Medtronic

Clinical Investigation Plan

Clinical Investigation Plan/Study Title	A Prospective, Multi-Center Study of the Medtronic Braive™ Growth Modulation System When Used in the Treatment of Pediatric Patients Diagnosed with Juvenile or Adolescent Idiopathic Scoliosis (BRAIVE IDE Study)
Clinical Investigation Plan Identifier	MDT19009SD1901 EUDAMED number will be provided under a separate cover, when applicable
Study Product Name	Braive™ Growth Modulation System (Braive™ GMS)
Sponsor/Local Sponsor	Medtronic Sofamor Danek USA, Inc. 1800 Pyramid Place Memphis, TN 38132 USA **Local sponsor – EU Legal Representative:** Medtronic Bakken Research Center BV Endepolsdomein 5 6229 GW Maastricht The Netherlands **Local Sponsor - Canada:** Medtronic of Canada ULC. 99 Hereford St. Brampton, ON L6Y 0R3 Canada +1-905-460-3800
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Confidentiality Statement

1. Investigator Agreement and Signature Page

Study product Name	Braive™ Growth Modulation System
Sponsor/Local sponsor	Medtronic Sofamor Danek USA, Inc. Local sponsor Europe: Medtronic Bakken Research Center BV Local sponsor Canada: Medtronic of Canada ULC
Clinical Investigation Plan Identifier	MDT19009SD1901
Version Number/Date	7.0 / 07 June 2023

I have read the protocol, including all appendices, and I agree that it contains all necessary details for me and my staff to conduct this study as described. I will conduct this study as outlined herein and will make a reasonable effort to complete the study within the time designated.

I agree to comply with all applicable regulations and guidelines under which the study is being conducted, e.g., United States Food and Drug Administration regulations (In US, 21 CFR part 11, 50, 54 and 812 apply and in Europe/Canada 21 CFR part 11 and 54 apply), International Standard ISO14155:2020 and ethical principles that have their origin in the Declaration of Helsinki 2013 and the clinical trial agreement.

I agree to conduct the study in compliance with country, local and internal institutional requirements. I agree to ensure that the confidential information contained in this document will not be used for any purpose other than the evaluation and conduct of the clinical investigation without the prior written consent of Medtronic.

I will provide all study personnel under my supervision copies of the protocol and access to all information provided by Medtronic. I will discuss this material with them to ensure that they are fully informed about the products and the study.

Investigator's Signature:	
Investigator's Name:	
Institution:	
Date:	

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2. Glossary

Term	Definition
ADE	Adverse Device Effect
AE	Adverse Event
AIS	Adolescent Idiopathic Scoliosis
APPT	Adolescent Pediatric Pain Tool
AVBT	Anterior Vertebral Body Tethering
CIP	Clinical Investigation Plan or Protocol
DD	Device Deficiency
DSM-5	Diagnostic and Statistical Manual of Mental Disorders 5
EC	Ethics Committee
eCRF	Electronic Case Report Form
EEA	European Economic Area
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
GMS	Growth Modulation System
IC	Informed Consent
ICH	International Conference on Harmonization
IDE	Investigational Device Exemption
Idiopathic Scoliosis	A lateral curvature of the spine that occurs during growth, the cause of which is unknown.
IFU	Instructions for Use
IRB	Institutional Review Board
IRB/EC/REB	Institutional review board/ethics committee/research ethics board

ISO	International Organization for Standardization
JIS	Juvenile Idiopathic Scoliosis
MEDDEV	Medical Device Directives
Medtronic	Medtronic Sofamor Danek USA, Inc.
PedsQL	Pediatric Quality of Life Inventory™
PHI	Protected Health Information
Protocol	Clinical Investigation Plan
SADE	Serious Adverse Device Effect
RA	Regulatory Authority
RDC System	Remote Data Capture System
REB	Research Ethics Board
SAE	Serious Adverse Event
SID	Subject Identification
SQV	Site Qualification Visit
SRS-22	Scoliosis Research Society 22 Patient Questionnaire
TPD	Therapeutic Products Directorate
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect
VAS	Visual Analog Scale
VBT	Vertebral Body Tethering

3. Synopsis

Title	A Prospective, Multi-Center Study of the Braive™ Growth Modulation System When Used in the Treatment of Pediatric Patients Diagnosed with Juvenile or Adolescent Idiopathic Scoliosis (BRAIVE IDE Study)
Clinical Study Type	Interventional, prospective, multi-center, single-arm study
Product Name	Braive™ Growth Modulation System (Braive™ GMS)
Sponsor	Medtronic Sofamor Danek USA, Inc. 1800 Pyramid Place Memphis, TN 38132 USA **Local sponsor– EU Legal Representative** Medtronic Bakken Research Center BV Endepolsdomein 5 6229 GW Maastricht The Netherlands **Local Sponsor (Canada)** Medtronic of Canada ULC. 99 Hereford St. Brampton, ON L6Y 0R3 Canada
External Organizations	Radiographic Review Core Lab (used for eligibility assessment of currently enrolled subjects): Medical Metrics, Inc 2121 Sage Road, Suite 300 Houston, TX 77056 USA This information may be subject to change during the course of the study. Periodic updates to study contact information will be sent to study sites as needed.
Indication under Investigation	The Braive™ GMS is indicated for use in the treatment of juvenile idiopathic scoliosis (JIS) or adolescent idiopathic scoliosis (AIS) in skeletally immature patients with Cobb angles between 30 and 60 degrees, who have failed conservative care, have a Sanders score of ≥2 to ≤5 or a Risser score of 0 to 2, have kyphosis of less than or equal to 40 degrees with a sagittal thoracic modifier N or negative, and have a Lenke Classification of 1A, 1B, or 1C. In the United States (US) the device will be investigational, and an investigational device exemption (IDE) approval was obtained before the study was initiated.

	In Canada, the device will be investigational and an Investigational Testing Authorization (ITA) was obtained before the study was initiated. In Europe the device was CE marked at the time of surgery and therefore the study will be conducted within the approved indication. Medtronic has decided to not renew EC certification for the Braive GMS 24th March 2023. This decision was not based on concerns regarding patient safety.
Investigation Purpose	The purpose of this study was to establish probable benefits and evaluate the safety and preliminary effectiveness of the Braive™ GMS when used in the treatment of JIS and AIS. A Humanitarian Device Exemption (HDE) was to be submitted to FDA when all available 24-month follow-up data had been collected. The collected data were to be used to support regulatory applications to seek market approval in US and potentially other geographies, and to confirm long-term clinical performance and safety of the CE-marked Braive™ GMS. In March 2023, Medtronic made the decision to discontinue the BRAIVE program. All sites, therefore, have been notified to discontinue study enrollment and there are no plans at this time to utilize collected data to obtain Humanitarian Device Exemption (HDE) approval. This decision is not associated with any safety or efficacy observations from the study, and Medtronic has not received stopping recommendations from the Data Monitoring Committee or any regulatory bodies.
Product Status	Braive™ GMS is investigational in the United States and Canada and it was CE marked in countries that require CE at the time of patient surgery.
Primary Safety Objective and endpoint	Considering the BRAIVE program closure, the primary safety objective is to summarize device-related adverse events up to 24 months. The primary safety endpoint is to summarize device-related adverse events up to 24 months.
Secondary Safety Objective and endpoint	The secondary safety objectives of the study are to assess all the secondary endpoints listed here. ○ Procedure-related adverse events up to 24 months ○ Secondary Spinal surgeries related to the original study device up to 24 months ○ Device deficiency up to 24 months (Note: “secondary spinal surgeries” and “subsequent spinal surgical interventions” are used interchangeably throughout the document). In addition, all data will be summarized up to skeletal maturity.
Additional Secondary Endpoints	The following is the list of additional secondary endpoints of this study: • Change from baseline in main thoracic Cobb angle at all available postoperative time points Change from baseline in proximal thoracic Cobb angle at all available postoperative timepoints • Change from baseline in thoracolumbar/lumbar Cobb angle at all available

	postoperative timepoints • Change from post-op baseline in Instrumented Cobb Angle at all available postoperative time points. • Change from baseline in thoracic kyphosis at all available postoperative timepoints • Change from baseline in Lumbar Lordosis at all available postoperative timepoints • Change from baseline in coronal balance at all available postoperative timepoints • Change from baseline in Sagittal Balance at all available postoperative timepoints • Change from baseline in total vertical thoracic spine height (T1- T12) at all available postoperative timepoints • Change from baseline in total vertical spine height (T1-S1) at all available postoperative timepoints • Change from baseline in Scoliosis Research Society-22 Patient Questionnaire (SRS-22) at all available postoperative timepoints Status of return to full activity within 3 months per SRS-22
Study Design	This is a prospective, multi-center, single-arm study of the Braive™ GMS. Eligibility requirements for the study require that subjects have failed conservative care. The baseline measurements will be collected prior to implantation of the device and compared against the measurements collected postoperatively. Data will be evaluated for safety and patient outcome. Subjects will continue to be followed through skeletal maturity. Clinical assessments will be completed at a preoperative visit, during surgery, at discharge, and postoperatively at 3 months, 6 months, 12 months, 18 months, and 24 months and then annually until the subject is skeletally mature (defined as Risser 5 as assessed by the investigator). Radiographic assessments will be completed at baseline, prior to hospital discharge, and at all follow-up time points.
Sample Size	The initial calculated sample size was 25 subjects at 10 sites across the US, Europe and Canada. When enrollment was stopped in March 2023, 10 subjects had been implanted with the Braive™ GMS at 4 sites across the US, Europe, and Canada. No more subjects will be enrolled after March 2023.
Inclusion/ Exclusion Criteria	A subject must meet ALL of the following inclusion criteria to participate: • Has a diagnosis of juvenile or adolescent idiopathic scoliosis • Is skeletally immature with a Sanders Score of ≥2 to ≤5 • Has failed conservative care as per investigator's assessment • Has a main thoracic Cobb angle between 30 and 60 degrees • Has a Lenke Classification of 1A, 1B, or 1C • Has kyphosis ≤40 degrees with a sagittal thoracic modifier N or negative • Informed Consent Form/Assent and Authorization to Use and Disclose Health Information (if applicable) have been signed by Parent/legal guardian

	and/or patient/participant per local requirement. A subject will be excluded from participating in this study for ANY of the following reasons: • Has undergone previous spinal fusion procedure(s) at the affected levels • Is pregnant or plans to become pregnant within the first 24- months of the study • Has a curve that requires instrumentation below L1 • Has spinal MRI abnormalities (e.g., CHIARI malformation, Syrinx greater than 4mm, tethered cord) • Has any type of non-idiopathic scoliosis • Has a left-sided curve • Has an associated syndrome • Has a history of malignant hyperthermia • Has an active or significant risk of infection (immunocompromised) • Has inadequate tissue coverage over the operative site as per investigator's assessment • Has a suspected or documented allergy or intolerance to implant materials • Has a major psychiatric disorder/ history of drug abuse that would interfere with the subject's ability to comply with study instructions or might confound the study interpretation as per investigator's assessment (DSM-5 can be used as a reference) • Is a ward of the court/state • Has had prior ipsilateral or contralateral chest surgery • Has severe chronic lung disease (e.g., asthma, bronchiectasis) • Has poor bone quality, as determined by the investigator, that may limit anterior fixation • Is unwilling or unable to return for follow-up visits and/or follow intra-operative and/or post-operative instructions • Concurrent participation in another clinical study that may add additional safety risks and/or confound study results* *Subjects in concurrent studies can only be enrolled with permission from Medtronic. Please contact Medtronic's study manager to determine if the subject can be enrolled in the BRAIVE IDE Study.
Study Procedures and Assessments	Clinical assessments will be completed at baseline (preoperatively), during surgery, and postoperatively at discharge, 3 months, 6 months, 12 months, 18 months and 24 months and then annually until subjects reach skeletal maturity (defined as Risser 5 as assessed by the investigator). Radiographic assessments will be completed at pre-op, prior to hospital discharge, and at all study follow-up visits. All subjects will be followed until skeletally mature.

Study Activity	PreOp	Surgery (Day 0)	Discharge	3 Mos.	6 Mos.	12 Mos.	18 Mos.	24 Mos.	Annually [4]	Unscheduled visit
Visit Window (Days)				±30	±30	±90	±90	±90	±182	
Inclusion/Exclusion Criteria	X									
Informed Consent / Assent	X									
Demographics	X									
Medical History	X									
Physical Assessment	X		X	X	X	X	X	X	X	
PedsQL	X									
SRS-22	X			X	X	X	X	X	X	
Neurological Status	X		X							
Spirometry	X									
Pregnancy Test[1]	X									
Operative Information		X								
Adverse Events and device deficiencies[2]	X	X	X	X	X	X	X	X	X	X
Subsequent Spinal Surgical Interventions[2]			X	X	X	X	X	X	X	X
Study Deviations	X	X	X	X	X	X	X	X	X	X
Study Exit	X	X	X	X	X	X	X	X	X	X
Radiographic Procedures										
X-Ray P/A Thoracolumbar Spine[3]	X		X	X	X	X	X	X	X	X
X-ray Neutral lateral Thoracolumbar Spine[3]	X		X	X	X	X	X	X	X	X
X-ray P/A Right Lateral Bending Spine[3]	X									
X-ray P/A Left Lateral Bending Spine[3]	X									
X-ray P/A Left Hand[3]	X									
MRI	X									
StealthStation DICOM[5]		X								
Intraoperative image[6]		X								
Risser Score								X[7]	X[7]	
Radiographic assessments as per the Radiographic Evaluation Protocol[8]	X		X[9]	X	X	X	X	X	X	X

Informed Consent/Assent must be obtained prior to performing any study specific procedure.

[1] A pregnancy test will be administered to all female subjects of child-bearing potential within 72 hours prior to surgery.

[2] Adverse events, device deficiencies and subsequent spinal surgical interventions are collected at intervals and as reported regardless of follow-up interval.

[3] The surgery procedure should occur as soon as possible after the eligibility report has been received from

	the imaging vendor but no later than 3 months after the date of acquiring the X-ray images. [4] After 24 months, subjects will be followed until skeletal maturity is reached (defined as Risser 5 as assessed by the investigator). [5] StealthStation DICOM collection is only applicable to study sites using imageguidance. [6] Intraoperative image collection is only applicable to study sites that are not using image guidance. [7] Risser score will be mandatory from 24 months onwards. [8] Radiographic assessments will be performed by the study site according to their standard of care. [9] Referred as Post-op baseline or immediate post-op.
Safety Assessments	All AEs will be collected for this study. The relationship between an AE and the device and/or procedure, as well as its severity and seriousness, will be assessed by the physician/investigator. All adverse events will be reviewed by Medtronic safety representative for safety assessments. A steering committee and Medtronic medical advisor will monitor the safety of the investigational treatment.
Statistics	<u>Analysis of Endpoints</u> For the primary safety endpoint and secondary safety endpoints, the rate of event along with the 2-sided 95% confidence interval will be calculated and presented. For the additional secondary endpoints related to the change from the baseline, when the distribution of data is approximately normally distributed, the change from baseline will be tested using a paired-sample t-test. When the distribution of the data is non-normal, a Wilcoxon signed-rank test may be used in place of the paired t-test. In addition, the descriptive statistics including but not limited to mean, standard deviation, median, minimum and maximum will be calculated and presented. For "Status of return to full activity within 3 months per SRS-22", the number and percentage of subjects returned to full activity within 3 months will be calculated and presented. <u>Analysis Populations</u> The primary analysis population will include all subjects who were enrolled and underwent the Braive™ GMS surgical procedure. The primary dataset will be used for all the analyses.

