# Pilot Trial Green Sun Medical Dynamic Brace

## Sponsor: Green Sun Medical

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NCT # 03641469

## STATEMENT OF COMPLIANCE

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the Institutional Review Board (IRB) for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. In addition, all changes to the consent form will be IRB-approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

# 1 PROTOCOL SUMMARY

## 1.1 SYNOPSIS

| | |
|---|---|
| **Title:** | Pilot Study of the Green Sun Medical Dynamic Brace |
| **Study Description:** | Preliminary investigation of safety and performance |
| **Objectives:** | Preliminary Safety and Performance of Green Sun Medical brace (GSM). |
| **Endpoints:** | Safety – ongoing review<br>Performance: In-brace Cobb angle correction and Cobb angle progression |
| **Study Population:** | Adolescent idiopathic scoliosis (AIS) patients currently treated with a standard of care thoracolumbosacral orthosis (TLSO) |
| **Phase:** | |
| **Description of Sites/Facilities Enrolling Participants:** | Multiple sites across the United States |
| **Description of Study Intervention:** | Green Sun Medical (GSM) brace |
| **Study Duration:** | unknown |
| **Participant Duration:** | variable |
| **Optional Substudy** | Pressure-Sensor Equipped Pad Clinical Validation |

# 1 INTRODUCTION

## 1.1 STUDY RATIONALE

The Green Sun Medical Dynamic Brace (GSM) brace was developed as an alternative to rigid thoracolumbosacral orthoses (TLSOs, braces) commonly used to prevent continued curve progression in patients with adolescent idiopathic scoliosis (AIS). The brace applies corrective forces to the muscular and bony structures of the spine while preserving range of motion (ROM). The orthosis is prefabricated and adjusted for each patient. A series of semi-rigid segments encircle the patient's torso in close contact and are joined by a structure of flexible elements. These flexible (or elastic) elements generate stabilizing forces, providing the necessary immobilization while allowing relative motion of the semi-rigid segments. To date, this brace has been tested in the lab on healthy volunteers.

The innovative design of this brace should provide an equivalent degree of correction of the scoliotic curvature as a rigid TLSO, with increased acceptability to the patient via improved comfort and spinal/chest wall mobility. Increased acceptability promotes increased adherence to treatment. Given the strong research evidence that bracing effectiveness is a function of correction and adherence, there is reason to believe that a future pivotal study of the GSM brace could demonstrate superior effectiveness to rigid TLSO designs.

This is a pilot study to collect preliminary short-term data concerning the safety and performance of the GSM brace in a sample of subjects with AIS who are currently being treated with a TLSO.

## 1.2 BACKGROUND

**Adolescent Idiopathic Scoliosis**

Adolescent idiopathic scoliosis is a structural lateral and rotatory curvature of the spine arising in otherwise normal children during puberty. Curvatures less than 10 degrees are viewed as a variation of normal because until a curvature has exceeded 10 degrees, it has little potential for progression. The 1982 report of the Scoliosis Research Society [1] stated that 2-3 percent of children younger than 16 years of age will have a curvature of 10 degrees or less, but only 0.3-0.5 percent will have a curvature of 20 degrees of more. The vast majority of AIS patients do not initially present due to symptoms, but due to the finding of truncal asymmetry noted during screening or incidentally during well-child examinations. Long-term follow-ups indicate that the population may have a higher prevalence of back pain, and of respiratory compromise if the curve becomes extremely large. [2] Therefore, the treatment of AIS during adolescence is mainly an attempt to prevent problems during adulthood by arresting the progression of the curve. Additionally, large curves are generally acknowledged to cause significant cosmetic deformity and associated psychological distress. Such deformity can only be corrected through surgery. Thus, many patients seek and receive essentially prophylactic non-operative treatment (bracing) for AIS.

**Biomechanics of Adolescent Idiopathic Scoliosis and Bracing**

Two major biomechanical principles are thought to contribute to the development and progression of AIS: Euler's theory of elastic buckling of a column; and the effect of the Hueter-Volkmann principle of vertebral body growth. Euler's theory, as applied to AIS by Gavin, Shurr and Patwardhan,[3] conceptualizes the vertebral column as a straight, flexible column fixed at the base, free at the upper end, and subjected to an axial compressive force. There exists an upper limit of the magnitude of this force at which point the column will buckle; this force is a function of its flexibility, length, and end support conditions. Due to the lateral curvature of the

scoliotic spine, an axial compressive load at the top results in internal bending moment and causes deformation of the curved column. If the axial load is removed, the curve will return to its original shape through an elastic response. This response is in keeping with the observation that curves are smaller with the patient in a supine vs. standing position. As the axial load is increased, the internal stresses increase, and there is further increase in the deformation of the column. At some point, the axial load may become large enough to cause the bending moment in the column to exceed the elastic limit and cause plastic, permanent deformity. The axial load sufficient to cause plastic deformation is termed the critical load of the column and is a function not only of the curve flexibility, length and support conditions, but also of the magnitude of the initial curvature. The larger the curve, the smaller the critical load, and therefore, the more likely large curves are to progress than smaller ones.

The action of a TLSO can be explained using the above principle of plastic buckling as three separate, but interactive, components: end-point control, transverse loading, and curve correction. Endpoint control describes the stabilizing forces placed on the pelvis by the orthosis that provide an increase in the critical load of a spinal curve. Another characteristic of scoliosis orthoses is some form of a transversely directed load on the apex of the curvature, through accessories such as slings and pads, or through the molding of a full-contact orthosis. The use of transverse forces alone directed at the apex of the curve increases the critical load the spine can carry and may be sufficient to prevent the curve from further progression. The curve correction produced by an orthosis has the single greatest effect on increasing the overall critical load of the spinal column. For example, reducing a curve from 30 degrees to 20 degrees increases the critical load from 50 percent to 80 percent. The results of the combined effects of these mechanisms are additive. Utilizing the proper biomechanical forces will theoretically allow any TLSO to achieve optimum correction.

**Use of Bracing in AIS**

Several brace designs have been proposed based on these biomechanical principles. Modern spinal braces began with the development of the Milwaukee brace. The Milwaukee brace, a cervicothoracolumbosacral orthosis, was first used as a post-operative device, then became the mainstay of non-surgical treatment for scoliosis in the 1960s. Although this brace is still in use for certain curvatures, lower profile rigid thoracolumbosacral orthoses (TLSOs) are now most frequently used. TLSOs were primarily designed to circumvent the objectionable characteristics of the Milwaukee, including a lower profile without the cervical extension, the use of lighter materials, and customization to the individual to improve comfort and cosmesis. [4] Despite these changes, TLSOs are poorly tolerated by many patients. Sanders and colleagues stated “many factors likely contribute to the low overall compliance with bracing, including comfort, social

issues and self-image. Some patients may decide that the risk of progression to surgery is more acceptable than wearing a brace." [5]

TLSOs are usually prescribed for curves with an apex caudal to the seventh thoracic vertebra, with a magnitude greater than 25 degrees and less than 45 degrees, or 20 degrees plus documented progression of greater than 5 degrees over 6 months in skeletally immature patients. [16] Some TLSOs have been developed for use only at nighttime or part-time (e.g. Providence and Charleston bending braces), while most others are worn 18 or more hours per day. Although TLSOs differ slightly in their design, all were developed based on the same principle of three-point control with the goal of correcting the curve in the brace, and stabilizing it throughout the duration of wear. [6] Curve correction is both a function of brace construction and of the characteristics of the individual curve, such as its severity and flexibility.

