation in the study will be assessed for inclusion and exclusion criteria appropriateness by the study coordinator. If they are candidates, consent will be obtained by the PI in a private room and they will be randomized into treatment or control group by the coordinator. At this time, the x-ray taken during routine care by the PI for diagnosis will be obtained and graded for severity. Demographic information including age and gender will also be collected.

   Research Visits: Baseline, 1 week and 2 week visits
Study procedures will be performed by the study coordinator in a patient room equipped with a hand table, if necessary, patient will be moved to an procedure room similarly equipped. Numeric Pain Rating Scale (NPRS), and Disabilities of the Arm, Shoulder, and Hand (DASH) will be administered to the participant by the study coordinator. Static range of motion will be tested with a wrist goniometer measuring flexion, extension, ulnar deviation, and radial deviation with the participant's elbow supported on a hand table. Strength testing will be performed with a hand dynamometer and pinch meter. These questionnaires/tests will be performed at the baseline, 1 week and 2 week visits. They should take approximately 10 minutes to complete. Study coordinator will also provide the participant with the foam and compression wraps and provide instructions for its use. The compression wrap is a cloth wrap (similar to an elastic bandage wrap) that will be saturated/treated with the Theraworx foam. Participants will be asked to apply the foam treated wrap nightly for a minimum of 6 and maximum 10 of hours and avoid use of lotions, topical creams, or topical NSAIDs during the study period. A study data sheet will be given at this time for the participant to document nightly compliance hours, daily Tylenol use, and daily pain rating. This sheet will be collected at the 2 week visit. This portion of the research visit should take approximately 5 minutes but will allow for time for questions.

2. **Upload a copy of all materials used to collect data about subjects: (Attach all surveys, interview/focus group scripts, and data collection forms except for case report forms, SCID or KSADS):**

Document	Unique Protocol ID: STUDY18090019 Official Title: Impact of Theraworx Foam on Pain and Motion and Patient-Reported Outcomes in Thumb Arthritis Document Date: August 1, 2020	Category	Date Modified	Document History
View	Foam%20Study%20Data%20Form.pdf(0.02)	Data Collection	10/9/2018	History
View	DASH_questionnaire_2010.pdf(0.02)	Data Collection	10/9/2018	History
View	Numeric%20Pain%20Rating%20Scale%20Instructions.pdf(0.01)	Data Collection	9/30/2018	History

3. * **Will blood samples be obtained for research purposes?**

○ Yes ● **No**

Data Safety and Monitoring

1. * **Describe your plan to periodically evaluate the data collected regarding both harms and benefits to determine whether subjects remain safe. The plan might include establishing a data monitoring committee and a plan for reporting data monitoring committee findings to the IRB and the sponsor:**
The primary investigator will monitor confidentiality and data on a monthly basis to ensure accuracy and recruitment of subjects. Monthly meetings, with the study coordinator will be held to verify compliance and testing procedures. These meetings will monitor recruitment, retention, data, adverse events, and breaches in confidentiality.

   The investigators will comply with the IRB's policies for the reporting of serious and unexpected adverse events as addressed in Chapter XVII of the IRB Policies and Procedures Manual.

   At the time of the IRB renewal, the PI will submit in writing the information about the frequency of the monitoring, the dates that the weekly meetings took place, a summary of the cumulative adverse events, external factors or relevant information that might have an impact on the safety or ethics of the study, and final conclusion regarding changes to the anticipated risk/benefit ratio to study participation and final recommendations related to the
   continuation, changing, or termination of the study. Also, at the time of the IRB annual renewal, reported documentation over the past year will be submitted to the IRB.

2. * **Describe your plan for sharing data and/or specimens:**
Though we currently do not have plans to share data/documents to external persons, if at a future time we wish to share information appropriate approvals will be obtained.

3. **If any research data is collected, stored, or shared in a paper format, address what precautions will be used to maintain the confidentiality of the data:**
Paper-based records will be kept in a locked filing cabinet and only be accessible to personnel involved in the study. Computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords and stored on an encrypted /firewall protected network.