4. Introduction

4.1. Background

Adolescent Idiopathic Scoliosis (AIS), is a complex three – dimensional structural spine deformity with unknown etiology and a prevalence of 1-4 % of adolescents in the early stages of puberty (1, 2).

The goals of AIS treatment are to improve esthetics, improve quality of life, reduce back pain, improve psychosocial well-being, preventing the risk for curve progression in adulthood, improving breathing function, Cobb angle correction and prevention of further treatment in adulthood (3). The absolute goals for all patients in every clinical situation are to avoid fusion surgery (3). It was recommended that treatment decisions should be individualized, considering the probability of curve progression, based on the curve magnitude, skeletal maturity, patient age and sexual maturity (3).

When focusing on curve progression, Charles et al. described in 2006 that curve pattern, Cobb angle at the onset of puberty, and curve progression velocity were strong predictive factors of curve progression. Juvenile scoliosis (of curves > 30 degrees) increased rapidly and presented a 100% prognosis for surgery for curves > 40 - 45 degrees (4). The time of peak growth velocity was indicated to occur around 11-13 years of skeletal age (girls) and 13-15 years (boys), with nearly 90% of all operated curves progressing during this growth phase. For Cobb angles of >40 - 45 degrees in the thoracolumbar region or >50 degrees in the thoracic region, there was an increased risk of curve progression in adulthood, and together represented 0.1 % of patients with AIS (5). An annual curve progression velocity of 6 - 10 degrees during the pubertal growth spurt resulted in a spinal fusion rate of 70%. An increase of 1 degree per month represented a 100% risk for spinal fusion surgery (4).

In general, there are three therapy options for AIS: observation, bracing or surgical fixation. A high variability in outcome results is reported for both bracing and fusion. Bracing is currently considered the primary method for treating moderate AIS during developmental phase of growth. The literature showed that bracing significantly decreased the progression of high-risk curves to the threshold for surgery, when the bracing was applied for at least 18 hours per day (6, 7).

Criteria for bracing treatment were 10 years or older, skeletally immature (Risser sign of 0, 1 or 2), and a Cobb angle of 25 - 40 degrees, no prior treatment, and if female, either pre-menarche or less than 1 year post-menarche (8). The (bracing) treatment was observed to be more effective in curves under 30 degrees (8). In summary (or in general), publications showed that the success rate for bracing ranged from 52% - 84% at 4 years follow-up, with 18% - 50% of curves progressing despite bracing, for Cobb angles of 20 - 40 degrees.

However, bracing effectiveness was limited by psychosocial impacts, patient's compliance to the treatment and patient preferences for alternative treatments, such as fusion. In addition, progression to

surgery was related to immature Risser status and initial curve magnitude, with curves measuring ≥ 30° progressing to surgical magnitude in > 50% of the patients (9).

Patients with an increased risk of curve progression during adult life are generally considered for fusion surgery if they are skeletally immature and have a Cobb angle of >40–45 degrees in the thoracolumbar region or >50 degrees in the thoracic region (5). Surgery was recommended not only based on the Cobb angle, but also based on cosmesis, patient preference, and the probability of achieving significant benefit. The advantages of spine curve correction were reported to be a high degree of patient satisfaction, as measured by SRS-22 questionnaires (10). Successful long-term effects on the health-related quality of life, satisfaction, physical function were reported for patients 10- 30 years after initial fusion surgery; the effects of which were comparable to those observed in a healthy patient population (11-16).

Many publications describe long-term risks associated with fusion. Several publications described that these risks were mainly related to degenerative changes (11, 17) reduced spinal mobility and muscle endurance (13), lowered psychological status (14), increased risk of mid- to long-term complications and revision surgery (18), or variability of results depending on the criteria for selective fusion (10, 19).

As an alternative to fusion relative new therapy option for fusionless surgical treatment of AIS is anterior vertebral body tethering (AVBT). Anterior vertebral body tethering is a minimally invasive, fusionless surgical procedure that aims to preserve motion of the instrumented segments and allow curve correction. It is a growth-modulation technique, which utilizes skeletally immature patients' growth potential to attain progressive scoliosis correction (20, 21). AVBT is currently being employed in AIS patients with growth remaining (Risser score of 0-3 and a Sanders digital hand score ≤ 5) in thoracic curves measuring 35 - 70 degrees and lumbar curves measuring 30 - 70 degrees (22). Ninety-one patients have been treated with unspecified AVBT devices which were likely Dynesys®, as it is the main AVBT device used in clinical practice. These patients had two years of post-op follow-up. In addition, another 32 patients were followed-up for one year, with a sub-cohort of 11 were followed-up for two years, treated with Dynesys®. The following AVBT related adverse events were reported: overcorrection in 13/116 patients (11.2%), with 2 more subjects with possible overcorrection pending curve progression requiring fusion in 3 patients with 3 more subjects pending fusion (6/123 subjects). Additionally, the following were reported: 4 tether breakages; 1 screw loosening in a subject who grew 17cm; 1 contralateral lumbar tether added; 7 with less optimal result; 3 atelectasis, of which two were reported to be resolved with physical therapy, and one required posterior spine fusion for lumbar decompensation below the tether. No neurological complications or infections were reported.

In conclusion, the current State of the Art (SOTA) treatment for AIS consists of three main options (observation, bracing and fusion). The choice of treatment depends on the magnitude of the deformity and the risk for curve progression. The time of peak growth velocity was indicated to occur around 11-13 years of skeletal age (girls) and 13-15 years (boys), with nearly 90% of all operated curves progressing during this growth phase. Bracing and fusion represent opposite treatment technologies. Bracing

maintains the flexibility of the growing spine but depends on the patients' adherence to (or compliance with) the treatment. Fusion achieves a deformity correction already at first erect, but at the cost of a stiff immature spine and risk for additional complications later in life.

The AVBT treatment has emerged as an alternative treatment positioned between bracing and fusion. The Braive™ GMS is designed as a growth-modulation, non-fusion technique, which utilizes patients' remaining growth potential to limit further progression of the curve, to provide correction of the thoracic spine, and allow continued growth while maintaining mobility. These results have demonstrated a positive benefit / risk ratio by eliminating the need for bracing compliance, reducing the risk for less optimal curve correction and maintaining flexibility of the spine. In addition, the need for fusion surgery in patients with larger Cobb angles and the associated risk for additional surgery later in life are reduced.

4.2. Purpose

The BRAIVE IDE Study is a prospective, multi-center, single-arm study. The purpose of this study was to establish probable benefits and evaluate the safety and preliminary effectiveness of the Braive™ GMS when used in the treatment of JIS and AIS.

In March 2023, Medtronic made the decision to discontinue the BRAIVE program. All sites, therefore, have been notified to discontinue study enrollment and there are no plans at this time to utilize collected data to obtain Humanitarian Device Exemption (HDE) approval. This decision is not associated with any safety or efficacy observations from the study, and Medtronic has not received stopping recommendations from the Data Monitoring Committee.

5. Objectives and Endpoints

5.1. Objectives

5.1.1. Primary Objective

The primary objective of the study is to summarize the safety data .

5.1.2. Primary Safety Objective

Considering the BRAIVE program closure, the primary safety objective is to summarize the Device-related adverse events up to 24 months follow up.

The summary will be based on both Investigators and Medtronic relatedness assessment.

5.1.3. Secondary Safety Objectives

The secondary safety objectives of the study are to assess all the secondary safety endpoints listed below in section 5.2.2.

5.1.4. Additional Secondary Objectives

The Additional Secondary objectives of the study are to assess all the secondary endpoints listed below in section 5.2.3.

5.2. Endpoints

5.2.1. Primary Safety Endpoint

The primary safety endpoint is any device-related adverse events up to 24 month follow up.

5.2.2. Secondary Safety Endpoint

The secondary safety endpoints are listed below.

- Procedure-related adverse events up to 24 months
- Secondary Spinal surgeries related to the original study device up to 24 months
- Device deficiency up to 24 months

(Note: "secondary spinal surgeries" and "subsequent spinal surgical interventions" are used interchangeably throughout the document).

In addition, all data will be summarized up to skeletal maturity.

5.2.3. Additional Secondary Endpoints

The additional secondary endpoints of this study include:

- Change from baseline in main thoracic Cobb angle at all available postoperative time points
- Change from baseline in proximal thoracic Cobb angle at all available postoperative timepoints
- Change from baseline in thoracolumbar/lumbar Cobb angle at all available postoperative timepoints
- Change from post-op baseline in Instrumented Cobb Angle at all available postoperative time points.
- Change from baseline in thoracic kyphosis at all available postoperative timepoints
- Change from baseline in Lumbar Lordosis at all available postoperative timepoints

- Change from baseline in coronal balance at all available postoperative timepoints
- Change from baseline in Sagittal Balance at all available postoperative timepoints
- Change from baseline in total vertical thoracic spine height (T1- T12) at all available postoperative timepoints
- Change from baseline in total vertical spine height (T1-S1) at all available postoperative timepoints
- Change from baseline in Scoliosis Research Society-22 Patient Questionnaire (SRS-22) at all available postoperative timepoints
- Status of return to full activity within 3 months per SRS-22

6. Study Design

This is a prospective, multi-center, single-arm study of the Medtronic Braive™ GMS. Eligibility requirements for the study require that subjects have failed conservative treatment as per investigator's assessment. The baseline measurements will be collected prior to implantation of the device and compared against the measurements collected postoperatively. Subjects will continue to be followed until skeletally mature.

The initial calculated sample size was 25 subjects at 10 sites across the US, Europe and Canada. A maximum of 5 subjects (20% of original population target) were to be enrolled and treated at a single site, to mitigate bias by limiting the number of subjects per site. When enrollment was stopped in March 2023, 10 subjects had been enrolled and treated at 4 sites, across the US, Europe and Canada.

Investigational sites were selected based on experience and expertise in managing patients with JIS and AIS, ability to recruit subjects and comply with the protocol and regulations, and clinical research expertise and resources. Investigators selected to participate in this clinical study are responsible for fulfilling the requirements of the investigator's agreement and investigational plan. All investigators signed an investigator agreement prior to initiation of screening or enrollment activities.

Only consented subjects were enrolled into the study. Sites were requested to make every effort to enroll subjects in a consecutive manner. Clinical assessments are scheduled at baseline (preoperatively), during surgery, and postoperatively at discharge, 3 months, 6 months, 12 months, 18 months and 24 months and then annually until subjects reach skeletal maturity (defined as Risser 5 as assessed by the investigator). Radiographic assessments are scheduled at pre-op and prior to hospital discharge, and at all study follow-up visits. All subjects will be followed until skeletally mature.

6.1. Duration

Enrollment in the study for each subject is defined as the date the parents/legal guardian and subject sign the informed consent/assent (as applicable).

Enrolled subjects who did not undergo the Braive™ GMS procedure as defined in this protocol could be exited (removed) from the study and be replaced when enrollment was still open. In such cases the Medtronic study manager had been contacted for guidance as to whether to exit the subject or not. The completion of the study is defined as the conclusion of the follow-up visit when the subject is skeletally mature (Study Exit). Each subject's participation in the study is expected to last from the date of the procedure until the subject is skeletally mature. Consequently, the total participation time in the study will vary for each subject. Each subject is evaluated prior to the procedure (baseline), during the procedure, prior to hospital discharge, and 3 months, 6 months, 12 months, 18 months and 24 months post procedure and then annually until skeletal maturity is reached (defined as Risser 5 as assessed by the investigator).

The expected duration of the study is approximately 8 years, including approximately 18 months for subject enrollment. The study is considered complete when all subjects have reached skeletal maturity (defined as Risser 5 as assessed by investigators).

6.2. Rationale

Figure 1 shows the spectrum of treatment options incorporating the Braive™ GMS. Conservative care, which primary consists of bracing, is often effective in treating small, flexible curves. Bracing does not correct the curve; rather it is intended to halt the progression of the curve. Studies have shown that the longer the brace is worn each day, the better the potential outcome (6). However, bracing has several disadvantages. The braces are often cumbersome, visible, and must be worn a minimum of 18 hours a day for several years, often resulting in a high rate of non-compliance by the young patients, especially with the psychosocial ramifications present in today's society (6, 23). Non-compliance leads to treatment failure, especially in patients with larger, stiffer curves. Thus, studies have reported that bracing has been shown to have a high rate of variable outcomes (24, 25). Further, while alternative treatments to bracing, such as physical therapy, electrical stimulation or chiropractic care, may provide symptom relief or core strengthening, these treatments have not been scientifically proven to treat or prevent curve progression (26).

If conservative care does not halt the curve progression, there are other treatment options: vertebral body tethers (VBT) like the Braive™ GMS, growing rods, and fusion surgery. Growing rods are used to treat a different population of scoliosis patients compared to Braive™ GMS. Growing rods are used for patients less than 10 years of age with severe scoliosis (curves > 60 degrees), while the Braive™ GMS is intended for patients with less severe, progressive scoliosis (curves 30 - 60 degrees) who have growth potential remaining. Patients with an increased risk of curve progression during adult life are generally considered for fusion surgery (fusion of the spine with rigid instrumentation to correct the deformity) if they are skeletally immature and have a Cobb angle of >40 - 45 degrees in the thoracolumbar region or >50 degrees in the thoracic region (5). Fusion surgery can result in reduced spinal growth and decreased spinal mobility that can negatively impact the quality of life for AIS patients and require further treatments

throughout their life. According to Crawford & Lenke, 2010 (27), fusion procedures do generate some concerns, which include "the cessation of spinal growth over the fused segments (which may negatively affect pulmonary function) and the potential for disc degeneration of segments adjacent to a long fusion construct. Since non-operative treatment does not control progression in all cases, the search for alternative treatment of juvenile idiopathic scoliosis is warranted." The main concerns with traditional posterior instrumentation and fusion in skeletally immature patients with scoliosis include: correction loss, crankshaft phenomenon, implantation failure and lack of spinal growth (28).