Despite a large body of research literature, the question of TLSO effectiveness wasn't definitively answered until 2013, when the results of the Bracing in Adolescent Scoliosis Trial (BrAIST) were published. [7] The use of a TLSO significantly reduced the incidence of curve progression to surgical threshold, relative to no treatment, in both the randomized and observation arms of the study. Additionally, a strong dose-response curve was noted, demonstrating that increasing average hours of wear per day decreases the risk of significant curve progression. The dose-response relationship is supported by several other studies, and evidence is emerging that longer hours of wear are required by younger patients with larger Cobb angles, who are at higher risk of curve progression. [8-11] Unfortunately, clinical experience and objective monitoring of wear time indicates that compliance/adherence is a serious issue in bracing treatment. [6, 12-14]. In the BrAIST study, [7] the median wear time was 13 hours per day, despite prescription of a minimum of 18 hours per day. Adherence improves when optimal levels of education and support are provided to patients and when barriers, such as comfort and appearance, are addressed. [9, 15-17]

The amount of Cobb angle correction obtained in the brace has also been linked to treatment outcomes. Historically, the goal has been in-brace correction of at least 50%, [18, 19] although successful outcomes have been shown with correction ranging from 10-50% or greater. [20-24] The amount of correction a TLSO can achieve is enhanced by appropriate customization, starting with accurate measurements of both the patient's trunk and their specific curve pattern and magnitude. [25] But the amount of correction achievable from even an optimally designed TLSO is limited by patient and curve characteristics which contribute to the stiffness of the curve. Therefore, comparison of correction between brace designs may best be demonstrated by within-patient differences if randomization to treatment with large samples is not possible.

It is clear that a high percentage of patients experience curve progression and subsequent spinal fusion surgeries which may have been prevented if appropriate corrective forces and adequate wear time had been achieved.

## 1.3 GSM BRACE

**Green Sun Medical Dynamic (GSM) Brace (also known as the Green Sun Medical Whisper Brace™)**

The GSM Dynamic External Orthosis is an externally applied device designed specifically for use with AIS and other spinal deformity patients. The GSM brace, like a TLSO, applies corrective forces at the apices of the scoliosis and supports the muscular and bony structures of the spine.

The engineering team designed the device to provide clinically-relevant forces and moments equivalent to those generated by TLSOs [26] while addressing issues with current rigid bracing technology. Addressing these barriers to successful bracing outcomes is critical. Failure of conservative therapy for AIS may result in spinal fusion, a major procedure that fuses an average of 10 vertebrae and results in expensive hospitalizations and the potential for life-long complications.

Key differences between the GSM brace and TLSOs are:

| Issue | Rigid Bracing | GSM Dynamic Orthotic |
|---|---|---|
| **Range of Motion** | Extremely limited in spinal motion during brace wear results in patient discomfort, muscular atrophy and reduced compliance | Allows range of motion, potentially improving patient comfort, paraspinous muscle tone and compliance |
| **Curve Correction** | Designed to prevent deformity progression<br>Ability to correct curvature limited by drop-off in support forces with any correction | Designed to minimize force drop-off with correction<br>Sustained corrective forces could potentially offer improvement of the spinal deformity |
| **Accommodate Growth** | Patient growth can result in altered support forces, reduced brace performance, discomfort and require new brace fabrication | Designed to accommodate growth<br>Modular nature allows device to accommodate growth with minimal effort and cost |
| **Ease of Fabrication and Adjustment** | Most rigid braces fashioned by hand<br>Fit issues or failure to achieve significant in-brace correction can result in re-fabrication<br>Limited ability to adjust with padding | Modular components and adjustable force mechanisms allow rapid adjustments to fit patient anatomy and in-brace correction |

The design of the GSM brace utilizes a series of semi-rigid segments that encircle the patient's torso in close contact joined by a structure of flexible elements. These flexible (or elastic) elements generate the necessary corrective forces while allowing relative motion of the semi-rigid segments. The orthosis is minimal in appearance and worn under the patient's garments.

The GSM brace also includes an integrated sensor system which allows the continuous collection of movement and pressure data for the purposes of tracking brace wear and effectiveness. Initially, the data are intended for information only while the system and algorithms are validated. The sensor system is comprised of the following:

- Hardware: The sensor system hardware includes a Bluetooth Low Energy (BLE) microcontroller board with rechargeable battery, 3-axis accelerometer, and an array of piezoresistive pressure sensors integrated into key locations on the orthosis. The board stores data in its internal memory.
- Software: The sensor system firmware samples accelerometer and pressure sensor data and writes to the board's internal memory. More than 60 days of data can be retained between syncs.

Please see the Investigator's Brochure for additional details concerning the development of the device. FDA classification: Sec. 890.3490 Truncal orthosis, Class I device, and is exempt from premarket notification and current good manufacturing practice requirements. The GSM brace is a non-significant risk device. The FDA defines a significant risk device under 21 CFR 812.3(m) as having the following uses and characteristics:

1) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
2) Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
3) Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
4) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

The FDA defines serious risk as potential harm to subjects that could be life-threatening, could result in permanent impairment of a body function, or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure.

A non-significant risk device is any device that does not meet those criteria. The GSM brace does not meet the criteria defined in 1 and 2 above. While the device is intended for treating the disease of scoliosis, it, like other TLSO's, does not pose a serious risk to the patient. The GSM Dynamic Orthosis is a brace worn externally over the torso of a patient. It has been designed to provide forces of similar magnitude to current standard-of-care braces.

# 2 OBJECTIVES AND ENDPOINTS

Primary

1. Safety of the GSM brace: To identify unanticipated adverse events associated with the GSM brace and patient characteristics likely to raise safety issues
2. Performance of the GSM brace:
    a. To assess immediate radiographic outcomes (in-brace Cobb angle) relative to those in the TLSO
    b. To assess short-term radiographic outcome (out of brace Cobb angle) after 3 months
    c. To assess adherence to the bracing prescription (hours of wear per day)
    d. To assess patient-reported outcomes including health-related quality of life and measures of acceptability of the GSM brace (e.g. comfort, stress, interference with activities) relative to experiences in the patient's previous TLSO

Secondary

1. To assess spinal range of motion in the GSM brace relative to the subject's TLSO
2. To assess lung vital capacity in the GSM brace relative to the subject's TLSO
3. To validate accelerometer data (obtained from an embedded sensor in the GSM brace) as an estimate of the average hours of wear per day.

# 3 STUDY DESIGN

## 3.1 OVERALL DESIGN

This is a pilot study to provide "proof of concept" data which will inform further refinements of the GSM brace and support the development of a subsequent pivotal multicenter clinical trial.

Our primary aims involve safety and performance.

This is a multi-center, open-label trial where subjects serve as their own controls. Baseline radiographic and patient report will reflect the effect of the subject's standard of care TSLO, providing data that can be directly compared to that obtained during use of the GSM brace.

# 4 STUDY POPULATION

## 4.1 INCLUSION CRITERIA AND EXCLUSION CRITERIA

Inclusion criteria are as follows:

1) Diagnosis of AIS
2) Current treatment with a TLSO, of ≥5 months' duration
3) Existing 3D surface scan of torso and out-of-brace x-ray within the past 6 months. If no scan exists, patient must be willing to undergo a scan to allow fabrication of the GSM brace.
4) One curve apex below T7
5) Female sex (85% of the AIS population is female)
6) Ability to read and write English
7) Age 10-15 years

Exclusion criteria:

1) Parents/patients who decline participation and/or do not sign the consent/assent documents
2) Pregnant women
3) Patients who are unwilling or unable to return for follow-up visits
4) Patients who are unable to read and write in English.

## 4.2 SCREEN FAILURES

Other than the pregnancy test, there will be no screening for participation after informed consent/assent is signed.

## 4.3 STRATEGIES FOR RECRUITMENT

1. Identification

Potential subjects will consist of patients currently being treated at a study center. We estimate that at any given time, the sites are treating approximately 60 patients who would meet the inclusion criteria.