Risk and Benefits

1. * Enter all reasonably foreseeable risks, discomforts, hazards, or inconveniences to the subjects related to subjects' participation in the research:

View

Research Activity	**Strength Testing**
Common Risks	***No Value Entered***
Infrequent Risks	**Isometric strength testing may result in muscle cramping, discomfort, or fatigue, although occurrence is rare (occurs in less than 1% of people).**
Other Risks	***No Value Entered***

View

Research Activity	**Randomization**
Common Risks	**Those being randomized to the placebo may not receive direct benefit compared to those randomized to foam.**
Infrequent Risks	***No Value Entered***
Other Risks	***No Value Entered***

View

Research Activity	**Use of Foam**
Common Risks	***No Value Entered***
Infrequent Risks	**Skin irritation, allergic reaction**
Other Risks	***No Value Entered***

View

Research Activity	**Storage of Research Data**
Common Risks	***No Value Entered***
Infrequent Risks	**Breach of Confidentiality**
Other Risks	***No Value Entered***

View

Research Activity	**Range of Motion Testing**
Common Risks	***No Value Entered***
Infrequent Risks	**The range of motion procedures may result in soreness, however it is rare (occurs in less than 1% of people).**
Other Risks	***No Value Entered***

Other Risks	***No Value Entered***

2. * **Describe the steps that will be taken to prevent or to minimize risks:**
Subject research records will be double-locked, with access only be research personnel listed. Electronic files will be stored in password protected systems. Subject research records and the data linking file will be destroyed after 7 years to decrease the risk of confidentiality being breached.

Subjects will be instructed to not exert themselves in a manner that will cause pain during the procedures. Those who experience any pain or discomfort during the testing procedures will be given the opportunity to rest or terminate the testing session.

Subjects with any prior adverse reactions to topical agents will be excluded.
In the event of any adverse event or injury, the investigator will provide the subject for proper medical treatment.

3. **Financial risks - will the subject or insurer be charged for any research required procedures?**
○ Yes ● **No**

4. **Describe the steps that will be taken to protect subjects' privacy:**
Examination and testing will be completed in a private examination room

5. **What steps will be taken in the event that a clinically significant, unexpected disease or condition is identified during the conduct of the study:**
The PI will notify the patient and either treat the condition or provide an appropriate referral.

6. **Describe the potential benefit that individual subjects may experience from taking part in the research or indicate if there is no direct benefit. Do not include benefits to society or others:**
There may be a direct benefit for participating in this study, if the study hypothesis is true, there is a chance that the treated wrap will provide more pain relief and inflammation reduction than the placebo wrap/bracing alone.

The data gathered will allow us to determine if there is a benefit to the test foam in reducing pain and inflammation in thumb

CMC OA. Having an understanding of the product in recovery may lead to future studies that investigate a wider array of measures related to conservative CMC OA treatment.

7. Do you anticipate any circumstances under which subjects might be withdrawn from the research without their consent?

● **Yes** ○ No

* **Describe the circumstances and any procedures for orderly termination:**
unforeseen illness or allergic reaction to foam or non-compliance

8. Describe procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection and data already collected:
The data already collected will continue to be used in the study.

Placebo Arm

1. * **Is there a commonly used diagnostic/treatment approach that is currently recognized as being effective for the proposed subjects' disease or condition, and that will be withheld from subjects assigned to the placebo arm of this research study:**
   Yes

2. **Describe the commonly used diagnostic/treatment approaches that will be withheld from subjects assigned to the placebo arm of this research study:**
   A commonly used treatment approach is corticosteroid injection, over the counter pain medications, and/or surgical treatment.

3. **Is enrollment into this study limited to individuals in whom the commonly used diagnostic/treatment approaches are known to be ineffective or intolerable?**
   no

4. **Provide a scientific justification for the placebo-control arm of this research study:**
   The study purpose is to compare the use of TheraWorx foam and compression wrap, with the placebo foam with wrap and Theraworx foam alone on subjects with thumb carpometacarpal osteoarthritis having thumb or wrist pain.

5. **How long will subjects participate in the placebo arm? Justify why this duration is necessary:**
   2 weeks. This is a short period of time. If no benefit in the placebo arm, can efficiently undergo other treatment options such as steroid injection.

6. **How frequently will the subject's condition or disease be monitored and compare that to the frequency of monitoring associated with standard care for this disease/condition?**
   weekly

7. **What specific endpoints will result in discontinuing a subject's participation due to worsening of the subject's disease or condition?**
   It is such a short study and examining a chronic condition (arthritis) that the PI does

not expect an acute worsening of the disease or condition.

8. **What is the risk to subjects who receive no active treatment for their disease or condition while in the placebo arm?**

Felay in treatment by usual care conservative measures resulting in pain

9. **Describe the planned involvement of a 'contact person' who interacts with the subject on a regular basis and who will notify the investigators immediately of any problems related to the subject's disease or condition:**

There is no reason why the subject could not contact the investigators in this study on thumb arthritis. No plans to involve a contact person.

Note: The involvement of the contact person must also be addressed in the consent form

Statistical Analysis Plan

The Primary Outcome is VAS pain score at 2 weeks

This will be analyzed with ANOVA which is the appropriate test for continuous data and multiple groups.

Significance will be set at 0.05

Secondary Outcomes

Will also be analyzed using ANOVA.

Significance will be set at 0.05