As an alternative to fusion, anterior vertebral body tethering (AVBT) has emerged as a relatively new therapy option for fusionless treatment of JIS or AIS. AVBT is a minimally invasive, fusionless surgical procedure that aims to preserve motion of the instrumented segments and allow curve correction. Specifically, the Braive™ GMS is intended to limit further progression of the curve, to provide correction of the thoracic spine, and allow continued growth while maintaining (spinal) mobility (or flexibility). As described in the background section, while some patients have been treated with AVBT devices, the purpose of this study is to establish probable benefit and evaluate the safety and preliminary effectiveness of the Braive™ GMS as an alternative to the treatments discussed above and as it fills a treatment gap for patients who have failed conservative care and are not yet appropriate patients for fusion surgery. For this reason, no control group is implemented for this study and where needed the comparison with bracing and fusion literature will be made. Additionally, as the Braive™ GMS preserves motion in the spine while allowing curve correction, it may address some of the risks associated with the treatment of patients who progress to fusion surgery.

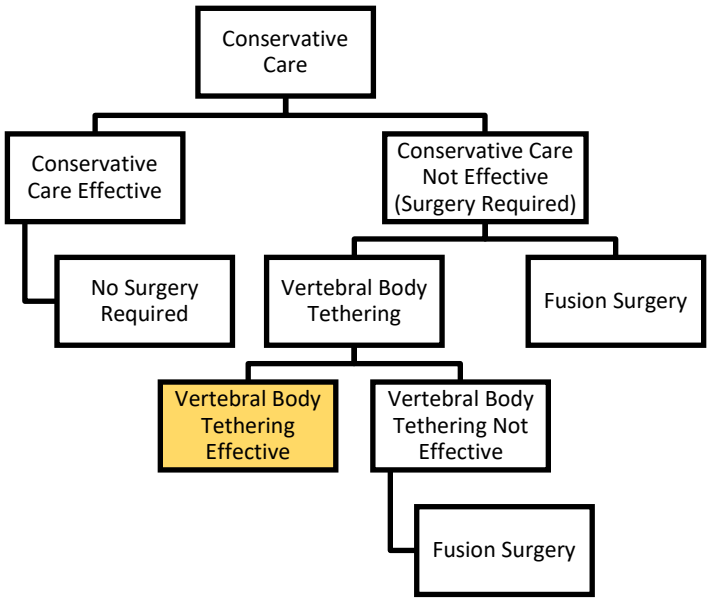

Figure 1: Spectrum of Treatment Options for Idiopathic Scoliosis

7. Product Description

7.1. General

The Braive™ GMS is an implantable device being evaluated for use in the treatment of JIS or AIS in skeletally immature patients with Cobb angles between 30 and 60 degrees, who have failed conservative care, have a Sanders score of ≥2 to ≤5, have kyphosis ≤40 degrees with a sagittal thoracic modifier N or negative, and have a Lenke Classification of 1A, 1B, or 1C.

The Braive™ GMS is intended to limit further progression of the curve, provide correction of the thoracic spine, and allow continued growth while maintaining mobility. The system consists of the following components: Braid, Fixed Angle Screws (FAS), Plate, and Break-Off Set Screw. The system is designed such that first the Plate and then FAS are implanted into the bone (or vertebral body). The Braid is then inserted into the slot of the screw and the Set Screw is threaded into the FAS (to secure the Braid in place). Per vertebral level 3 components are implanted and the different levels are connected to each other by 1 Braid. On average it is expected that the subject will require 6 to 8 levels implanted. The system is implanted using an anterior thoracoscopic approach across multiple vertebral levels (usually five to seven). The implants are placed along the lateral vertebral wall on the convex side of the scoliotic curve. **Figure 2** includes images of the implant assembly and the implanted construct on the anterior-lateral side. The system can be implanted freehand or through image guidance using Medtronic's O-Arm ™ Surgical Imaging System and Medtronic Stealth Station™.

Figure 2: Screw Plate Assembly (left) and Anterior Lateral Braid Placement (right)

The design of the Braive™ GMS is based on the Hueter-Volkmann principle in which the rate of epiphyseal growth is affected by pressures applied to its axes. As such, decreased stress on the growth plate leads to an increased growth rate and an excessive stress leads to growth retardation. AVBT has become a general term to describe such a procedure when applied to the vertebrae of the spinal column.
For Medtronic's Braive™ GMS, compression is applied to the convex side of the scoliotic curve using a flexible braid, which is affixed to the anterior spinal column using metallic vertebral body screws, plates and set screws. The applied compression modulates growth on the convex side of the curve and allows the continued growth of the concave side of the curve, resulting in the concave side "catching up" and correcting the deformity (**Figure 3**).

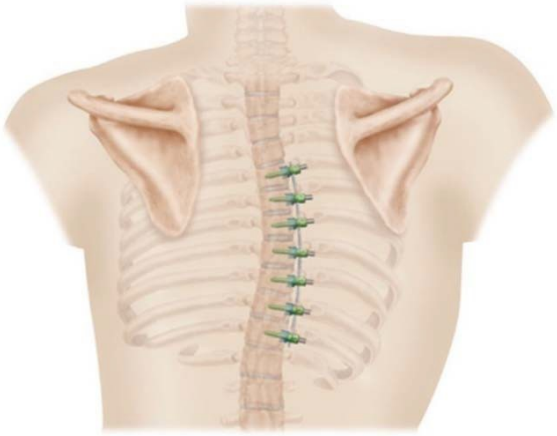

Figure 3: Braive™ GMS, compression applied on convex side of the curve.

The Braive™ GMS consists of the components and corresponding material composition outlined in Table 1.

Table 1. Braive™ GMS Implantable Components and Material Composition

Component	Material Composition
Fixed Angle Screws (FAS)	Titanium Alloy (Ti-6Al-4V)
Plate	Titanium Alloy (Ti-6Al-4V)
Break-off Set Screw	Titanium Alloy (Ti-6Al-4V)
Braid	UHMWPE Fibers

A description of the different implants and available sizes is provided in Table 2 and 3. An overview of the different instruments is provided in Table 4.

Table 2. Braive Metal Implant Set

PART TYPE	Investigational CFN	CE mark CFN	DESCRIPTION	Sterile
FAS	677105520	777105520	5.5X20MM SELF-TAPPING FAS	STERILE
FAS	677105522	777105522	5.5X22.5MM SELF-TAPPING FAS	STERILE
FAS	677105525	777105525	5.5X25MM SELF-TAPPING FAS	STERILE
FAS	677105527	777105527	5.5X27.5MM SELF-TAPPING FAS	STERILE
FAS	677105530	777105530	5.5X30MM SELF-TAPPING FAS	STERILE
FAS	677105532	777105532	5.5X32.5MM SELF-TAPPING FAS	STERILE
FAS	677105535	777105535	5.5X35MM SELF-TAPPING FAS	STERILE
FAS	677105540	777105540	5.5X40MM SELF-TAPPING FAS	STERILE
FAS	677105545	777105545	5.5X45MM SELF-TAPPING FAS	STERILE
FAS	677106520	777106520	6.5X20MM SELF-TAPPING FAS	STERILE
FAS	677106522	777106522	6.5X22.5MM SELF-TAPPING FAS	STERILE
FAS	677106525	777106525	6.5X25MM SELF-TAPPING FAS	STERILE
FAS	677106527	777106527	6.5X27.5MM SELF-TAPPING FAS	STERILE
FAS	677106530	777106530	6.5X30MM SELF-TAPPING FAS	STERILE
FAS	677106532	777106532	6.5X32.5MM SELF-TAPPING FAS	STERILE
FAS	677106535	777106535	6.5X35MM SELF-TAPPING FAS	STERILE
FAS	677106540	777106540	6.5X40MM SELF-TAPPING FAS	STERILE
FAS	677106545	777106545	6.5X45MM SELF-TAPPING FAS	STERILE
Set Screw	677501000	777501000	BREAKOFF SET SCREW	STERILE
Plate	677603000	777603000	PLATE	STERILE

Table 3. Braive Braid Implant Set

PART TYPE	Investigational CFN	CE mark CFN	DESCRIPTION	Sterile
Braid	677700000	777700000	UHMWPE BRAID	STERILE
Braid	677700750	777700750	UHMWPE BRAID LONG	STERILE

Table 4. Braive Instrument Set

PART TYPE	Investigational CFN	CE mark CFN	SAP DESCRIPTION	Sterile
Navigated Instrument	NAV677000008	NAV777000008	NAVIGATED AWL-PLATE HOLDER	NO
Instrument	677000008	777000008	AWL-PLATE HOLDER	NO

Navigated Instrument	NAV677000014	NAV777000014	NAVIGATED FAS DRIVER	NO
Instrument	677000014	777000014	FAS DRIVER	NO
Instrument	677000015	777000015	FAS HEAD POSITIONER	NO
Instrument	677000016	777000016	3MM ASSEMBLY BOLT	NO
Instrument	677000020	777000020	SET SCREW BREAK-OFF	NO
Instrument	677000021	777000021	OBTURATOR	NO
Instrument	677000026	777000026	BLUNT-TIP PROBE	NO
Instrument	677000028	777000028	BRAID GRASPER	NO
Instrument	677000029	777000029	DEPTH GAUGE	NO
Instrument	677000034	777000034	PROVISIONAL DRIVER	NO
Instrument	677000035	777000035	COUNTER TORQUE	NO
Instrument	677000037	777000037	PLATE TEMPLATE	NO
Instrument	677000041	777000041	PLATE HOLDER	NO
Instrument	677000023	777000023	TENSIONER	NO
Handle	G900000	G900000	Quick Connect Ratcheting Handle	NO
Handle	9339012	9339012	Egg Handle	NO
Handle	7578011	7578011	Threaded Handle	NO

Table 5: Braive Licensing Disc

PART TYPE	Investigational CFN	CE mark CFN	SAP DESCRIPTION	Sterile
Software Part	9736353	9736313	BRAIVE Licensing Disc	NO

The Braive™ GMS is investigational in the US and Canada and will be labeled as such. The label will be provided separate from this CIP. Outside the US, the Braive™ GMS was CE marked, at the time of the surgeries and is labeled as such. Labeling will be provided in local language for CE marked devices. The CE marked devices will be used within intended use as described in the approved IFU for which CE mark has been obtained. In countries where no market release is obtained, the use of the Braive™ GMS is limited to the clinical investigation and according to the Clinical Investigation Plan. Instructions for Use are available separate from this CIP.

Medtronic has decided to not renew CE certification for the Braive GMS on 24th March 2023. This decision was not based on concerns regarding patient safety.

7.2. Route of Administration

Information regarding the surgical technique for implantation of the device is provided in the Surgical Technique and the Navigated Surgical Technique that are available separate from this CIP.

7.3. Manufacturer

Medtronic Sofamor Danek USA, Inc
1800 Pyramid Place
Memphis, TN 38132
USA

7.4. Packaging

All study implants will be provided in an intact sterile package provided by the sponsor and will be clearly labeled sterile. The instruments as listed in Table 4 will be provided non-sterile in metal sets to the clinical sites. Investigational devices will be labeled according to local requirements as per local authorities. Please refer to the IFUs that are available separate from this CIP for additional information regarding packing and labeling of the study devices and instruments.

CE marked devices will be labelled in respective local language.

7.5. Intended Population

The Braive™ GMS is indicated for use in the treatment of JIS or AIS in skeletally immature patients with Cobb angles between 30 and 60 degrees, who have failed conservative care, have a Sanders score of ≥2 to ≤5, have kyphosis ≤ 40 degrees with a sagittal thoracic modifier N or negative, and have a Lenke Classification of 1A, 1B, or 1C.

The Braive™ GMS is intended to limit further progression of the curve, to provide correction of the thoracic spine, and allow continued growth while maintaining mobility.

7.6. Equipment

Imaging: The site should have the ability to perform or access to equipment or facility to perform the following: Posterior/Anterior, Neutral and Lateral Bending radiographs, and MRI as applicable.

Sites will be able to choose to implant the system non navigated according to the standard Surgical Technique or navigated following the Navigated Surgical Technique (both Surgical Techniques are available separate from this CIP). Study sites intending to implant the system using image guidance shall have access to Medtronic's O-Arm Surgical Imaging System and Medtronic StealthStation. O-Arm and StealthStation are recommended to be used according to their applicable instructions for use. Study sites using image guidance will be provided a licensing disc to access the Braive™ GMS in navigated views.

Any test equipment critical to be used for assessing safety endpoints (X-ray) will be maintained/calibrated according to the manufacturer's specifications. Maintenance and calibration reports will be monitored periodically by the monitor for images collected at study sites.

7.7. Product Use

The Braive™ GMS will be used according to the surgical technique provided separately from this CIP. The operating surgeon should refer to the product's IFU and the instruments IFUs, provided separately from this CIP.

7.8. Product Training Requirements

To reduce the potential for surgical technique variations, Medtronic will supply a surgical technique to describe the implantation of the Braive™ GMS. The Surgical technique (non-navigated) and the Navigated Surgical Technique are provided separate from this CIP. All surgeons will undergo certified training on the surgical techniques prior to performing their first implantation of the device and will receive case support for the first case and subsequent cases, as needed.

In addition, an interactive educational application will be provided to investigators that will allow access to representative examples of curves in the range of the intended patient population. The examples will include the pre-operative Cobb angle, the initial, post-operative curve correction, and subsequent simulations of the growth and curvature over time. This application is intended to illustrate the general principle of growth modulation for training purposes. It is not indicative of or based on actual clinical outcomes with the Braive™ GMS. This application is not used to make individual patient treatment decisions or to predict patient outcomes.

7.9. Product Receipt and Tracking

Device accountability logs will be maintained by the sites for the investigational devices and instruments and for the CE marked devices and instruments if they are provided free of charge. Investigational and free of charge CE marked devices, (navigated) instruments and BRAIVE Licensing Disc will not be shipped to the site until receipt and tracking training has occurred, and the investigator has delegated authority to personnel to manage receipt and tracking of the devices. Records of shipment and receipt will be maintained both at the clinical site and by the sponsor or sponsor's representative.

7.10. Product Storage

The investigational devices and instruments will be provided for this study and must be stored in a secure location (i.e., limited access area or in a locked cabinet). The principal investigator (or qualified designee) must agree not to dispense the devices and instruments from, nor store them at, any site other than the study sites designated at the beginning of the study. This section also applies for CE marked devices and

instruments provided free of charge.

7.11. Product Return

Any component that is explanted should be returned for analysis according to Medtronic standard procedures for complaint product analysis. Note, this does not include any components that were implanted and removed during the initial procedure. These were to be returned to the sponsor or sponsor's representative. The device accountability log should be updated accordingly. Additionally, any components where the packaging is not intact or that are opened but not implanted should be returned to the sponsor or sponsor's representative, and the device accountability log should be updated accordingly. The Retrieval and Analysis of Explanted Devices protocol provided separate from this CIP is no longer applicable.