Under a partial HIPAA waiver or other institutional authorization allowing examination of records for research screening, study staff will identify patients who meet the inclusion criteria using the results of their most recent clinical visit and their orthotic care to date. To otherwise approach all patients would be impractical due to the large volume of patients seen in the clinic who do not meet these criteria (i.e. patients with other diagnoses, adults, or patients with other characteristics outside the inclusion criteria). If the patient meets the inclusion criteria, her name and contact information will be entered into an electronic log. Once the patient

makes a decision about participation, the entry will be deleted. The entire log will be deleted once study data collection is completed.

2. Recruitment

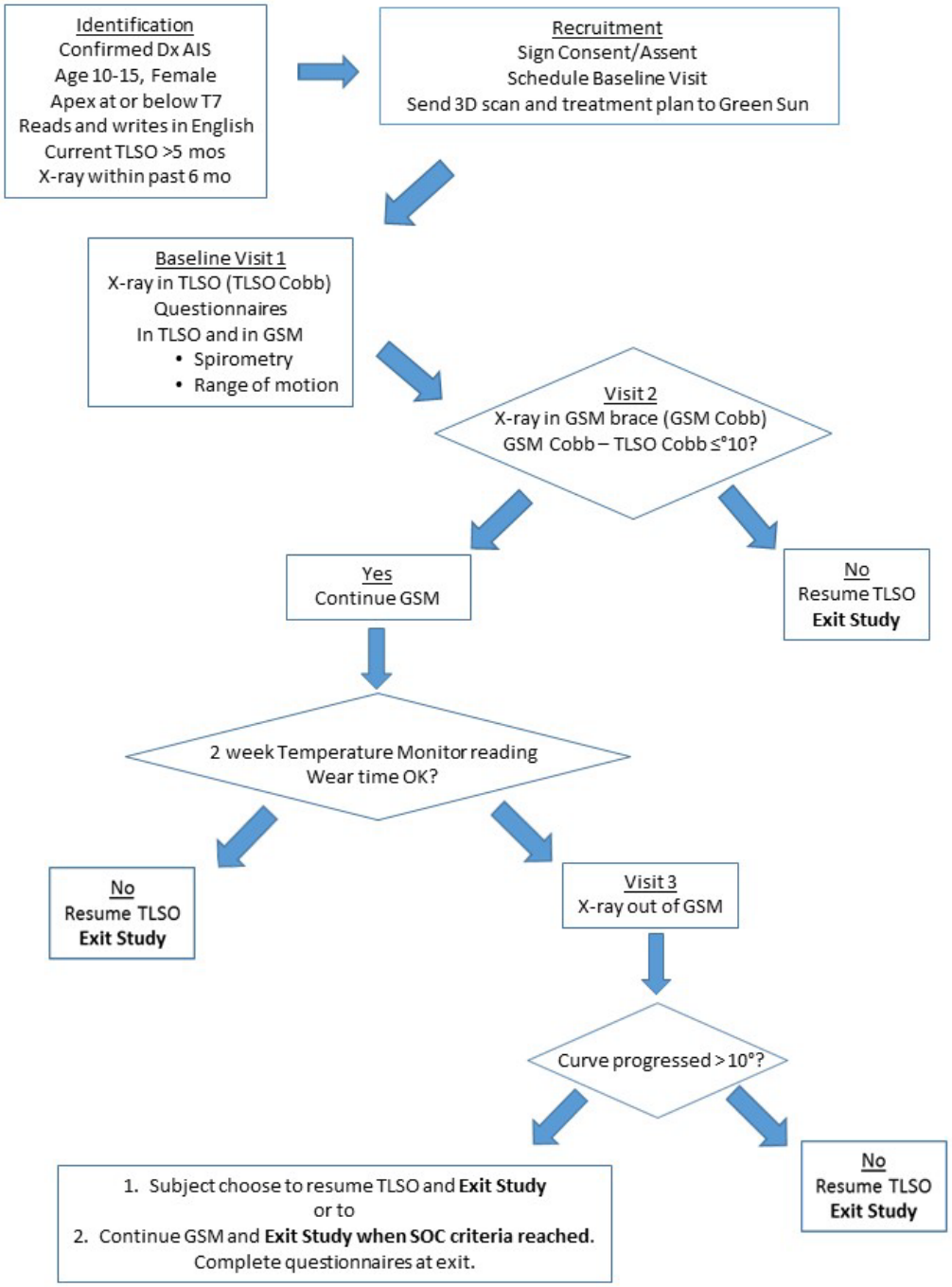
Recruitment can occur in two ways.

1) Patients encountered in clinic. If a patient meets the inclusion criteria, study staff will introduce the study and answer questions. The family will be given the option to see the GSM brace, and further discuss the study prior to enrolling. If the family is interested in the study, study staff will go over the Informed Consent and Assent documents with the family, and answer any questions they may have. The family will be given the opportunity to see the GSM brace. Families will be encouraged to take as much time as they need to consider participation. No study procedures will occur until signed consent/assent is obtained.

2) Patients identified via a search of medical records. If a patient meets the inclusion criteria, study staff will mail out an introductory letter with an overview of the study and copies of the Informed Consent and Assent documents (See Introductory Letter). One week later, study staff will call the family and introduce the study (See Introductory Phone Script). The voluntary nature of the study will be emphasized and parents/patients will be assured that declining participation will not impact their continued care. The family will be given the option to see the brace, and further discuss the study prior to enrolling by visiting the clinic. Families will be encouraged to take as much time as they need to consider participation. If the family is interested in the study, during the introductory phone call, study staff will read the Informed Consent and Assent documents with the family, and answer any questions they may have. Consent/assent could be obtained either via the mail or in person. No study procedures will occur until signed consent/assent is obtained.

# 5 STUDY INTERVENTION

## 5.1.1 STUDY INTERVENTION SUMMARY FLOWSHEET



### 5.1.2 STUDY PROCEDURES

**Immediately After Consent is Signed and Received by Study Team**

The following will be sent to Green Sun so that an appropriately-configured GSM brace can be made for the subject:

1) A de-identified copy of the most recent 3D scan of the patient's torso (tagged with a study ID number)
2) The individualized treatment plan devised by the PI which specifies the location and direction of applied forces (e.g. push on the patient's left axilla, push on the patient's right rib cage roughly 4 inches lateral of midline around T9) and tagged with a study ID number

The Baseline Visit will be scheduled approximately 2 weeks after consent is signed and the 3D scan and treatment plan have been sent to Green Sun to allow Green Sun time to fabricate the brace.

**Instructions for Radiographs**

1. All study-related radiographs will be obtained using the EOS® Imaging system Micro Dose protocol (when available). If an EOS system is not available, please see **Additional Information on Assessments.** Radiographs and Assessments, and **5.2.1 Risks** for further information).
2. The number of study-related radiographs is NOT to exceed 6.
3. Three radiographs are required:
    a. In the TLSO (Baseline Visit 1)
    b. In the GSM (Visit 2)
    c. Out of brace (Visit 3)
4. A maximum of **3** optional in-brace radiographs may be taken at any time prior to Visit 3 to maximize the fit, correction and comfort of the GSM brace.

**Baseline Visit 1 (approximately 2 hours)**

1. A urine pregnancy test will be conducted. Pregnant subjects will exit the study.
2. Completion of the Brace Questionnaire and the Italian Spine Youth Quality of Life (ISYQOL) questionnaire (5 minutes)
3. Assessments while wearing current TLSO
    a. Vital capacity using Spiropet spirometer (average of 3 trials, 5 minutes)
    b. Measurement of spine range-of-motion (flexion, extension, rotation) using a tape measure (5 minutes)

   c. In-brace standing coronal full-spine radiograph (5 minutes)
4. The subject will be fitted with the customized GSM brace. The fit and corrective forces will be fine-tuned by adjusting the drive mechanisms until the corrective forces are matched to the surface anatomy of the patient and to the spinal deformity. The subject is involved in this process by providing feedback concerning the comfort of the brace. A log will be kept of all adjustments made to the brace during the course of the study. The brace will include the embedded force and acceleration sensors, as well as two temperature monitor units.
5. Assessments while wearing Green Sun Brace
   a. Vital capacity using Spiropet (average of 3 trials, 5 minutes)
   b. Measurement of spine range-of-motion (flexion, extension, rotation) using a tape measure (5 minutes)
6. Subject sent home with daily GSM Brace Diary
7. Extraction of data from medical/orthotic records: date of birth, gender, date of menses onset, and historical measures of height, weight, skeletal maturity (Risser grade, status of triradiate), Scoliosis Research Society curve classification, Cobb angle(s), kyphosis, lordosis, coronal and sagittal balance, apical vertebral rotation, in-brace Cobb angle(s) and estimated brace wear time. Data from TLSO brace initiation to baseline study visit will be extracted. These data define the spinal deformity, and the risk for continued progression.
8. OPTIONAL: Subject Appraisal of the GSM Brace Wear Mobile App
   Subjects will be given the option to use and provide feedback concerning the GSM mobile app (Dynamic Scoliosis Brace Monitoring App, Version 1.5.1, developed by Green Sun Medical and Mindset Medical). This app pairs the subject's mobile device with the GSM sensor in the brace and offloads date, accelerometer and pressure sensor data to estimate the number of hours per day that the brace is being worn by the patient. The app graphically displays the estimated hours/day the brace was worn for the current day and for the week. The app provides real-time feedback using graphical displays that should be easily understandable by adolescents. There is research evidence that providing subjects with brace wear time feedback results in better compliance to brace wear recommendations. [9, 16] Subjects will be given the option to use the app and to complete the GSM App feedback form at Visit 2 and Visit 3. The purpose of the app in this study is not to assess brace wear time or the influence of the app on wear time, but only to gather subjects' opinions for ongoing refinement of the app. The accuracy or reliability of the app is not being tested in this study. Subject PHI will not be used for registration; subjects will be instructed to enter their Study ID and City instead of their First and Last names; DOB as January 1, 2019; their email will be entered as the

StudyID@greensunmedical.com. More information about the app is provided in the section: **Additional Information on Assessments**

**Visit 2 (1-2 weeks after Baseline, approximately 1 hour)**

1) Standing coronal full-spine radiographs in the GSM brace (5 minutes).
2) Completion of GSM App Feedback Questionnaire (optional)
3) Safety Check: Query for adverse events and other issues
4) Performance Check
    a) If the Cobb angle obtained in the GSM brace is less than, or no more than, 10 degrees greater than that measured in the TLSO (measurement from Baseline Visit 1) then the GSM in-brace correction will be considered equivalent to the standard brace, and the subject will be sent home for a 2-week trial of the GSM brace
    b) If the in-brace Cobb angle is >10 degrees than that in the TLSO, the subject will exit the trial and continue with their current TLSO.
5) The subject will be provided with 1) instructions for removal and return of 1 temperature monitor at 2 weeks, 2) an extra sensor system rechargeable battery and charger, with instructions for use, 3) mailing labels and envelopes, and 4) GSM brace diaries.

**Phone Visit and Performance Check (2 weeks after baseline)**

1. Study staff will contact the subject and parent/guardian to see how well the subject is adapting to the GSM brace and remind the subject/parent to remove the temperature monitor from the brace and send by courier overnight to the study site.
2. Safety Check: Query for adverse events and other issues
3. Performance Check – to ensure adherence to prescribed number of hours per day in the GSM brace:
    1. If any problems are noted during the phone contact the PI will determine whether adjustments to the brace could alleviate the issues and, if so, ask the subject return to clinic
    2. If the temperature monitor data indicate the subject is wearing the GSM brace an average of 2 or more hours less per day than prescribed
        a. The PI will determine whether adjustments to the brace could alleviate the issues and have the subject return to clinic; if not, the subject will exit the study and return to their current TLSO
        b. If after adjustments to the brace, the subject feels that the brace is still incompatible with the prescribed wear time, the subject will exit the study and return to their current TLSO

**Phone Visits (Weeks 4, 6, 8, and 10 after baseline)**

1. Study staff will contact the subject and parent/guardian to see how well the subject is adapting to the GSM brace and remind the subject/parent to continue completion and return of the diaries to the study site in the prepaid envelopes.
2. Safety Check: Query for adverse events and other issues

**Visit 3 (3-4 months after baseline, approximately 1 hour)**

1. Standing coronal full-spine radiographs out of the brace and measurement of the Cobb angle
2. Download of temperature monitor data from GSM brace
3. Collection of GSM Brace Diary
4. Completion of the Brace Questionnaire and the Italian Spine Youth Quality of Life (ISYQOL) questionnaire
5. Completion of GSM App Feedback Questionnaire (optional)
6. Safety Check: Query for adverse events and other issues
7. Performance Check:
    a. If the Cobb angle measures no more than 10 degrees greater than that obtained from the subject's most recent out of brace radiograph (prior to enrollment), we will conclude the curve is stable or has progressed within the expected limit. If not, the subject will resume use of the TLSO.
    b. If curve stabilization is seen, subjects may opt to continue the GSM brace or resume use of their TLSO based on subject and parent preferences.

**Ongoing Evaluations after Visit 3 (following the standard-of-care until GSM brace is discontinued)**

For subjects continuing to use the GSM brace after Visit 3: Subject clinical care and evaluations (x-rays, clinical exams) after Visit 3 will be limited to that typically performed as the standard of care (SOC). The exception to the SOC will be the administration of the BrQ and ISYQOL at the end of treatment, ongoing monitoring and recording of AE's discovered during routine clinic visits or other communications, and temperature monitoring (at sites where this is not typically SOC). Clinical and radiographic data from these visits will be collected for study purposes (height, weight, onset of menses, Cobb angle(s), kyphosis, lordosis, coronal and sagittal balance, apical vertebral rotation, in-brace Cobb angle(s), and skeletal maturity indicators) as available.

GSM brace treatment will be discontinued using individualized SOC parameters such as Cobb angle and skeletal maturity indicators, at which time the subject will exit the study.

**Exit From Study**

Subjects will exit the study upon occurrence of the following events

1. Visit 2. GSM in-brace Cobb is >10° more than the TLSO in-brace Cobb
2. Subject not wearing or tolerating GSM brace (per temperature monitor reading 2 weeks after baseline, or at any time during study period)
3. Visit 3. GSM out-of-brace Cobb indicates curve progression
4. GSM brace is discontinued using standard of care criteria

**Additional Information on Assessments**

Radiographs and Assessments: When available, radiographs will be obtained using the EOS® Imaging system Micro Dose protocol. The EOS® system provides low dose, full body, stereo-radiographic images of patients in a functional position. It is a bi-planar device using two perpendicular fan beams of X-rays and proprietary detectors that travel vertically while scanning the patient. In a few seconds, the EOS® exam produces two simultaneous frontal and lateral, low dose images of the whole body or an anatomical segment. The Micro Dose option for pediatric follow up exams further reduces the radiation exposure. http://www.eos-imaging.com/us/professionals/eos/eos.

Participating sites who do not have access to the EOS® Imaging system Micro Dose protocol are allowed to use their existing equipment. However, they are responsible for calculating the amount of research-related radiation and the potential risks, to include this information in IRB/human subjects research application materials, and to relate this information to the subject via the informed consent document as required by the IRB or equivalent review board.