Upon completion of all surgeries or study completion at the latest, all unused devices including the Braive™ Instrument Set and licensing CD will be returned to the sponsor or sponsor's representative. Records of device shipment and receipt will be maintained both at the clinical site and by the sponsor or sponsor's representative. At study completion, the software will need to be deinstalled.

For CE marked devices and instruments that are obtained via the commercial route (not provided free of charge) only the explant process applies.

7.12. Product Accountability

Device accountability logs will be maintained for the components of the devices. Upon completion of the study, unused devices must be returned to the sponsor or sponsor's representative. Records of shipment and receipt will be maintained both at the investigational site and by the sponsor or sponsor's representative.

The device accountability log will track at least:

a) the date of receipt and received by name,
b) identification of each device (lot number/serial number or unique code),
c) expiry date, if applicable
d) the date of use,
e) subject identification,
f) the date of return and returned by name (including reason for return)
g) the date on which the device was explanted from the subject and returned for analysis, if applicable

Product accountability does not apply for CE marked devices and instruments that are obtained via the commercial route (not provided free of charge).

8. Selection of Subjects

8.1. Study Population

As reflected in the inclusion and exclusion criteria below, all subjects will have failed conservative treatment prior to enrollment in the study. The baseline measurements will be collected prior to implantation of the device and compared against the measurements collected postoperatively.

8.2. Subject Enrollment

Subjects planning to undergo an anterior vertebral tethering procedure with the Braive™ GMS will be screened for eligibility to participate in the study. All subjects that are considered for the study should be included on the subject screening log. The reason for non-eligibility should also be recorded on the subject screening log. Subjects will be considered enrolled in the study once the informed consent form/assent is signed by the parent/legal guardian and/or the subject (as applicable). Those who do not undergo the implantation of the Braive™ GMS as defined in this protocol might be exited from the study and can be replaced if enrollment is still open. In such cases the Medtronic study manager should be contacted for guidance as to whether to exit the subject or not. The initial calculated sample size was 25 subjects. When enrollment was stopped in March 2023, 10 subjects had been enrolled and treated with BRAIVE GMS. Subjects who receive the study treatment will be considered study subjects.

8.3. Inclusion Criteria

A subject must meet all of the following inclusion criteria to participate in this study:

- Has a diagnosis of juvenile or adolescent idiopathic scoliosis
- Is skeletally immature with a Sanders Score of ≥2 to ≤5
- Has failed conservative care as per investigator's assessment
- Has a main thoracic Cobb angle between 30 and 60 degrees
- Has a Lenke Classification of 1A, 1B, or 1C
- Has kyphosis ≤ 40 degrees with a sagittal thoracic modifier N or negative
- Informed Consent Form/Assent and Authorization to Use and Disclose Health Information (if applicable) have been signed by Parent/legal guardian and/or patient/participant per local requirement.

8.4. Exclusion Criteria

A subject will be excluded from participating in this study for any of the following reasons:

- Has undergone previous spinal fusion procedure(s) at the affected levels

- Is pregnant or plans to become pregnant within the first 24-months of the study
- Has a curve that requires instrumentation below L1
- Has spinal MRI abnormalities (e.g., CHIARI malformation, Syrinx greater than 4mm, tethered cord)
- Has any type of non-idiopathic scoliosis
- Has a left-sided curve
- Has an associated syndrome
- Has a history of malignant hyperthermia
- Has an active or significant risk of infection (immunocompromised)
- Has inadequate tissue coverage over the operative site as per investigator's assessment
- Has a suspected or documented allergy or intolerance to implant materials
- Has a major psychiatric disorder/ history of drug abuse that would interfere with the subject's ability to comply with study instructions or might confound the study interpretation as per investigator's assessment (DSM - 5 can be used as a reference)
- Is a ward of the court/state
- Has had prior ipsilateral or contralateral chest surgery
- Has severe chronic lung disease (e.g., asthma, bronchiectasis)
- Has poor bone quality, as determined by the investigator, that may limit anterior fixation
- Is unwilling or unable to return for follow-up visits and/or follow intra-operative and/or post-operative instructions
- Concurrent participation in another clinical study that may add additional safety risks and/or confound study results*

*Subjects in concurrent studies can only be enrolled with permission from Medtronic. Please contact Medtronic's study manager to determine if the subject can be enrolled in the BRAIVE IDE Study.

9. Study Procedures

9.1. Schedule of Events

The study schedule, procedures, and methods of assessment are defined in detail to enable compliance with the required activities, and to ensure that the resulting data meet the criteria for evaluability. See Table 6 for visit schedule. The relevant electronic Case Report Forms (eCRFs) along with the applicable source documentation will be completed for each subject. The case report forms are provided separate from this CIP.

Table 6. Schedule of Events

Study Activity	PreOp	Surgery (Day 0)	Discharge	3 Mos.	6 Mos.	12 Mos.	18 Mos.	24 Mos.	Annually [4]	Unscheduled visit
Visit Window (Days)				±30	±30	±90	±90	±90	±182	
Inclusion/Exclusion Criteria	X									
Informed Consent / Assent	X									
Demographics	X									
Medical History	X									
Physical Assessment	X		X	X	X	X	X	X	X	
PedsQL	X									
SRS-22	X			X	X	X	X	X	X	
Neurological Status	X		X							
Spirometry	X									
Pregnancy Test[1]	X									
Operative Information		X								
Adverse Events and device deficiencies[2]	X	X	X	X	X	X	X	X	X	X
Subsequent Spinal Surgical Interventions[2]			X	X	X	X	X	X	X	X
Study Deviations	X	X	X	X	X	X	X	X	X	X
Study Exit	X	X	X	X	X	X	X	X	X	X
Radiographic Procedures										
X-Ray P/A Thoracolumbar Spine[3]	X		X	X	X	X	X	X	X	X
X-ray Neutral lateral Thoracolumbar Spine[3]	X		X	X	X	X	X	X	X	X
X-ray P/A Right Lateral Bending Spine[3]	X									
X-ray P/A Left Lateral Bending Spine[3]	X									
X-ray P/A Left Hand[3]	X									
MRI	X									
StealthStation DICOM[5]		X								
Intraoperative image[6]		X								
Risser Score								X[7]	X[7]	
Radiographic assessments as per the Radiographic Evaluation Protocol[8]	X		X[9]	X	X	X	X	X	X	X

Informed Consent/Assent must be obtained prior to performing any study specific procedure.

[1] A pregnancy test will be administered to all female subjects of child-bearing potential within 72 hours prior to surgery.

[2] Adverse events, device deficiencies and subsequent spinal surgical interventions are collected at intervals and as reported regardless of follow-up interval.

[3] The surgery procedure should occur as soon as possible after the eligibility report has been received from the imaging vendor but no

later than 3 months after the date of acquiring the X-ray images.
[4] After 24 months, subjects will be followed until skeletal maturity is reached (defined as Risser 5 as assessed by the investigator).
[5] StealthStation DICOM collection is only applicable to study sites using imageguidance.
[6] Intraoperative image collection is only applicable to study sites that are not using image guidance.
[7] Risser score will be mandatory from 24 months onwards.
[8] Radiographic assessments will be performed by the study site according to their standard of care.
[9] Referred as Post-op baseline or immediate post-op.

9.1.1. Enrollment

All subjects and the parent(s)/legal guardian need to provide their informed consent/assent in accordance with the informed consent/assent regulations per geographic region. If the subject agrees to participate in the study, he/she and/or the parent/legal guardian will be asked to sign the informed consent form (ICF)/Assent form (as applicable). Once the ICF/Assent forms are signed, a copy of the signed ICF/Assent forms will be provided to the parent/legal guardian and/or the subject. The Informed Consent and Assent forms are provided separate from this CIP.

The subject and/or parent or legal guardian must sign the ICF/Assent prior to performing any study specific procedure. A subject is considered enrolled in this study at the time the subject and/or parent/legal guardian signs the ICF/Assent form. The subject will be assigned a unique, sequential code linked to their name, alternative subject identification or contact information. The investigator will maintain a log of all subjects enrolled (enrollment log) in the study. The total enrollment for the study is 10 treated subjects.

9.1.2. Pre-op

The following information will be collected at the preoperative visit:

- Verification of Inclusion/Exclusion criteria
- Demographics
- Medical History
- Physical Assessment (weight and height)
- Imaging (PA, lateral, lateral bending, and left-hand X-rays, MRI)
- Radiographic assessments as per standard of care
- PedsQL
- SRS-22
- Neurological Status
- Pulmonary Function (Spirometry)
- Pregnancy test (administered to all female subjects of child-bearing potential within 72 hours prior to surgery)
- Adverse Events
- Study Deviations

9.1.3. Surgery

The surgery procedure should occur as soon as possible after the eligibility report has been received from the imaging vendor but no later than 3 months after the date of acquiring the X-ray images. If the images cannot be done within the required window, new images should be obtained.

The following information should be collected during surgery:

- Surgery procedure data
- Surgery Time
- Blood loss and Transfusion
- Device information
- Adverse Events and/or device deficiencies
- Study Deviations
- StealthStation Images (only collected at study sites using image guidance – standard of care images)
- Intraoperative images (only collected at study sites not using image guidance – standard of care images)

It is recognized that a subject might be enrolled but not implanted with the Braive™ GMS due to the investigator's discretion. If this occurs, it shall be documented on a study deviation eCRF, including the rationale for not implanting the device and the study exit form will be completed in the eCRF system.

9.1.4. Discharge Assessment

The following information will be collected at the discharge assessment (at the time of hospital discharge):

- Physical Assessment (weight and height)
- Imaging (P/A and lateral X-rays)
- Radiographic assessments as per standard of care
- Neurological Status
- Adverse events and/or device deficiencies
- Study Deviations

9.1.5. Post-operative Assessment at 3, 6, 12, 18, 24 months and annually

The following information will be collected at 3-month, 6-month, 12-month, 18-month, 24-month post-operative visits and annually thereafter until skeletal maturity is reached:

- Physical Assessment (weight and height)
- SRS-22
- Imaging (PA and lateral X-rays)
- Radiographic assessments as per standard of care
- Adverse Events and/or device deficiencies
- Study Deviations

- Risser score (only required on and after 24 months)

9.2. Diagnostic Tests

The following medical imaging and laboratory assessments will be performed during the study.

9.2.1. Spirometry Assessment

Pulmonary function will be assessed at the pre-operative visit by collecting the following parameters:

- Forced Vital Capacity (FVC)
- Forced Expiratory Volume in one second (FEV1)
- Total Lung Capacity

9.2.2. Radiographic Assessment

Images collected will be evaluated by investigators for adverse event, device deficiency and additional secondary endpoints analysis. The following series of radiographs will be obtained per the Schedule of events.

- P/A Thoracolumbar Spine
- Neutral Lateral Thoracolumbar Spine
- P/A Right Lateral Bending Spine
- P/A Left Lateral Bending Spine
- P/A Left Hand
- StealthStation DICOM
- Intraoperative AP fluoroscopy

With the early enrolment stop, the decision was taken to use Core Lab assessments for patient eligibility assessment only. The remaining radiographic assessments will be performed by the study sites as per their standard of care. For relevant endpoints, study site will follow the Radiographic Evaluation Protocol for radiographic measurements. The Radiographic Evaluation Protocol is maintained separate from this CIP.

9.2.3. O-Arm™ Imaging System and Stealth Station Image Acquisition

Sites using image guidance in the procedure workflow may have imaging collected from Medtronic O-Arm Surgical Imaging System and Medtronic StealthStation. Images being obtained off the systems are from the procedure workflow following the Navigated Surgical Technique. The StealthStation DICOM will be obtained per the Schedule of Events for potential future use:

- To confirm the post-operative position of the Braive™ GMS System
- To verify the amount of correction achieved by the Braive™ GMS System during surgery
- To further develop the Braive™ GMS System and the surgical technique
- To develop future capabilities that improve O-arm™ Imaging System image quality, reduce X-ray dose

to the patient, and aid in the development of segmentation and other algorithms/features that can enhance a surgeon or radiologist's decision-making ability

- To develop future capabilities that improve algorithmic segmentation of anatomy and aid in new development or enhancement of current surgical planning features for Medtronic platforms (i.e., StealthStation™, Mazor X™ Stealth Edition, BraiveSim)
- To validate a patient-specific computer modeling software that will generate patient-specific simulations of growth and curvature over time (only applicable for those patients that provide separate consent for this since the data may need to be shared with an external vendor)

9.2.4. Intraoperative Image Acquisition

For sites that are not using image guidance, intraoperative AP fluoroscopy images will be collected before and after implantation of the Braive™ system during surgery to:

- Confirm the post-operative position of the Braive™ System
- To verify the amount of correction achieved by the Braive™ GMS System during surgery
- Further development of the Braive™ GMS System and the surgical technique
- To validate a patient-specific computer modeling software that will generate patient-specific simulations of growth and curvature over time (only applicable for those patients that provide separate consent for this since the data may need to be shared with an external vendor)

9.2.5. Risser Score

Risser Score will be assessed by the investigator to evaluate the skeletal maturity of the subject in accordance with the following definitions:

Grade 0: No iliac apophysis visible.
Grade 1: Initial appearance of ossification of the iliac apophysis.
Grade 2: Migration halfway across the top of the iliac wing.
Grade 3: Three-fourths of the distance.
Grade 4: Ossification crossing the iliac wing, but not fused to the ilium.
Grade 5: Complete ossification of the iliac apophysis with fusion to the ilium.

When grade 5 is reached on or after 24-month follow up visit, subject will be exited from the study.

9.2.6. Pregnancy Testing

All subjects of childbearing potential must receive a pregnancy test (urine or serum test) within 72 hours prior to the study surgery. If the result of the pregnancy test is positive, the subject will be withdrawn from the study prior to surgery and will not receive the study treatment.

9.3. Subject Consent

The informed consent process in this study will be conducted in compliance with the Informed Consent regulations in 21 CFR 50 (US only), Declaration of Helsinki 2013, ISO 14155:2020 and national/local data protection laws and regulations. All subjects and/or parents/legal guardians for this study will be provided with an Informed Consent/Assent (as applicable) describing this study and providing sufficient information to make an informed decision about the subjects' participation in this study. The Informed Consent and Assent templates will be submitted with the protocol for review and approval by an IRB/EC/REB and the Regulatory Authorities, where applicable.

The investigator or authorized designee must obtain written informed consent/assent from the subject and/or parent(s)/legal guardian before any clinical study related activity takes place. Prior to entering the study, the investigator, or his/her designee, will inform all potential subjects and parent(s)/legal guardian about all aspects of the study (e.g., the purpose and nature of the study, procedures, potential risks, follow-up schedule, and expected duration).

All items addressed in the Informed Consent Form/Assent Form must be explained. The language used shall be as non-technical as possible and must be understandable to the subject.

The investigator or designee will discuss the foreseeable risks as well as potential benefits that may result from participating in the study and the available alternative therapies.