In addition to the Cobb angle, other components of the deformity will be measured, including kyphosis, lordosis, apical vertebral rotation, and coronal and sagittal balance.

Spiropet

Vital capacity will be estimated using the Spiropet portable spirometer. Subjects will be instructed to inhale as deeply as possible and to then exhale completely over 5 to 6 seconds through the spirometer. This will be repeated 2 times, with a minimum of 30 seconds in between trials. Disposable mouthpieces are used to prevent contamination across subjects. https://www.fitnessmart.com/products/spiro-pet-small-dry-spirometer-model-64450?variant=29708592263

Temperature Monitors to Estimate Brace Adherence

Participating sites are encouraged to use their standard-of-care brace temperature monitors/loggers. If the site has not been using a monitor to estimate brace wear, the sponsor will provide iButtons and the required hardware/software.

The iButton™ is a commercially available electronic device which records and stores time, date and temperature readings. The logger will be set to record date, time and temperature every 15 minutes. The temperature range at which the brace is assumed to on will be set at 82.4°F and 110°F. Validation of the accelerometer data as an estimate of the number of hours per day that the subjects are wearing the brace will be done via comparison with data from a temperature logger. The reliability and validity of iButton™ data for estimating wear time has been demonstrated in several published reports. [27-29] (iButton™ DS1922L" https://www.thermochron.com/product/ds1921g-thermochron/?gclid=EAIaIQobChMI5t-G1K6G3QIVRMDICh1A2gDSEAAYASAAEgL1YvD_BwE (Maxim Integrated Products, Inc.; 120 San Gabriel Drive, Sunnyvale, CA 94086).

Questionnaires

The Brace Questionnaire (BrQ, 34 items [30]) and the Italian Spine Youth Quality of Life Questionnaire (ISYQOL, 20 items [31]) are validated measures of health-related quality of life in patients being treated for spinal deformities. An item directly asking the subject how much they like their brace was added for this study. The GSM Brace Diary was created specifically for this study based on the Scoliosis Compliance Questionnaire. [17] The diary lists several daily activities (e.g. time at home, time at school, sports, being with friends, walking, bending, taking brace on and off) and asks the subject to rate how challenging they were that day on a 5-point Smiley Face scale from laughing to crying. The diary also includes questions about pain and discomfort in the brace, and a free text area for the subject to record any other comments they have related to brace wear.

GSM Brace Mobile App (optional)

Subjects will be able to opt in or out of use of the app. The app was developed by GSM specifically for this pilot and is available free-of-charge to interested subjects. The app is available for IOS and Android via the App Store and Play Store. Security functions have been built into the app to maintain confidentiality, integrity and availability as referenced by the NIST cybersecurity framework, HIPAA and the FDA. Updates are validated through Apple and Google stores. The app is not intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation or treatment or prevention of disease and is therefore not considered a medical device and is outside of FDA purview. According to FDA guidance, the app poses minimal risk to the user as it is solely intended to help users self-manage their disease (track brace wear time) and does not provide any specific treatment suggestions.

The mobile app connects to the sensor in the brace and downloads the data. Once the data are downloaded, the app uploads the data to a cloud-based server. The mobile app queries the server for the wear-time estimates and displays them graphically on the mobile device. All data

transfers (brace to app, app to cloud, cloud to app) are encrypted, as are the data stored on the server. The server keeps a record of the transfer details for an audit trail, including the following: Serial number of the sensor in the brace, unique user ID, battery level in the sensor, sensor firmware version, mobile app version, records transferred and time of transfer. The permissions required by the app include: Location, USB storage, and network access, Bluetooth settings and Bluetooth pairing. The app's Privacy Policy (as of July 2, 2019) discusses sharing data from the app with health care professionals via an interactive platform if permission is granted by the user and the provider. This function is not available at this time, and there are no plans to share app data with anyone but the subject during this pilot study. Directions for accessing and using the app will be provided to the families (GSM App Instructions, attached). The server (and the software residing on the server) are managed by Mindset Medical. Green Sun Medical has a Business Associate Agreement with Mindset Medical that satisfies HIPAA requirements.

### 5.1.2 BRACE CUSTOMIZATION, DOSING AND ADMINISTRATION

The GSM braces will be provided directly to the research team by the company at no cost. Each GSM brace will be custom-fabricated via computer-assisted design using the 3D torso scans and a treatment plan (e.g. placement of corrective forces) devised by the treating orthotist as inputs. The brace components are then assembled. Once assembled, the GSM brace will be fit to the subject by representatives of the manufacturer and in consultation with the treating orthotist.

The GSM brace will be prescribed for the same number of hours per day as was the TLSO (generally 18-22 hours per day, individualized based on patient characteristics). Subjects and the family will be shown how to don and doff the brace, how to remove the temperature monitor, and how to exchange and recharge the battery in the GSM sensor board.

## 5.2 RISK/BENEFIT ASSESSMENT

### 5.2.1 KNOWN POTENTIAL RISKS

GSM brace: The GSM brace is a non-significant risk device. The FDA defines a significant risk device under 21 CFR 812.3(m) as:

1) Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
2) Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;

3) Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
4) Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject

A non-significant risk device is any device that does not meet those criteria. While the device is intended for treating the disease of scoliosis, as are TLSO's, the GSM is not an implant and does not meet the criteria defined in 1 and 2 above. The FDA defines serious risk as potential harm to subjects that could be life-threatening, could result in permanent impairment of a body function, or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure. There are no risks associated with this device that could be categorized as serious.

The GSM Dynamic Orthosis is a brace worn externally over the torso of a patient. It has been designed to provide forces of similar magnitude to current standard-of-care braces.

There are no known or suspected risks directly associated with the GSM brace. The performance and safety checks built into the protocol should theoretically insure that use of the GSM brace does not adversely affect the longer-term outcome relative to what was anticipated if only the TLSO was used. However, it is difficult to predict the results of a TLSO for any individual patient and we cannot know with any certainty, given the design of this pilot study, whether or not the GSM brace influences the risk of a successful outcome.

Rare adverse events have been reported related to the use of TLSOs. [7] Most events involve loss of skin integrity (rash, bruise, irritation) due to pressure from the brace on the skin. Some change in the skin is expected in response to the corrective forces, but loss of integrity should not occur. The risk of these events will be mitigated by careful fitting of the GSM brace and by advising subjects to immediately report any areas of discomfort so the brace can be adjusted. In addition, patients using rigid TLSOs have reported issues with body image and self-esteem, depression and anxiety, although it is not clear that these concerns are directly related to brace wear or to the diagnosis itself. There is no reason to believe that these events or concerns would be any more frequent or severe during the use of the GSM brace, and may be less frequent. Subjects will be followed closely via phone calls every 2 weeks and queried about concerns/events related to brace wear.

Study-related Radiation: All subjects will have research-related coronal radiographs while 1) wearing their TLSO at baseline, 2) in the GSM brace after 1 week of wear, and 3) out of the brace after 3 months of wear. Three additional in-brace coronal radiographs may be obtained at the discretion of the orthotist or investigator in order to maximize the fit, correction, and comfort of the brace and/or check the effect of brace modifications. The total number of research-related radiographs will not exceed 6.

Other than ionizing radiation, here are no valid and reliable methods currently available to directly assess the spine's response to a scoliosis brace. The frequency of radiographs during brace treatment for AIS varies, but in general, radiographs are obtained prior to initiation of a brace, in the brace anywhere from the day the brace is fit to 6 months afterward, and then every 4-6 months until criteria for brace discontinuation is met. Since subjects will enter this study at different times during their treatment, we cannot anticipate which, if any, of the radiographs obtained in this study should be considered standard of care. Therefore, all radiographs obtained between consent and Visit 3 will be considered study-related.

A urine pregnancy test will be administered to all subjects who are of child-bearing potential. If the test is positive, the subject will exit the study.

When available, participating sites should obtain the study radiographs using the EOS® Micro Dose protocol. Use of this protocol results in significantly decreased radiation exposure to the subject relative to standard digital radiography. Comparisons of the EOS® Micro Dose protocol with digital radiography indicate a significant decrease in radiation exposure (0.02 mGy vs. 1.66 mGy; [32] 2.6µSV vs. 67.5 µSV [33]) for a full spine coronal plane radiograph. Attached correspondence from the University of Iowa Medical Radiation Protection Committee (advisory to the University of Iowa Institutional Review Board) estimates 1 coronal full spine radiograph using the EOS® Micro Dose protocol would expose the subject to an effective dose equivalent of 0.25 mrem, which is about equal to the average environmental radiation everyone experiences in 1 day. The maximum study-related effective dose equivalent will total approximately 3 mrem of radiation. The maximum total exposure for all study-related radiation is approximately equal to the amount of radiation everyone experiences in 3 days.

**Participating sites who are not using the EOS® Micro Dose protocol will be responsible for calculating the amount of research-related radiation and the potential risks, to include this information in IRB/human subjects research application materials, and to relate this information to the subject via the informed consent document as required by the IRB or equivalent review board.**

Spirometry: There are no risks associated with use of the Spiropet spirometer. Subjects may stop the testing at any time if they feel uncomfortable.

Privacy and confidentiality: The risk to privacy will be minimized by performance of study procedures in a private area whenever possible. Only data necessary to address the study aims will be collected. Subjects will be informed they can skip any questions they do not feel comfortable answering. Risk to confidentiality will be minimized by using study ID's in lieu of other identifiers to identify subject data. ID's will be assigned in order of enrollment within site (e.g. 2-digit site ID_01, 2-digit site ID _02, etc.), and their link to the subject's identity will be maintained in a file separate from study data. Other risks to confidentiality will be minimized by storage of paper forms in a locked office and electronic data in a password-protected file in a password-protected computer. Only data conforming to the definition of a HIPAA limited dataset will be transmitted over the Internet. Entries in the screening log will be deleted as soon as a decision about participation is made, or at the close of the study if the patient has not yet made a decision.

Subjects opting to install and use the GSM Brace Mobile App may risk loss of confidentiality if their mobile device is lost, stolen, borrowed or if the subject accesses the app in view of others. The App or Play stores may track download and installation. Loss of confidentiality is minimized by using non-identifying information to register; subjects will use their Study ID and City in lieu of their name, DOB will be entered as January 1, 2019 and a non-functioning email address (Study ID@greensunmedical.com) will be entered. Additionally, the permissions required by the app include: Location, USB storage, network access, Bluetooth settings and Bluetooth pairing, but not other data such as contacts, photos, texts, or email. Persons other than the subject will not be able to access data from the sensors unless they 1) download the app and 2) are in close proximity to the subject's brace (<10 feet) to pair with their device. All data transfers (brace to app, app to cloud, cloud to app) are encrypted, as are the data stored on the server. The server (and the software residing on the server) are managed by Mindset Medical. Green Sun Medical has a Business Associate Agreement with Mindset Medical that satisfies HIPAA requirements.

Only for subjects enrolled at sites where compensation will come directly from the Sponsor/U of Iowa: If subjects agree to share their name and contact information with the University of Iowa for purposes of compensation, this information will be given to Lori Dolan over the phone or via fax.

### 5.2.2 KNOWN POTENTIAL BENEFITS

The subject may benefit from treatment in the GSM brace in terms of curve correction, curve stabilization and increased comfort (relative to their standard of care TLSO) while wearing the GSM brace, although the potential for longer-term benefit is unknown.

### 5.2.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

This study presents minimal risk with the potential for benefit.

## 5.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

It will not be possible to blind the subject or the assessors to the study condition (type of brace) due to their unique characteristics (which is also visible in the radiographs). All radiographic measurements will be made by the site PI's or their delegates and verified by the medical advisor (Weinstein).

## 5.4 COMPLIANCE WITH STUDY INTERVENTION

The use of the device will be primarily monitored via the temperature monitor data. A secondary aim involves using the temperature monitor data to validate inferences about compliance using data from the force and accelerometer sensors built into the GSM brace.

## 5.5 CONCOMITANT THERAPY

Subjects will be encouraged to continue with any concomitant therapy and activities during the study (e.g. physical therapy, chiropractic, massage, yoga, school, sports).

## 5.6 COMPENSATION TO SUBJECTS

Subjects will be compensated $25 after visits 1 and 2, $25 for Visit 3 and then $10 for each additional week during the 3 month period (10 weeks), for a possible total compensation of $175. Payment will be issued within 1 month after Visit 2, and within 1 month after the subject exits the study. Payments will be pro-rated according to the number and type of visits completed.

# 6 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

## 6.1 DISCONTINUATION OF STUDY INTERVENTION

The intervention will be halted by the investigators if:

1. Equivalent or improved in-brace correction is not obtained at the Week 1 visit
2. If the subject is not able/willing to wear the GSM brace for approximately the same number of hours as the TLSO
3. Safety concerns are noted by the PI, study staff and/or the medical monitor
4. Radiographic evaluation at Visit 3 suggests that the curve is not stable (has progressed more than 10 degrees)
5. If the parent/subject, investigator or medical monitor feel that continuation of treatment in the GSM brace is not in the best interests of the subject. Ongoing care will be individually determined based on standard of care considerations.

Once the GSM brace is discontinued, continued follow-up for safety and efficacy are not required.

## 6.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

1. Participants will be withdrawn from the study in the event of a positive pregnancy test or reports of a suspected pregnancy.
2. Participants may withdraw voluntarily from the study or discontinue use of the GSM brace at any time. Participants who wish to stop wearing the GSM brace will be instructed to notify study staff so that treatment can be resumed using the TLSO brace.

Participants will be instructed to contact the study staff (PI, orthotist or coordinator) at any time to discuss issues they may be having with the GSM brace or with any other aspect of the protocol. Study staff will attempt to make any modifications to the brace or other aspects of the protocol necessary to mitigate these issues and maintain the participant on protocol.

## 6.3 LOST TO FOLLOW-UP

Participants will be considered lost to follow-up if they cease to report for study visits and do not respond to our attempted contacts. Staff will contact participants by phone at 2 weeks after GSM brace initiation and at least monthly to address questions and issues. Subjects will be queried for any questions or concerns, and for the occurrence of anticipated and unanticipated adverse events.

Study staff will accommodate the participants' schedule in order to minimize missed study visits. In the case of a missed visit, staff will attempt contact via three phone calls and/or emails each 1 week apart.

Completion of the questionnaires and diaries will be encouraged but not required.