The subject and/or parent(s)/legal guardian must have ample time and opportunity to read and understand the Informed Consent Form/Assent Form, to inquire about details of the clinical study, and to decide whether to participate in the clinical study. All questions about the clinical study should be answered to the satisfaction of the subject and/or the parent(s)/legal guardian.

Neither the investigator, nor the investigation site staff shall coerce or unduly influence a subject and/or parent(s)/legal guardian to participate or to continue to participate in the clinical study. The informed consent/assent process shall not waive or appear to waive the subject's rights. Subjects and/or parent(s)/legal guardian will be informed by the investigator or designee that they are free to refuse to participate in the study, and if they choose to participate, that they may withdraw from the study at any time without compromising further medical care. In addition, subjects and/or parent(s)/legal guardian will be informed that the investigator may terminate their participation at any time without their consent. Written informed consent/assent will be obtained prior to subject enrollment and before any study-specific procedures are initiated.

Whenever new information becomes available that may be relevant to the subject's confirmed participation in the clinical study, Medtronic will revise the written Informed Consent Form/Assent Form and inform the investigators. The revised information will be sent to the investigator for approval or

notification by the IRB/EC/REB and the Regulatory Authorities, where applicable. An approved copy of this information must be provided to the participating subjects and/or parent or legal guardian, and the informed consent process as described above needs to be repeated. The investigator should inform the subject in a timely manner whenever new information becomes available that may be relevant to the subject's confirmed participation in the clinical study.

The investigator or designee will also determine that the subject/parent(s)/legal guardian can read, comprehend and make a decision regarding study participation of the subject (as applicable).

The original, signed and dated ICF/Assent Form must be retained in the subject's study records. The informed consent process must be documented in the subject's medical records and signed copies ofthe ICF/Assent Form will be provided to the subject and/or parent(s)/legal guardian. The date the subject and/or parent(s)/legal guardian signed the Informed Consent Form and data protection authorization (if applicable), and/or Assent must be documented in the subject's medical records.

9.4. Assessment of Safety

The criteria outlined in this section will be used to evaluate each subject before, during, and after surgery to determine the safety associated with the subject's treatment and study procedures. The safety of the Braive™ GMS will be assessed by evaluating the nature and frequency of AEs and additional surgical procedures (such as reoperations, revisions, or removals) and overcorrection.

9.4.1. Primary Safety Endpoint

The safety endpoint is any device-related adverse events up to 24 months. For this endpoint, the summary will be based on both Investigators and Medtronic relatedness assessment.

9.4.2. Secondary Safety Endpoint

The secondary safety endpoints are listed below:

- Procedure-related adverse events up to 24 months
- Secondary Spinal surgeries related to the original study device up to 24 months
- Device deficiency up to 24 months

For these endpoints, the summaries will be based on both Investigators and Medtronic relatedness assessment.

9.4.3. Adverse Events

All AEs will be collected (see section 11 for further details). AEs will be evaluated before, during and after surgery to determine the safety associated with the subject's treatment and study procedures.

The AEs will be classified according to the classification in Table 7: AE Definitions/Classifications.

The safety of the investigation will be assessed by evaluating the nature and frequency of AEs and subsequent spinal surgical procedures, as well as overcorrection, if applicable.

A steering committee and Medtronic medical advisor will monitor the safety of investigational treatment.

All adverse events will be reviewed by a Medtronic safety representative.

9.4.4. Neurological Status

Neurological status will be evaluated prior to the study treatment and at discharge. Neurological status can be performed at the investigator's discretion according to their standard of care at study follow up visits. Abnormalities should be reported as adverse event.
Neurological status is based on four types of measurements (sections): motor, sensory, reflexes, and straight leg raising. Each of the sections is comprised of a number of elements. Following scales will be used to evaluate neurological status: reflexes (0 = Absent, 1= Hypo-reflexia, 2 = Normal, 3 = Hyper-reflexia), sensory function (Light Touch T1 to S1, 1=Absent, 2=Impaired, 3=Normal), motor function (using 0-5 scores whereas 0= Total Paralysis, 1 = Palpable or Visible Contraction, 2 = Active Movement, Gravity Eliminated, 3 = Active Movement, Against Gravity, 4 = Active Movement, Against Some Resistance and 5 = Active Movement, Against Full Resistance (full strength) and straight leg raise (1 = positive, patient experiences radiating leg pain below the knee on elevating the leg between 15 and 70 degrees with the knee extended, 2 = negative, no pain is experienced on elevating the leg between 15 and 70 degrees with the knee extended).

Neurological change will be defined as deteriorate, maintenance or improvement in all sections (motor, sensory, reflex, and straight leg raising) between baseline and discharge. In order for a section to be considered a success, each element in the section must remain the same or improve from the time of the baseline evaluation to discharge. Therefore, if any one or more elements in any section does not stay the same or improve, then a patient will not be considered a success for neurological status. Note: For reflex, a change from Hypo-reflexia to Hyper-reflexia or a change from Hyper- reflexia to Hypo-reflexia is considered as maintained.

9.4.5. Overcorrection

When the growth modulation occurs at a relatively rapid rate, the spine may grow past a corrected (e.g., 0 degree or neutral) alignment. This phenomenon is termed overcorrection as it represents an overshoot of the desired clinical account of a 0 degree Cobb angle. A negative main thoracic Cobb angle indicates reversal of the curve, i.e., from right-sided to left-sided curve.

The risk of overcorrection is mitigated by the following:

- Limiting enrollment to subjects with a Sanders Score equal or greater than 2 to allow sufficient growth time for the Braive™ GMS to correct the curve without allowing extra time for overcorrection.
- Requiring investigators to review the educational tool and to follow the surgical technique.
- The risk reduction is achievable by understanding the potential for a rapid growth spurt (e.g., Sanders score) and the surgeon's control to avoid excessive compression with the Braid (e.g., surgical technique). Prior to skeletal maturity, clinically significant overcorrection of the curve can be treated by removing the Braid or releasing tension by cutting the Braid, which will allow increased growth of the vertebrae on the operated side and may reduce the overcorrection. After skeletal maturity, clinically significant overcorrection of the curve can be treated by fusion surgery, which is the standard of care for skeletally mature patients who have failed bracing and were not treated with vertebral body tether. The potential sequelae for overcorrection are the same as those for scoliosis; however, the degree of overcorrection curvature is likely to be less than the degree of curvature at baseline. Potential complications include: cosmetic such as uneven shoulders, one hip or rib cage prominent, and body tilted to one side, low back pain, lower self-esteem, decreased social functioning, depression, persistent pain if there is wear and tear of the spine bones, spinal infection after surgery, spine or nerve damage from curve or spinal surgery, and lung and heart problems (in severe scoliosis with curves > 70 degrees).

If overcorrection occurs, it will be at the discretion of the physician, in consultation with the patient and family, to determine if surgical intervention is necessary. Overcorrection is considered clinically significant if it is greater than 20 degrees and/or if it requires a secondary spinal surgery classified as treatment failure and will be considered a device-related adverse event.

9.4.6. Subsequent Spinal Surgical Intervention

Some adverse events or treatment failures may lead to additional surgical interventions. Relatedness of these subsequent spinal surgical interventions will be assessed as described in the following sections.

9.4.6.1. Types of Subsequent Spinal Surgical Interventions

Secondary spinal surgeries (equivalent to subsequent spinal surgical interventions) will be classified using the definitions as specified in section 11.1 Table 7.

Any subsequent spinal surgical intervention will be reviewed by Medtronic safety to determine whether it is a true treatment failure. Subjects with a treatment failure will only be followed up for safety (AEs and subsequent spinal surgical interventions) and radiographic imaging (Qualitative assessments only: Risser score, device integrity and additional observations) until the patient reaches skeletal maturity.

Total events and total number of subjects who have additional surgeries will be summarized. The numbers

of revisions (total, preventive and non-preventive), removals, reoperations and other surgeries will also be summarized.

9.4.6.2. Relatedness of Subsequent Spinal Surgical Interventions

A relatedness determination will be made by the investigator to the original study device and the original study surgery to a subsequent surgical intervention.

For the purpose of harmonizing reports, each subsequent spinal surgical intervention will be classified according to five different levels of causality. The investigator will use the following definitions to assess the relationship of the subsequent spinal surgical intervention to the original study device (i.e., investigational device), other surgical components, or study procedures.

- Not Related: Relationship of the subsequent spinal surgical intervention to the original study device or study procedures can be excluded.
- Unlikely: The relationship with the use of the original study device or study procedures seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
- Possible: The relationship with the use of the original study device or study procedure is weak but cannot be ruled out completely. Alternative causes are also possible (e.g., an underlying or concurrent illness/clinical condition or/and an effect of another device, drug, or treatment). In cases where relatedness cannot be assessed, or no information has been obtained, the relationship should also be classified as possible.
- Probable: The relationship with the use of the original study device or surgical procedure seems relevant and/or the need for a subsequent spinal surgical intervention cannot reasonably explained by another cause, but additional information may be obtained.
- Causal Relationship: The event is associated with the original study device or original surgical procedure beyond reasonable doubt.

A subsequent spinal surgical intervention determined as having “possible,” “probable,” or “causal” relationship to the Braive™ GMS will be conservatively considered as being “related” to the device.

9.5. Assessment of Effectiveness

9.5.1. Radiographic secondary endpoints

The radiographic secondary endpoints for this study are listed below. These endpoints are assessed as per site standard of care:

- Change from baseline in main thoracic Cobb angle at all available postoperative time points
- Change from baseline in proximal thoracic Cobb angle at all available postoperative timepoints
- Change from baseline in thoracolumbar/lumbar Cobb angle at all available postoperative timepoints

- Change from post-op baseline in Instrumented Cobb Angle at all available postoperative time points.
- Change from baseline in thoracic kyphosis at all available postoperative timepoints
- Change from baseline in Lumbar Lordosis at all available postoperative timepoints
- Change from baseline in coronal balance at all available postoperative timepoints
- Change from baseline in Sagittal Balance at all available postoperative timepoints
- Change from baseline in total vertical thoracic spine height (T1- T12) at all available postoperative timepoints
- Change from baseline in total vertical spine height (T1-S1) at all available postoperative timepoints

9.5.2. PedsQL (Pediatric Quality of Life Inventory™)

PedsQL will be evaluated prior to the study treatment.

The PedsQL Measurement Model is a modular approach to measuring health-related quality of life (HRQoL) in children and adolescents and those with acute and chronic health conditions. The 23-item PedsQL Generic Core Scales are designed to measure the core dimensions of health as delineated by the World Health Organization, as well as role (school) functioning. The 4 Multidimensional Scales are physical functioning, emotional functioning, social functioning and school functioning. The 3 Summary Scores are Total Scale score, Physical Health Summary score, and the Psychosocial Health Summary score. Two versions of this assessment will be filled out, one by the subject and one by the parent or legal guardian. Information from these versions will be analyzed separately.

9.5.3. SRS-22

The SRS-22 will be evaluated prior to the study treatment and postoperatively at 3 months, 6 months, 12 months, 18 months, 24 months and annually until skeletal maturity is reached.

The SRS-22 Patient Questionnaire has become the most widely used patient-reported outcome (PRO) instrument for evaluating individuals with idiopathic scoliosis. The SRS-22 contains 22 questions covering 5 domains: function/activity 5 items; pain 5 items; self-perceived image 5 items; mental health 5 items; and satisfaction with treatment 2 items. Each item is scored from 1 (worst) to 5 (best). Each domain has a total sum score ranging from 5 to 25, except for satisfaction, which ranges from 2 to 10. The sum of the first 4 domains gives a maximum subtotal of 100, and when the satisfaction domain is included, the maximum total is 110.

9.6. Imaging Guidelines

Study subjects are required to undergo imaging procedures at specified time points during the study. To ensure consistency in the type and quality of all images obtained throughout this study some requirements have been defined:

- Clinical sites must use imaging equipment (X-ray) that are maintained and calibrated according to the manufacturer's specifications when performing imaging procedures on subjects for this study.
- Imaging equipment maintenance and calibration will be monitored.
- To reduce the radiation exposure to study subjects, all X-ray examinations should be realized at the lowest radiation dose that still provides the minimally required image quality.

A Radiographic evaluation protocol will be kept separate from this document.

9.7. Recording Data

The investigator must ensure that the data reported in the eCRF and all other required study reports are accurate, complete and reported in a timely manner. Data reported on the eCRFs must be consistent with the source documents, and discrepancies between the eCRF and source documents need to be justified in writing, signed and dated by the investigator, and filed in the subject's medical file or appropriate location.

Subject neurological status and instrument accountability can be recorded directly on the eCRF and is considered source data. All other data entered in the eCRFs should be documented in the subject's medical records/source document (electronic or paper), (e.g., hospital records, surgery reports, x-rays, MRIs, CTs, or any other material that contains original information used for data collection including the documentation of AEs and study source document completed by the investigator or site staff). Subject/parent(s)/legal guardian completed questionnaires as well as data collected during subject/parent(s)/legal guardian phone calls will be considered as source data.

This study will be conducted using a Remote Data Capture (RDC) system. The RDC system allows the study centers to enter study data into the sponsor's database over a secure internet connection. Required data will be taken from source documents and directly entered into the study database by authorized site personnel in accordance with applicable regulations.

Every attempt should be made to complete the required onsite clinic visit. However, if the subject is unable to return to the investigational site for their scheduled follow-up visit, the study site can contact the subject and collect the following data remotely using the source document worksheet:

- SRS-22 – phone version or web-based application
- Adverse events and/or device deficiencies

The Principal Investigator or an individual delegated by the Principal Investigator on the Delegation of Authority Log is responsible for documenting and entering data for the study on the eCRFs. Only authorized site study staff can complete eCRFs. eCRFs shall be signed by the Principal Investigator or Sub-investigators (physicians only) as specified on the Delegation of Authority Log included in the Investigator Site File. The Principal Investigator or delegated Sub-Investigator is required to approve all data on eCRFs via electronic signature.

Procedures used for data review, database cleaning, and issuing and resolving data:

- Data will be reviewed using programmed and manual data checks.
- Data queries will be made available to centers for resolution.
- Study management reports may be generated to monitor data quality and study progress.

9.8. Deviation Handling

A study deviation is an event where the investigator or site personnel did not conduct the clinical study according to the Clinical Investigational Plan or Clinical Investigation Agreement.

The investigator is not allowed to deviate from the above-mentioned documents except under emergency circumstances to protect the rights, safety and well-being of human subjects. All deviations shall be documented in the eCRF and explained, regardless the reason for the deviation. Multiple deviations of the same type at the same visit may be reported on one e-CRF.