# 7 STUDY ASSESSMENTS AND PROCEDURES

## 7.1 PERFORMANCE ASSESSMENTS

1. Primary performance measures
    1. Visit 2 GSM in-brace Cobb angle compared to that in the TLSO at baseline
    2. Visit 3 out of brace Cobb angle compared to measurements from the most recent out of brace radiograph
    3. Average hours of GSM brace wear per day over the 3-month trial period (temperature monitor data)
    4. Change in scores on the Brace Questionnaire and the ISYQOL
2. Secondary measures
    1. Vital capacity and range-of-motion relative to that obtained in the TLSO at Visit 1
    2. Accelerometer data (obtained from an embedded sensor in the GSM brace) as an estimate of the average hours of wear per day (to be validated by comparison with temperature monitor data)

## 7.2 SAFETY ASSESSMENTS: ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

Safety will be monitored continuously during the trial

### 7.2.1 DEFINITION OF ADVERSE EVENTS (AE)

The following AE's are anticipated and related or possibly related to brace wear or to the diagnosis of AIS:

- Skin Issues (on the trunk, shoulders or any other area in contact with the brace): bruising, lacerations, ulcers, pressure sores, rash. Most skin issues are classified as mild and can be alleviated by minor adjustments to the brace.
- Back pain
- Anxiety
- Problems sleeping
- Shortness of breath
- Altered body image or self-esteem

### 7.2.2 DEFINITION OF SERIOUS ADVERSE EVENTS (SAE)

Death

Life-threatening conditions

Hospitalization

Disability

A condition requiring intervention to prevent permanent impairment/damage

## 7.3 CLASSIFICATION OF AN ADVERSE EVENT

### 7.3.1 SEVERITY OF EVENT

Mild = not requiring treatment

Moderate = resolved with treatment

Severe = unable to carry on normal activities and required professional medical attention

### 7.3.2 RELATIONSHIP TO STUDY INTERVENTION

Unrelated

Possibly related

Related

### 7.3.3.3 EXPECTEDNESS

Unexpected

Expected (described in the protocol and/or Investigator's Brochure)

### 7.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

AE's will be solicited at each study visit, during the scheduled phone contacts and as often as daily via subject report on the questionnaires

Unsolicited AE's may be identified via observations and general discussions with the subject and/or parent at the study visits

### 7.3.5 ADVERSE EVENT REPORTING

Events will be recorded on the Adverse Event case report form as they are identified

All events will be reported to the sponsor upon identification

All unanticipated events will be reported to the IRB on continuing review applications or close of study (or according to local IRB policy).

Adverse event forms will be sent to the medical monitor every 2 weeks during the study, who will then summarize the AE's in a report to the sponsor and IRB.

### 7.3.6 SERIOUS ADVERSE EVENT REPORTING

All unanticipated serious adverse events will be reported within 48 hours of identification to the sponsor, medical monitor and the IRB (or as required using local standards)

### 7.3.7 REPORTING EVENTS TO PARTICIPANTS

All moderate or severe, possibly related or related events will be reported to subjects who are currently wearing the GSM brace via a phone call from the PI within 48 hours of identification

## 8 STATISTICAL CONSIDERATIONS

### 8.1 SAMPLE SIZE DETERMINATION

Study-wide, recruitment will continue until at least 10 but no more than 30 subjects have completed 3 months in the GSM brace. The final sample size will depend on an ongoing examination of the results, patient comments, input from medical monitor and the discretion of the sponsor. Therefore, if a subject exits the study prior to that point, another subject will be enrolled. The sample size is appropriate for initial field testing of this device and no sample size calculations were conducted.

### 8.4 STATISTICAL ANALYSES

This is a pilot study and no formal hypothesis testing will be done.
Descriptive statistics of selected variables will be calculated.

Primary Aims

1. Safety of the GSM brace: Summary of all adverse events; number and nature of adjustments made to the GSM brace
2. Performance of the GSM brace:
    a. Difference between in-brace Cobb angle measurements obtained in each brace
    b. Difference in out of brace Cobb angles (pre- and 3 months post-GSM brace)
    c. Average hours of wear per day relative to the prescription and to historical wear data (from chart and temperature monitor)
    d. Change in BrQ and ISYQOL scores baseline to 3-month visit; summary of GSM acceptability during various activities and qualitative analysis of free text entries recorded in GSM Brace Diary

Secondary Aims

1. Difference in range-of-motion testing between TLSO and GSM brace
2. Difference in vital capacity testing between TLSO and GSM brace

3. Correlation of accelerometer data and temperature monitor data; development and testing of an algorithm to convert accelerometer data to an estimate of the average hours of wear per day.

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# Appendix 1.

## Green Sun Medical Pressure-Sensor Equipped Pad Clinical Validation

**Substudy of the Pilot Trial Green Sun Medical Dynamic Brace**

**Protocol Version 1.0**

**14 Jan 2021**

Substudy participation is optional for subjects newly enrolled in the Pilot trial. Twelve subjects at select participating sites will be enrolled.

### 1. BACKGROUND

Spinal orthotics (braces) are effective in preventing curve progression in patients with adolescent idiopathic scoliosis. Braces work by providing corrective forces to relevant areas of the spine, but little is known about the amount of force required, or how forces change during activities and over time in response to changes in the shape of the patient's spine and torso. Therefore, it is important to be able to accurately measure these forces over the patient's course of treatment and to understand how much variation is normal, and when variation indicates that modifications need to be made to the brace in order to optimize its effectiveness.

The GSM engineering team has developed a smart pad sensor system capable of detecting changes in force magnitude and direction, but to date, the sensor system has only been evaluated on a test fixture. The smart pad sensor system of the GSM brace captures force data in two ways: interval and conditional. As the name implies, interval sampling captures sensor data at a consistent sampling rate. The objective of the conditional sampling is to capture force data when the patient and their brace are in a consistent state. This conditional sampling allows for a much more meaningful relative measure of brace performance. A conditional sample is triggered by the donning of a brace after the brace has been off the patient. Each interval force log includes the following data: 1) timestamp 2) voltage measurements for each of eight sensors embedded in the pad, and 3) readings from a 3-axis accelerometer. Each conditional force log includes the following data: 1) timestamp, 2) voltage measurements for each of the eight sensors, 3) readings from a 3-axis accelerometer, 4) the algorithmically determined force value (FV), and 5) the algorithmically determined X-Y coordinates for an equivalent point load. The smart pad system integrates with the standard sensor system placed in all braces and the data can either be stored and downloaded by the research team at study visits, or, if the subject is participating in the optional GSM Brace Wear Mobile App substudy, the data are uploaded to cloud storage when the subject syncs with the sensor.

## 2. OBJECTIVE

The primary goal of this substudy is to validate the ability of a pressure-sensor equipped pad (GSM Smart Pad, smart pad) to accurately and reliably measure static and dynamic forces through a combination of lab and field testing using human subjects enrolled in the GSM Pilot study.

## 3. PROTOCOL

Evidence for the accuracy and reliability of the force values generated by the smart pad system will be inferred via a series of comparisons to known forces and to a gold-standard measurement system (Tekscan pressure map/I-Scan™ system) both in the lab and in field testing with patient subjects. Analyses of repeated measures within each smart pad and between smart pads will be performed.

Lab Testing Materials and Methods

Lab Testing Phase 1. Twelve smart pads will be fabricated for testing and serialized in order to track performance over time. A benchtop test fixture will apply loads of 100N, 110N, 136N and 150N maintained for five minutes each with a 0-N dwell of 5 minutes in between loads. Loads will be applied in four rotational positions: neutral, 10-degree rotation from neutral, 20-degree rotation from neutral, and 30-degree rotation from neutral. Each of the 16 unique loading scenarios (magnitude x direction) will be run 10 times. The average force value under each of these conditions will be saved and analyzed. These 12 smart pads will then be used in field testing.

Lab Testing Phase 2. The smart pads removed from the brace at the 30-day follow-up visit will undergo repeat testing on the bench test fixture under the same 16 loading conditions.

Field Testing Materials and Methods

*Subjects*

Twelve subjects will be recruited from multiple sites to participate in the field testing. We will draw from the pool of patients who have consented to participate in the GSM Brace Pilot study. They will be told that participation in both studies is completely voluntary. Enrolled subjects may choose to stop participating at any time.

*Visits and Procedures*

Subjects in the substudy will undergo all procedures/assessments as those in the Pilot study. Participation in the substudy will last for approximately 1 month. One additional study visit will be required at approximately 1 month after Baseline. Otherwise, substudy procedures will

occur coincident with the Baseline, 1-week and 3-month follow-up visits in the Pilot protocol.