Examples of study deviations include but are not limited to:

- Informed Consent procedures
- Enrolled subject does not meet Inclusion/Exclusion criteria for those criteria assessed by the investigator. The Radiographic Review Core Lab will perform an independent subject eligibility review for the following in/exclusion criteria after the patient has been enrolled:
    - Is skeletally immature with a Sanders Score of ≥2 to ≤5
    - Has a main thoracic Cobb angle between 30 and 60 degrees
    - Has a Lenke Classification of 1A, 1B, or 1C
    - Has kyphosis ≤ 40 degrees with a sagittal thoracic modifier N or negative

  In case the patient does not meet any of the in/exclusion criteria as listed above this will not be considered a protocol deviation, but the patient will be exited and can be replaced if enrollment is still open.
- Visit not done
- Assessment(s) at the visit not performed
- Visit outside the defined visit window
- Subject did not undergo Braive procedure as defined in this protocol
- Improper reporting of AEs, serious adverse events (SAEs), adverse device effects (ADEs), serious adverse device effects (USADEs or SADEs) and device deficiencies (DDs).
- IRB/EC/REB approval not obtained, if required
- Is pregnant or becomes pregnant within first 24-months of the study
- COVID-19 impact

9.8.1. Request for approval of study deviations

Prior approval by Medtronic is expected in situations where the investigator anticipates, contemplates, or makes a conscious decision to deviate. Prior approval is not required when a deviation is necessary to

protect the safety, rights or well-being of a subject in an emergency or in unforeseen situations beyond the investigator's control (e.g., inability to perform required procedures due to subject inability or illness).

For medically justifiable conditions which preempt a subject's ability to complete a study-required procedure, it may be permitted to report only one deviation which will apply to all visits going forward. This may also apply for other unforeseen situations (e.g., the subject permanently refuses to complete a study required procedure and the data will not contribute to the primary endpoint analysis). However, prior approval from Medtronic is required for such situations.

9.8.2. Reporting requirements for study deviations

The Investigator shall adhere to IRB/EC/REB requirements and procedures for reporting study deviations and shall report the deviation as soon as possible to Medtronic. Medtronic is responsible for analyzing deviations, assessing their significance, and identifying any additional corrective and/or preventive actions (e.g., amend the CIP, additional training, terminate the study, etc.). Repetitive or serious investigator compliance issues may result in the need to initiate a corrective action plan, and in some cases, freeze enrollment or ultimately terminate the investigator's participation in the clinical study.

In the event the deviation involves a failure to obtain a subject's consent or is made to protect the life or physical well-being of a subject in an emergency, the deviation must be reported to the IRB/EC/REB as well as Medtronic per IRB/EC/REB and local reporting requirements. Reporting of all other study deviations should comply with IRB/EC/REB and Regulatory Authorities (where applicable) policies and/or local laws and must be reported to Medtronic as soon as possible upon the center becoming aware of the deviation. Medtronic is responsible for reporting all study deviations to Regulatory Authorities as applicable.

9.8.3. Amendments to the Clinical Investigation Plan

The investigator will propose any appropriate modification(s) of the CIP or investigational device or investigational device use. Medtronic will review this proposal and decide whether the modification(s) will be implemented.

Medtronic will submit any significant amendment to the CIP, including a justification for this amendment, to the appropriate regulatory authorities and to the investigators to obtain approval from their IRB/EC/REB and Regulatory Authorities, where required by local law/regulations. Administrative amendments to the CIP will be submitted to the IRB/EC/REB and appropriate regulatory authorities for notification, where required by local law/regulations.
Furthermore, investigators shall sign any approved amendment for agreement.

9.9. Subject Withdrawal or Discontinuation

Subjects are free to voluntarily withdraw from the study at any time and for any reason. The Investigator can only withdraw a subject from the study with a valid reason. Withdrawn or exited subjects will be followed under normal medical practice. Examples of reasons for subject discontinuation include, but are not limited to, those listed below:

- Informed Consent procedures not followed
- Subject does not meet all eligibility criteria
- Subject death
- Subject lost to follow-up
- Subject voluntarily withdraws from the study
- Subject did not undergo the Braive procedure as defined in this protocol

If a subject is withdrawn from the study, the reason for withdrawal (if known) shall be recorded in the eCRF and in the subject's hospital record.

Subjects withdrawn from the study were only replaced when subjects did not meet baseline eligibility or did not undergo the Braive procedure as defined in this protocol while the enrollment was still open.

Compliance with the required follow-up schedule is essential to enable the analysis of the results in a scientifically sound and meaningful way. If, for whatever reason, the subject follow-up visit cannot be scheduled within the time window, it is still essential to schedule a follow-up visit and to document the subject data at a date as close as possible to the calculated follow-up date.

As much as possible, subjects should not be lost-to-follow-up and investigators are urged to do their utmost best to maintain subject follow-up compliance as per CIP.

9.9.1. Withdrawal of consent

Subjects/parent(s)/legal guardian may withdraw from the study at any time and for any reason. If a subject withdraws from the study, the reason for withdrawal will be documented, if given by the subject/parent(s)/legal guardian, in the source documents and in the subject's eCRF. If a subject withdraws consent after undergoing the Braive procedure, they will not be replaced. The follow up of these subjects will be according to the standard of care at the site.

If a subject withdraws, study staff should make a reasonable effort to determine the reason for the subject's withdrawal from the study and to complete the Exit eCRF. Telephone calls, registered letters, and offers of transportation to the investigational site are considered reasonable effort. Documentation of communication attempts should be kept in the subject's chart to document the site's efforts in securing follow-up compliance. If a subject is withdrawn from the study, any missed visits or remaining evaluations will not be considered study deviations. If the subject agrees, he/she is to be followed via

telephone/mail/electronic media for the duration of the study to assess for AEs and/or subject survival and pregnancy outcome (if applicable).

Subjects who withdraw prior to surgery will not be counted in the total number of treated study subjects and will not be included in the efficacy analyses of the data. For subjects who are withdrawn during surgery due to an AE, the AE will be recorded on an Adverse Event eCRF and included in a summary of subject discontinuations.

9.9.2. Lost to follow up

Before considering a subject as lost to follow up, the investigator should make every attempt to contact the subject and the parent(s)/legal guardian (or relevant other persons associated with the subject) to have the subject return for follow-up to determine their clinical status and the occurrence/resolution of AEs, if any.

Before documenting a subject as lost to follow up, the investigator should document in the eCRF and source documents at least 3 contact attempts with the subject, subject's relatives or other persons associated with the subject. In addition, the investigator should make a reasonable effort to ascertain the reason(s), while fully respecting the subject's rights (e.g., if a subject is deceased, the date of death should be completed or if the subject is alive, the date of last contact with subject should be provided).

When subjects are lost to follow-up the investigator will make efforts to confirm the vital status of the subject, as described in the informed consent.

10. Risks and Benefits

10.1. Potential Risks

Medtronic has conducted a risk analysis for subjects in this study. Potential risks associated with participation in this study include those that might reasonably be expected to occur in association with the underlying medical diagnosis, surgical procedure(s), and use of the proposed study device. The clinical investigation has been designed to involve as little pain, discomfort, fear and any other foreseeable risk as possible for the subjects, and both the risk threshold and the degree of distress are specifically defined in the clinical investigation plan and constantly monitored. In the clinical study, the products will be used in accordance with the Surgical Technique and the IFUs that are available separate from this CIP. Reference is made to the IFUs for a detailed list of all risks and contra-indications associated with the devices and surgery. Additional risks are those associated with radiation exposure for x-rays beyond the standard of care for the purpose of study follow-up. X-rays will be taken prior to enrollment, during surgery and at each follow-up visit. Females of childbearing age should be aware that radiation exposure may be harmful to an unborn fetus.

Radiation doses may be potentially harmful, but the exact risks are difficult to measure. Subjects who are still concerned with the radiation exposure will be counseled that they may discuss this with their study doctor at any time.

Medtronic follows rigorous Quality Assurance and Control procedures throughout the life of a product, from the business analysis phase through development, market release, and post-market surveillance. The risk analysis process for the BRAIVE IDE study was performed in accordance with ISO 14971 to ensure that the level of risk was acceptable prior to starting the study.

10.2. Risk Minimization

A comprehensive set of risk mitigation actions will be undertaken before, during and after the device implantation.

10.2.1. Overall Mitigation Factors

Overall study factors to mitigate risks include:

- Investigator Selection

  Investigational sites will be selected based on experience and expertise in managing patients with JIS/AIS, ability to comply with the protocol and regulations, and clinical research expertise and resources. Only surgeons capable of performing the surgical procedure will be selected, which will mitigate the risks associated with the general surgery and with the treatment. Investigators selected to participate in this clinical study will be responsible for fulfilling the requirements of the investigator's agreement and investigational plan. All investigators will sign an investigator agreement prior to initiation of screening or enrollment activities.

  Each investigator will be trained in all aspects of the protocol, including the surgical technique and completion of subject documentation. The Investigators will receive procedure and device specific educational tools, that will provide specific training on the targeted patient group and pathology. This training will assist the investigators with optimal patient selection and in all aspects regarding the pre-operative planning and implantation of the device.

  Additionally, each investigator will be expected to make every effort to attend periodic Investigator's Meetings or conference calls when requested (or send a representative, if unavailable) to assure familiarity and compliance with the study protocol.

- Subject Selection

  Appropriate subjects will be carefully selected according to the specified inclusion and exclusion criteria, which will ensure that all the criteria from the approved intended use of the Braive GMS are met.

10.2.2. During Surgery

- Risks of Braive™ GMS

  Investigators will be chosen based on relevant surgical experience and qualifications. Each investigator will be trained in all aspects of the protocol, including the surgical technique and completion of subject documentation. Furthermore, a minimally invasive, endoscopic approach with 20 mm skin incisions is used to implant the Braive GMS. This approach provides improved visualization of the spine, which reduces the risks associated with open surgery and eliminates the risk of a poor cosmetic result from a thoracotomy incision. Navigation and fluoroscopy alternatives are also available, thus further increasing the precision of the procedure and reducing the surgical risks.

- Risks of Medtronic Reusable Instruments and Accessories (with/without StealthStation)

  Investigators will be chosen based on relevant surgical experience and qualifications. Selection of appropriate patients, as well as knowledge and understanding of the surgical technique, are important considerations in the successful use of the instruments and accessories by the investigator. Thus, each investigator will be trained in the surgical technique. Additionally, the inclusion and exclusion criteria specified in the protocol ensure that appropriate patients are selected.

10.2.3. During Post-operative Care

Clinical and radiographic assessments including collection of Adverse Events, Reoperations and Revisions/Removals will be performed prior to hospital discharge (immediate post-op), postoperatively at 3 months, 6 months, 12 months, 18 months and 24 months and annually thereafter until the subject reaches skeletal maturity (defined as Risser 5 as assessed by investigator), and as reported, regardless of follow-up interval. These assessments will mitigate the risks associated with the device including:

- Overcorrection Risk

  The risk for overcorrection is the main risk with the anterior vertebral tethering procedure as many patients will experience a spine growth spurt after the device implantation. This growth spurt will render a faster spine deformity correction but also may increase the risk of overcorrection, which may require revision or removal. Therefore, follow up visits are scheduled at least every 6 months for the first 24 months following surgery and then annually until the subject reaches skeletal maturity (defined as Risser 5 as assessed by investigator). This provides the Investigators the opportunity to detect and treat curve corrections that may be approaching overcorrection.
- Other Device and/or Procedure-Related Risks

Other reported risks with the procedure are implant loosening and implant failure, which may require revision or removal. The follow up visits that are scheduled until the subject reaches skeletal maturity ensure that these potential risks will be detected and can be treated before they have progressed.

- Radiation Exposure Risk

  Subjects will be exposed to radiation from X-rays taken during follow-up visits. However, some of these X-rays would likely be taken as standard of care for this condition, regardless of whether the patient was in the study. The ALARA (as low as reasonably possible) principles of reducing radiation exposure to the subjects enrolled will be recommended to all sites participating in the BRAIVE IDE study.

10.2.4. Oversight of Safety

The following oversight of safety mitigates the risk of device and/or procedure related adverse events being underreported or reported as either not related to the device and/or procedure or as nonserious.

- Monitoring

  This study will be monitored according to a study specific monitoring plan. Therefore, it is expected that all adverse events will be captured and documented.
- Safety representative

  All Adverse Events will be reviewed by Medtronic safety representative according to the Clinical Safety Management and Potential Complaint Plan.
- Steering Committee and Medtronic Medical Advisor

  A steering committee and Medtronic medical advisor will monitor the safety of investigational treatment.

10.2.5. Warning and Precautions

The following Warnings and Precautions will mitigate the risks of subject selection, the surgical procedure and the Braive GMS device.

A successful result is not always achieved in every surgical case. Spinal deformity may be unrelieved or worsened. There are general risks related to surgery, and specific risks related to the anterior procedure with the Braive™ GMS. These risks have been considered and mitigated as above. Careful patient selection, preoperative planning and surgical technique should be executed according to the training and education provided, and according to the study protocol and Instructions for Use. Unexpected events and variable patient biologic characteristics may still occur.

Multiple factors contribute to the amount of curve correction including initial Cobb angle, growth potential remaining, and degree of intraoperative correction. Both under- and overcorrection are

possible, the latter being more prevalent in literature to date. Determining the amount of bone age remaining at the time of surgery and understanding general principles of growth modulation are critical to mitigating correction variables. Care should be taken to consider relevant patient parameters in preoperative planning and extent of intraoperative correction. Patients should be closely monitored postoperatively.

Intervention may be necessary in the form of revision to cut, remove, or replace the braid or convert to fusion. An implanted device should never be re-used. Implants are designed for single patient use only. Do not reuse, reprocess, or re-sterilize used implants. Reuse, reprocessing, or re-sterilization may compromise the structural integrity of these implants and create a risk of contamination of the implants which could result in patient injury, illness, or death

10.3. Potential Benefits

The primary benefits expected for the subjects treated with the Braive™ GMS include the prevention of curve progression and/or improvement of the curve, maintenance of spine flexibility with preservation of neurologic status, improved cosmesis and quality of life, and diminishing the need for spinal fusion surgery and its related potential risks. Advantages of the vertebral tethering technique compared to fusion include less blood loss, faster recovery time, spinal motion sparing, and less hardware placement resulting in decreased complications. Another cosmetic benefit due to the thoracic approach is the very small surgical incision below the armpit compared to the long incision along the spinal column for spinal fusion.

Additionally, information collected from this study may assist in the modification of the existing system, the design of new product (s)/therapy(ies), and/or IFUs.

10.4. Risk-Benefit Rationale

Treatment of JIS and AIS patients via an anterior procedure with Braive™ GMS is expected to prevent the curve progression and/or improvement of the curve, to maintain a flexible spine into adulthood and to reduce the risk of fusion surgery later on in life. The treatment is also expected to result in improved subject spine cosmesis, improved self-esteem, social activities status and improved quality of life. These subjects will have failed conservative treatment such as monitoring, physiotherapy and bracing, and are at risk of continued curve progression. Progression of the curve to the threshold where a spine fusion would be necessary, later in life, would be associated with increased morbidity risk, reduced quality of life and increased risk for re-operation. Any risks associated with participation in this clinical study will be minimized and managed in accordance with and full compliance to 21 CFR Parts 50 (US only), 56, and 812 (US only) and ISO14155:2020. The risks are minimized by selecting only qualified investigators experienced in the field of application and trained in the use of the study device(s) and qualified by education, training, and experience to assume responsibility for the proper conduct of the clinical investigation. In addition, this protocol outlines a follow-up period designed to monitor the subjects until

skeletal maturity, with the majority of the visits taking place in the first 24 months to allow for the early detection of any adverse event. To reduce the risk of overcorrection, a subject's remaining growth potential is limiting enrollment to subjects with a Sanders Score between 2 and 5. Additionally, the surgeon's understanding of operative factors and the surgical technique reduce the risk of overcorrection. Prior to skeletal maturity, clinically significant overcorrection of the curve can be treated by removing the device, replacing and re-positioning the device, or cutting the braid component to release tension, all of which will allow increased growth of the vertebrae on the operated side and may reduce the overcorrection. After skeletal maturity, clinically significant overcorrection of the curve can be treated by fusion surgery, which is the standard of care for skeletally mature patients that have failed bracing and were not treated with the AVBT. The potential sequelae for overcorrection are the same as those for scoliosis; however, the degree of overcorrection curvature is likely to be less than the degree of curvature at baseline.

All the risks with the device have been deemed acceptable and the benefits of participating in the study outweigh the risks.

11. Adverse Events and Device Deficiencies

All AEs, DDs, and deaths, regardless of relatedness to surgical procedure or outcome, should be reported from the time the subject signs the informed consent form throughout the study in the eCRF and should be made available to the Medtronic study team. If applicable, these AEs and DDs will be reported to other countries where studies are conducted with the same or a similar product.

11.1. Definitions/Classifications

Investigator will classify each adverse event according to ISO 14155:2020. Adverse events and device deficiencies are defined as follows. Where the US and European terminology differs, the US term is listed first, followed by the European term.

Table 7: AE Definitions/Classifications

ISO Definitions for Clinical Investigations of Medical Devices for Human Subjects
Adverse Event (AE): *(ISO14155:2020 section 3.2)* Untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated *NOTE 1:* This definition includes events related to the investigational medical device or the comparator. *NOTE 2:* This definition includes events related to the procedures involved.

NOTE 3: For users or other persons, this definition is restricted to events related to investigational medical devices or comparators.

Adverse Device Effect (ADE): *(ISO14155:2020 section 3.1)*

Adverse event related to the use of an investigational medical device

NOTE 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

NOTE 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

NOTE 3: this includes 'comparator' if the comparator is a medical device.

Device Deficiency (DD): *(ISO14155:2020 section 3.19)*

Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance.

NOTE 1: Device deficiencies include malfunctions, use errors and inadequacy in the information supplied by the manufacturer including labeling.

NOTE 2: This definition includes device deficiencies related to the investigational medical device or the comparator.

SERIOUSNESS

Serious Adverse Event (SAE): *(ISO14155:2020 section 3.45)*

Adverse event that led to any of the following

a) death,
b) serious deterioration in the health of the subject, users or other persons as defined by one or more of the following:
1) a life-threatening illness or injury, or
2) a permanent impairment of a body structure or a body function, including chronic disease, or
3) in-patient or prolonged hospitalization, or
4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
c) Fetal distress, fetal death or a congenital abnormality or birth defect including physical or mental impairment

NOTE 1: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.

Serious Adverse Device Effect (SADE): *(ISO14155:2020 section 3.44)*
Adverse device effect that has resulted in any of the consequences characteristic of a Serious Adverse Event.

Unanticipated Adverse Device Effect (UADE): *(21 CFR 812.3(s))*

Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death, was not previously identified in a nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Unanticipated Serious Adverse Device Effect (USADE): *(ISO14155:2020 section 3.51)*

Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk assessment

NOTE 1: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.

Serious Health Threat: *(ISO14155:2020 section 3.46)*

Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons

NOTE 1: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.

RELATEDNESS	
Relationship of Adverse Events	Assessment of causality will be assessed for this study on the following basis: **1. Not related**: The relationship to the device or procedures can be excluded when: • The event is not a known side effect of the product category the device belongs to or of similar devices and procedures; • the event has no temporal relationship with the use of the investigational device or the procedures; • the event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible; • the discontinuation of medical device application or the reduction of the level of activation/exposure when clinically feasible and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious event; • the event involves a body site or an organ not expected to be affected by the device or procedure; • the event can be attributed to another cause (e.g., an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors); • the event does not depend on a false result given by the investigational device used for diagnosis, when applicable; • harms to the subject are not clearly due to use error. To establish the non-relatedness, not all the criteria listed above might be met at

	the same time, depending on the type of device/procedures and the serious event.
	
	2. Unlikely: The relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
	
	3. Possible: The relationship with the device is weak but cannot be ruled out completely; alternative causes are also possible (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases where relatedness cannot be assessed, or no information has been obtained should also be classified as possible.
	
	4. Probable: The relationship with the use of the device seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be obtained.
	
	5. Causal relationship: the event is associated with the investigational device or procedures beyond reasonable doubt when:
	• the event is a known side effect of the product category the device belongs to or of similar devices and procedures;
	• the event has a temporal relationship with the investigational device use/application or procedures;
	• the event involves a body-site or organ that
	  ○ the investigational device or procedures are applied to;
	  ○ the investigational device or procedures have an effect on;
	• the event follows a known response pattern to the medical device (if the response pattern is previously known);
	• the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the event (when clinically feasible);
	• other possible causes (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out;
	• harm to the subject is due to error in use;
	• the event depends on a false result given by the investigational device used for diagnosis, when applicable;
	
	To establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device /procedures and the serious event.

SEVERITY	
Mild (Grade 1): Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated. **Moderate (Grade 2):** Minimal, local or noninvasive intervention indicated; limited age appropriate instrumental activities of daily living (preparing meals, shopping, using the phone, managing	

money, etc.).

Severe (Grade 3): Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting age appropriate self-care activities of daily living (bathing, dressing and undressing, feeding self, toileting, taking medications, and not bedridden).

Life Threatening (Grade 4): Life threatening consequences; urgent intervention indicated; death.

SUBSEQUENT SPINAL SURGICAL INTERVENTION

Subsequent spinal surgical interventions will be classified using the following definitions, based on the description provided:

- Revision is a procedure that adjusts, or in any way modifies or removes, *part* of the original implant configuration, with or without replacement of a component. A revision may also include adjusting the position of the original implant configuration.
  Revisions will be considered in two categories:
  - Preventive surgery: Any braid manipulations (e.g., cutting or loosening the braid). *Preventive surgery for overcorrection will not be considered a treatment failure*
  - Non-preventive surgery: The revision is the result of an adverse event, i.e., the initial positioning of the device contributed to the adverse event and must be repositioned, or additional instrumentation is added to the original implant configuration. *Non-preventive surgery will be considered as a treatment failure.*
- Removal is a procedure where *all* of the original system configuration is removed with or without replacement. *Removal surgery will be considered a treatment failure.*
- Reoperation is a surgical procedure at the study treatment level(s) that does not involve removal, modification, or addition of any components to the original system. Examples include debridement of a surgical wound, scar revision or evacuation of a hematoma. *These will not be considered a treatment failure.* Spinal fusion or extension of the fixation due to the progression of initial scoliosis *will be considered a treatment failure*.
- Other is any other subsequent spinal surgical procedure not classified as a revision, removal or reoperation. Examples include spinal surgery not at the study treatment level(s) such as microdiscectomy or hernia repair.

11.2. Reporting of Adverse Events

All Adverse Events (except unavoidable events listed in Section 11.3), regardless of relatedness or outcome, must be reported. The investigator is responsible for reporting all AEs to Medtronic and for their follow up.

Pain, neurological, and function symptoms should be reported as an adverse event when a subject's

complaint for any of these symptoms results in an unscheduled visit or when a subject presents with clinically significant new or worsening pain, neurological and/or function symptoms as compared to the previous visit.

All adverse events will be classified using the following responsibility matrix:

Table 8. Adverse Event Classification Responsibilities

What is classified?	Who classifies?	Classification Parameters
Relatedness	Investigator	Device, Procedure
	Sponsor	Device, Procedure
Seriousness	Investigator	SAE, DD with SADE potential
	Sponsor	SAE, DD with SADE potential
Severity	Investigator	Mild, Moderate, Severe, Life Threatening
Diagnosis	Investigator	Based on presenting signs and symptoms and other supporting data
	Sponsor	MedDRA term assigned based on the data provided by Investigator
Expectedness	Sponsor	UADE/USADE

From the time that the assent/informed consent forms are signed, all reportable events must be recorded in the subject's medical record and on the Adverse Event and/or Device Deficiency eCRF and promptly reported to Medtronic. IRB/EC/REB reporting must be completed in accordance with the policies of the governing IRB/EC/REB. Regulatory Authority reporting should be in accordance with applicable local regulations.

It is the responsibility of the investigator to identify the occurrence of adverse events and device deficiencies and to ensure the required information is accurately documented on the eCRF.
Reports of adverse events and device deficiencies will include the following information, at a minimum:

- Date of event
- Date site became aware of the event
- Diagnosis or description of the event
- Assessment of the seriousness and relationship to the device and/or surgical procedure
- Treatment provided

- Outcome and date of resolution

The clinical course of each adverse event must be followed until resolution, subject discontinuation from the study or last study follow up visit, whichever comes first. “Not resolved” adverse events and device deficiencies must be assessed at each protocol required visit, and new or updated information must be documented on the Adverse Event and/or Device Deficiency eCRF and promptly reported to Medtronic and where applicable to the IRB/EC/REB. At time of study exit, the status of all unresolved Adverse Events should be evaluated and should reflect the subject's status at time of study exit.

Upon request of Medtronic, de-identified source documentation should be provided to Medtronic. When printouts of original electronic source documents are obtained, these shall be signed and dated by a member of the investigator site team with a statement that this is a true reproduction of the original source document.

Upon request of Medtronic, de-identified images should be provided to Medtronic.

Medtronic study personnel will promptly review all reported adverse events and device deficiencies and if necessary, request clarification and/or additional information from the investigator. If Medtronic disagrees with the Investigator’s assessment of the adverse event seriousness and relationship to the device and/or procedure, Medtronic study personnel will document the disagreement and report or ensure reporting of both opinions to the IRB/EC and regulatory authority as necessary. In addition, aggregate safety data will be reviewed and analyzed to identify potential safety issues, signals, and trends at minimum, annually.

Investigators must report applicable events and product deficiencies to Medtronic and where appropriate, to an IRB/EC/REB or regulatory authority. Details (e.g., date of event, treatment, resolution, seriousness, relationship to the product) of the events and product deficiencies must be documented in the medical record and reported to Medtronic per Table 10.

11.3. Not reportable events

Examples of events that are not reportable as adverse events for this study are:

- A documented pre-existing condition unless there is a worsening of the nature, severity, duration, or frequency of that condition.
- Elective or Preventative medical procedures (e.g., tooth extraction, cosmetic surgery); however, the condition leading to the procedures might be a reportable event if there is a worsening of the nature, severity, duration, or frequency of that condition.

Table 9 provides a list of Unavoidable Adverse Events (UAE). An UAE will not be considered reportable unless it worsens or is present outside the stated timeframe post-procedure.

Table 9. Unavoidable Adverse Events (UAEs)

Event Description	Timeframe from the Surgical Procedure
Anesthesia related nausea / vomiting	24 hours
Low-grade fever (<100°F or 37.8°C)	48 hours
Mild to moderate bruising / ecchymosis	7 days
Seroma	72 hours
Sleep problems (insomnia)	72 hours
Back pain related to laying on the table	72 hours
Shoulder pain/discomfort/stiffness	72 hours
Pneumothorax, non-serious	72 hours
Supplemental Oxygen with no other	24 hours
Blood loss less than 800 cc	24 hours

11.4. Device Deficiencies

A device deficiency (DD) is an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Device deficiencies include malfunctions, use errors, and inadequate labeling. All device deficiencies must be documented and submitted to Medtronic on the Device Deficiency eCRF. In addition, the investigator must also determine and document on the eCRF device deficiencies that did not lead to adverse event but could have led to a serious adverse device effect:

- If either suitable action had not been taken,
- If intervention had not been made, or
- If circumstances had been less fortunate
- Refer to Table 10 for investigator reporting timelines for device deficiencies.

11.5. Reporting Adverse Events to Medtronic

Investigator reporting timelines can be found in Table 10. The preferred way of transmission of AEs and DDs is the RDC system, but in case the eCRF cannot be accessed, the investigator should contact study personnel by e-mail to report. The AE/DD worksheet provided to investigators may be used for completion of available information, preferably signed by investigators and attached to the email. The same CIP reporting timelines apply for all types of reporting as if the eCRF would be available.

Table 10. Required timeframes for Adverse Advent Reporting by Investigator

Required Timeframes for Adverse Event reporting from Investigator to Medtronic	
Event Type	**Timeframe for Reporting**
Serious Adverse Event (SAE)	Immediately (but no later than 3 calendar days) after the investigator first learns of the event or of new information in relation with an already reported event.
Serious Adverse Device Effect (SADE)	
Unanticipated Adverse Device Effect (UADE)	
Unanticipated Serious Adverse Device Effect (USADE)	
Device Deficiencies with SADE potential	
All Other Adverse Event (AE)	In a timely manner after the investigator first learns of the event
All other Device Deficiencies	
Required Timeframe for Adverse Event reporting from Investigator to Health Canada (for Canadian sites only)	
Serious Adverse Device Effect (SADE)	In Canada, SADEs on the subject, the user or any other person must be reported to Health Canada and to the sponsor within 72 hours after it comes to the attention of the qualified investigator.
Unanticipated Adverse Device Effect (UADE)	In Canada, UADEs on the subject, the user or any other person must be reported to Health Canada and to the sponsor within 72 hours after it comes to the attention of the qualified investigator.
Unanticipated Serious Adverse Device Effect (USADE)	In Canada, USADEs on the subject, the user or any other person must be reported to Health Canada and to the sponsor within 72 hours after it comes to the attention of the qualified investigator.
Device Deficiencies with SADE potential	In Canada, DDs that have resulted in any of the consequences characteristic of an SAE on the subject, the user or any other person or could do so were it to reoccur must be reported to the regulator and the Sponsor within 72 hours after it comes to the attention of the qualified investigator.