Baseline Visit. Subjects in the substudy will receive a GSM brace that includes one of the serialized smart pads tested during Lab Testing Phase I. No additional procedures or assessments for the substudy occur at this visit.

Visit 2 (1-2 weeks after Baseline). Substudy procedures will add approximately 1 to 1.5 hours to the total duration of this study visit. The following procedures/assessments will take place in addition to the Pilot study activities (in-brace x-ray, safety check):

1. Calibration of the pressure map. The Tekscan pressure map is a very thin, flexible material embedded with force sensors to measure the magnitude and distribution of force exerted over an area. This map must be calibrated prior to use. To calibrate the map, the orthotist and research team will establish the area where the brace's thoracic pad would contact the subject's torso. The pressure map is then placed against the subject's torso with the smart pad (not yet attached to the brace) is centered over the map. A handheld force gauge (Mark 10 Series 4) is pressed on the smart pad to successively apply 80-N and 120-N forces to the patient for a period of less than 1 minute each. These known forces are then used by the I-Scan™ system to calibrate the pressure map for subsequent readings.
2. The smart pad is then placed in the GSM brace. The subject will don (put on) the brace, and the research team will place the pressure map between the subject's torso and the smart pad. The orthotist will assist the subject to adjust the strap tension and position of the brace. The subject is then asked to stand for 5 minutes in a normal posture with minimal spinal flexion or extension.
3. The subject will then be asked to doff (remove) the brace for 5 minutes.
4. Steps 2-3 are repeated for a total of four don-doff trials. During these trials, both the pressure map and the smart pad will capture force data. The smart pad will capture interval data once per minute; the don and doff trials will trigger the algorithm to capture one conditional sample for each trial.

Interim Between Visit 2 and the 1-Month Visit. The subject will continue to wear the GSM brace with the smart pad for a period of approximately 30 days. During this time, the smart pad will continuously capture data. These data will stored on the device and transmitted to the cloud when the device is paired with the GSM mobile app (if the subject is also participating in the optional GSM Brace Wear Mobile App study). If the subject does not pair with the device during this period, the data will be retrieved by the research team at the 1-month visit.

1-Month Visit (substudy subjects only). The smart pad will be removed from the subject's brace for Lab Testing Phase II and a replacement smart pad will be installed. The same set of

procedures completed during Visit 2 will be repeated (calibration of the Tekscan pressure map system via application of known 80-N and 120-n forces, data collection during donning and doffing). This visit will last approximately 1-1.5 hours.

## 4. RISKS

Subjects in the substudy should experience no additional risks beyond those encountered during participation in the Pilot study. The same safety and performance checks will be completed (e.g. if a subject does not have adequate correction in the GSM brace, or is unable to wear the brace the recommended number of hours, then the subject will exit the Pilot and the Validation substudy).

Tekscan pressure maps and the sensors embedded in the smart pad have been used in both lab and field tests without safety concerns. Applying forces of 80-N and 120-N should not cause the subject any discomfort as similar forces are applied by a typical scoliosis brace during normal wear. However, if a subject complains of discomfort, the team will withdraw the pressure immediately.

The data offloaded from the Tekscan pressure map/I-Scan™ system and the smart pad will be tagged only with the subject's study ID but no direct identifiers. These data will be treated with the same confidentiality measures as data from the Pilot study.

## 5. BENEFITS

The subjects in the substudy will experience no direct benefit from participating. However, we hope their participation will lead to a sensor pad-based pressure monitoring system that can be used to optimize scoliosis brace treatment in the future.

## 6. COSTS

Subjects in the substudy may incur uncompensated costs associated with the longer Visit 1 duration and the additional 1-month visit. These costs are in addition to those already incurred by participation in the Pilot study (e.g. travel, parking, loss of work/school time).

## 7. COMPENSATION

Subjects will be compensated $50 for their participation in the 1-month substudy visit.

## 8. SAMPLE SIZE CALCULATIONS AND STATISTICAL ANALYSIS

No formal sample size/power calculations were done to arrive at the sample of 12 subjects. Given the large number of repeated measures data to be collected, and given the results from earlier bench work, we anticipate data from 12 subjects are adequate to attain the precision necessary to make informed decisions about the accuracy and reliability of the sensors in this study.

Lab Testing Analysis: The distribution of force values generated by each smart pad unit under each scenario will be characterized by the mean, standard deviation and coefficient of variation (CV, ((mean/s.d)*100)).

1. The inter- and intra-unit reliability of the force measures will be inferred by testing the variation of the means and the CsV within and between the 12 smart pad units under each of the 16 scenarios using the R package cvequality (Version 0.1.3; Marwick and Krishnamoorthy 2019) and repeated measures ANOVA. The quality control standard will be set at a CV of 5% or less. Units that demonstrate CsV >5% will not be used in the field testing.
2. Reproducibility/durability of smart pad measurements will be assessed using repeated measures ANOVA comparing Test 1 to Test 2 measures.

Field Testing Analysis

1. The force values measured by the I-Scan system and the smart pad during the Baseline and 1-Month visits will be compared using repeated measures analysis of variance.
2. The means and CsV of the force values over the 30-day wear period will be evaluated, looking for changes over time, and within and between Active and Rest periods using repeated measures ANOVA.
3. A regression model will be derived to convert each 24-hour set of force values to an estimate of the number of hours the brace was worn, using the temperature monitor output as the gold standard. The predictive accuracy of the smart pad model will be assessed using calibration plots and other error estimates.

# Appendix 2.

Protocol Amendment Version 1.3/1.4 to Version 2.0
Summary of Changes
Version Date 14 Jan 2021

Summary of Major Revisions Made:

Adding Appendix 1.0 Optional Substudy Protocol "GSM Pressure-Sensor Equipped Pad Clinical Validation"

| | Version Number | Version Date |
|---|---|---|
| Current Approved Protocol | 1.3/4 | 27 Aug 2019 |
| Amended Protocol | 2.0 | 14 Jan 2021 |

1. **Section 1.3 Green Sun Medical Dynamic (GSM) Brace**

New Text: Green Sun Medical Dynamic (GSM) Brace (also known as the Green Sun Medical Whisper Brace™)

2. **5.1.2 Study Procedures**

Old Text: All study-related radiographs will be obtained using the EOS® Imaging system Micro Dose protocol.

New Text: All study-related radiographs will be obtained using the EOS® Imaging system Micro Dose protocol (when available). If an EOS system is not available, please see **Additional Information on Assessments.** Radiographs and Assessments, and **5.2.1 Risks** for further information).

Rationale for Change: The original intent was to only enroll subjects at sites with access to EOS® Imaging systems. The trial has since been opened up to sites who use other digital imaging systems.

3. **5.1.2. Study Procedures**

Old Text: Orthotimer

The Orthotimer is a commercially available electronic device which records and stores time, date and temperature readings. Software converts the readings to estimates of brace wear time. These devices have been used at the National Scoliosis Center for several years. The Orthotimer results will be used to determine the average daily hours of wear in the GSM brace and to validate estimates of wear time using data from the accelerometer built into the GSM brace. http://www.orthotimer.com/en/

New Text: Deleted description of the Orthotimer.

Rationale for Change: No sites in the study are using the Orthotimer. Text changed to allow sites to use their standard-of-care compliance monitors, or to be provided with iButtons by the sponsor.

4. **Appendix 1.** Green Sun Medical Pressure-Sensor Equipped Pad Clinical Validation
   Rationale for Change: Appended Protocol Version 1.0 14 Jan 2021 for the optional substudy.

5. **Administrative changes:** Minor changes involving grammar, wordsmithing, punctuation, and other editorial changes have been made throughout the document. All are clearly identified in the track-changes version of the amendment.