The AE reporting period for each subject starts when the subject and/or parent/legal guardian signs the Informed Consent/Assent and continues at all subsequent visits through the end-of-study. Any pre-existing conditions that are detected as part of the screening procedures should be reported on the

prior medical history form and not as AEs. However, pre-existing conditions that worsen during the study will need to be reported as AEs.

If possible, a specific diagnosis should be recorded, rather than a listing of individual signs and symptoms.

In addition, investigators are obligated to report adverse events in accordance with the requirements of their reviewing IRB/EC/REB and regulatory authority (where applicable). The Sponsor is obligated to report AEs that occur during this trial to the Regulatory Authorities and IRB in compliance with applicable local requirements.

Any necessary follow-up reports should be completed by updating the original AE eCRF in a timely manner. All follow-up reports should give full details of the event, including an updated assessment of the relationship to the procedure and/or device. When contacting the sponsor regarding SAEs/UADEs, site personnel should be prepared to provide as much information as is available at the time.

Detailed sponsor contact information including emergency contact details will be provided under a separate cover.

11.6. Pregnancy Reporting

Pregnancy itself is not considered to be an adverse event; however, it is a study deviation if the subject becomes pregnant within 24 months postoperatively. If the subject experiences untoward medical occurrences during pregnancy or at delivery, these should be recorded as an adverse event and reported to the sponsor immediately after becoming aware of the event. Female subjects who become pregnant during the study will be followed until the completion of the study. If available, outcomes will be collected on both mother and child.

11.7. Deaths

All subject deaths must be reported to Medtronic and the IRB/EC/REB as soon as possible (but no later than 3 calendar days), after learning of a subject's death, regardless of whether or not the death is related to the device system and/or procedure. The investigator should also attempt to determine, as conclusively as possible, whether such deaths are related to the device system and/or procedure. If the death is evaluated as device and/or procedure related and unanticipated, the event will be reported as a UADE/USADE by Medtronic or its designee to the appropriate Regulatory Authorities.

Any subject death will be reported on the Adverse Event and Study Exit eCRFs. If limited information is known, the Adverse Event eCRF must be completed with available information as soon as possible. The cause of death will be reported on the Adverse Event and death will be reported on the Study Exit eCRFs.

12. Data Review Committees

12.1. Data Monitoring Committee

Ongoing oversight for this study was provided by an independent DMC (Data Monitoring Committee) until enrollment was stopped. Considering enrolment stop and the changes in study design the decision was made to close the DMC and institute a periodic data review by a steering committee and Medtronic medical advisor to monitor the safety of the investigational treatment. The BRAIVE IDE Clinical Study steering committee is a group of at least 3 scientific or subject matter experts which includes pediatric orthopedic surgeons and neurosurgeons and physicians involved in juvenile and adolescent scoliosis. A chairperson from among those members will be identified and the steering committee will operate according to a charter. A review of the FDA annual report and event rate of the study will be made at least annually by steering committee, active investigators and Medtronic medical advisor.

12.2. CRO / Core labs

The information below maybe subject to change during the course of the study. Periodic updates to study contact information will be sent to study sites as need.

Table 11. CRO and Core Laboratory Information

Contact Information	Role
Medical Metrics, Inc 2121 Sage Road, Suite 300 Houston, TX 77056 USA	Radiographic analysis lab & Image Transfer of intraoperative images Used for eligibility assessment of currently enrolled subjects

13. Statistical Design and Methods

The initial plan was to conduct the primary analysis when all subjects have reached the 2-year visit and an updated analysis when all subjects have reached skeletal maturity. Due to the decision to stop study enrollment, a final analysis will be conducted when all subjects have reached skeletal maturity. An interim analysis may be conducted when all subjects reach 24-month visit in addition to the progressive report requested by FDA. .

13.1. Analysis of Baseline Data

Baseline and pre-operative data will include but are not limited to height, weight, age, and preoperative clinical and radiographic measurements. Demographics and other pre-treatment characteristics will be summarized and characterized with appropriate descriptive statistics. Categorical variables will be

summarized using frequency and percentage. Continuous variables will be summarized using mean, median standard deviation, minimum, and maximum.

13.2. Sample Size

This initial study was designed to show that the investigational device can be used to obtain a statistically significant improvement (>0) in the main thoracic Cobb angle. The initial sample size required to demonstrate a statistically significant improvement of Cobb angle at 24 months as compared to that in the preoperative visit is 24. Medtronic planned to treat 25 subjects. Due to the decision to stop enrollment early, the sample size is 10 at the time of enrollment stop.

13.3. Primary Analysis Population

The primary analysis population will include all subjects who are enrolled and undergo the Braive™ GMS surgical procedure. The primary dataset will be used for all the analyses. For subjects who are treatment failures, the last postoperative observation before the first treatment failure will be carried forward for all additional secondary endpoints and neurological status. No imputation for missing data will be made for other subjects.

13.4. Analyses for Additional Secondary Endpoints

All additional secondary endpoints are listed in the section 5.2.3. For the additional secondary endpoints related to the change from the baseline (pre-op or post-op baseline for instrumented Cobb angle), when the distribution of data is approximately normally distributed, the changes from baseline will be tested using a paired-sample t-test. When the distribution of the data is severely non-normal, a Wilcoxon signed-rank test may be used in place of the paired t-test. In addition, the descriptive statistics including but not limited to mean, standard deviation, median, minimum and maximum will be calculated and presented. For “Status of return to full activity within 3 months per SRS-22”, the number and percentage of subjects returned to full activity within 3 months will be calculated and presented.

Additional analysis will be performed by comparing the postoperative measurements at follow up visits with the measurements at immediate post-op.

13.5. Missing Data Considerations

All analyses will be conducted based on the observed data with no missing data imputation.

13.6. Safety Analysis

13.6.1. Primary Safety Endpoint

The primary safety endpoint is device-related adverse events up to 24-month visit postoperatively.

The number of events, the number and percentage of subjects experiencing device related AE up to 24 months postoperatively will be presented.
In addition, all device-related adverse events up to skeletal maturity (Risser 5) will be summarized.

13.6.2. Secondary Safety Endpoint

The secondary safety endpoints include:

- Procedure-related adverse events up to 24 months
- Secondary spinal surgeries related to the original study device up to 24 months.
- Device deficiency up to 24 months

In addition, all procedure-related and device related adverse events up to skeletal maturity, all secondary surgeries related to the original study device up to skeletal maturity and device deficiency up to skeletal maturity will be summarized.

13.6.3. Adverse events

A listing of all AEs will be provided, and a narrative of each device or procedure related AEs, secondary spinal surgeries, and death will be generated. In addition, summaries of AEs, both overall and by visit, will be provided.

Summaries will be presented for all AEs, SAEs, device or procedure-related AEs and device or procedure-related SAEs. Time course distributions will be provided in addition to cumulative summaries. Time course distributions will be based on the surgery date of the subject and onset dates of AEs, based on continuous time intervals. For overall AE summaries, a subject reporting the outcome at least once during the study period will be included in the frequency count. The percentage of subjects reporting the event at least once during the study period will be reported, and the denominator used in this calculation will be the total number of subjects who are enrolled and who receive the study treatment.

For AE summaries by visit, a subject reporting the outcome at least once during each visit window will be included in the frequency count. The percentage of subjects reporting the outcome at least once during each visit window will be reported, and the denominator used in this calculation will be the number of subjects who have any data reported at that visit (clinical or safety).

13.6.4. Neurological status

The number and percentage of subjects with normal and abnormal neurological status for each

component and overall at pre-op and discharge, and number and percentage of subjects with "improved", "maintained" and "deteriorated" neurological status from pre-op to post-op for each component and with "success" and "failure" for overall neurological status will be summarized.

13.6.5. Subsequent Spinal Surgical Interventions

Subsequent spinal surgical interventions including those that are related to the original study device or not related will be summarized in a similar way as for AEs. The summary will list different types of subsequent spinal surgical interventions. The numbers of events and subjects who undergo subsequent spinal surgical interventions and the associated time course distribution will be presented.

14. Ethics

14.1. Statement of Compliance

- The study will be conducted according to the protocol, ISO14155:2020, federal, national and local laws, regulations, standards, and requirements of the countries/geographies where the study is being conducted. The study will also be conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki 2013. The principles of the Declaration of Helsinki are implemented in this study by means of the Subject Informed Consent (IC) process, IRB/EC/REB approval, study training, clinical trial registration, pre-clinical testing, risk benefit assessment, and publication policy.
- In the US, the study will be conducted under an FDA Investigational Device Exemption (IDE) in compliance with 21 CFR Parts 11, 50, 54 and 812. In Canada and Europe, the study will be conducted in compliance with 21 CFR Part 11 and 54 and any national/local laws or regulations that apply. Study Investigators will be required to sign an Investigator Statement stating their intent to adhere to applicable regulations. Regulatory authority notification/approval to conduct the trial is required in all participating geographies, when applicable. Clinical sites will not begin enrolling subjects until the required approval/favorable opinion from the respective regulatory authority and IRB/EC/REB has been obtained (as appropriate).
- If any action is taken by an IRB with respect to the investigation, the information will be forwarded to the sponsor.
- This study will be publicly registered prior to first enrollment in accordance with the 2007 Food and Drug Administration Amendments Act (FDAAA) and Declaration of Helsinki on http://clinicaltrials.gov (PL 110-85, Section 810(a)).

The clinical investigation shall not begin at any site until the required approval/favorable opinion from the US Food and Drug Administration (FDA) or other appropriate regulatory authority, the IRB/EC/REB has been obtained, if appropriate.

Any additional requirements imposed by the IRB/EC/REB or regulatory authorities shall be followed, if appropriate.

14.2. Institutional Review Board (IRB) / Ethics Committee (EC) / Research Ethics Board (REB)

This study will be conducted in full compliance with the IRB/EC/REB regulations. It is the investigator's obligation to maintain an IRB/EC/REB correspondence file and to make this file available for review by the sponsor's representatives as part of the study monitoring process.

14.3. Principal Investigator Obligation

Each site will have a Principal Investigator (PI). The PI has overall responsibility for the day-to-day conduct of the trial at the site and for the integrity of the trial data generated by their site. Specifically, the PI is responsible for the following:

- Protecting the rights, safety, and welfare of the subjects in their care
- Obtaining written informed consent/assent of all subjects prior to any trial-related procedures, and only after Ethics Committee and regulatory approval (where applicable) of the trial
- Obtaining and maintaining Ethics Committee approval
- Conducting the investigation in accordance with the signed agreement, CIP, applicable laws and regulations, and any conditions of approval imposed by an Ethics Committee or regulatory authorities
- Providing accurate financial disclosure to the sponsor, including any relevant changes during the course of the trial and for 1 year after the completion of the trial
- Reporting adverse events and device deficiencies in accordance with the CIP and according to country regulations (excluding European sites: sponsor is responsible for reporting AEs and DDs to EC and Competent Authority)
- Approving all case report forms (or authorizing a sub-investigator to do so); approval of the case report form indicates the data represented are accurate and have been reviewed
- Maintaining accurate, complete, and current records, including:
- All correspondence with another investigator, the sponsor, the monitor, the Ethics Committee (including required reports), or regulatory agency
- Records of each consented subject's case history, signed and dated informed consent(s)/Assent(s), exposure to the device, eCRFs, and source documents
- The CIP, and documentation of dates of and reasons for each protocol deviation
- Any records required by a regulatory agency
- Ensuring that clinical records are clearly marked to indicate that the subject is enrolled in the study
- Allowing time with the trial monitor and Sponsor trial staff members during Sponsor site visits
- Informing the sponsor if any action is taken by an Ethics Committee or regulatory authority
- Failure to perform the investigator obligations or to complete corrective and preventive actions identified during monitoring or auditing activities may result in Principal Investigator or site personnel disqualification, and/or lead to suspension or termination of the study at the site.

14.4. Oversight of Study Personnel

The Principal Investigator may delegate study-related tasks to appropriately trained and qualified personnel to ensure alignment between contractual obligations and delegated study responsibilities.

The delegation of study-related tasks will be documented on the Delegation of Authority Log and the Principal Investigator will provide ongoing oversight of all delegated study-related tasks.

The Principal Investigator will ensure training is provided, completed and documented for all staff performing delegated study-specific tasks.

Study center personnel participating in the clinical study will be trained in study activities relevant to their role. Training must be completed and documented prior to that individual conducting any study related activities.

Investigator and/or study coordinator meeting(s) or telephone conference call(s) may be held to discuss the CIP, training, study results, etc. Continued training may occur through interim meetings or telephone conference calls to discuss relevant study issues.

14.5. Medtronic Representative Role

Medtronic representatives may provide support as required for the study under the direct supervision of the investigator as described below. The Principal Investigator or a person designated on the Delegation of Authority Log must be present to collect source documentation, record the study activities, and to be responsive to the subject's needs during an activity performed by a Medtronic representative.

Medtronic personnel may:

- Provide technical support during the procedure and follow-up visits
- This support may include the training of site personnel on the use of the Medtronic equipment or CIP-related procedures and data collection
- Clarify device behavior, operation, or diagnostic output as requested by the Principal Investigator or other health care professional
- Assist with the collection of device and technical data during the procedure (technical worksheets)
- Assist with collecting image data from the StealthStation and O-arm
- Assist with device and tissue explant retrieval (e.g., labeling the ruler, bags and containers, taking photographs of retrieved implant components and tissue)

Medtronic personnel may not:

- Practice medicine, provide medical diagnoses or make decisions related to subject treatment/care
- Express opinions about the product/feature under study
- Assist the subject by direct physical contact except as required by the specific protocol-related task to be conducted
- Discuss a subject's condition or medical treatment with the subject or a member of the subjects' family
- Provide the subject with any form/questionnaires related to the product(s) under investigation
- Enter data on eCRFs, except on the Medtronic Use Only Field

Any data collection completed by Medtronic personnel will be clearly identified as such.

15. Study Administration

15.1. Site Activation

During the activation process (prior to subject enrollment), Medtronic will train site personnel on the CIP, relevant standards and regulations, informed consent process, and on data collection and reporting tools. If new members join the investigation site team afterwards, they will receive training on the applicable clinical study requirements relevant to their role before contributing to the clinical study.

Prior to performing study related activities, all local regulatory requirements shall be fulfilled, including, but not limited to the following:

- IRB, EC or REB approval (and voting list, as required by local law) of the current version of the CIP and Informed Consent/Assent (as applicable).
    - US IRBs will maintain compliance with 21 CFR 50, 56 and 45 CFR Part 46 and/or appropriate local law.
    - It is the investigator's obligation to maintain an IRB/EC/REB correspondence file and to make this file available for review by the sponsor's representatives as part of the study monitoring process.
- Regulatory authority approval or notification (as required per local law)
- Fully executed Clinical Trial Agreement (CTA) - Medtronic contracts with participating institutions/investigators through a Clinical Trial Agreement that defines the scope and responsibilities and associated compensation related to carrying out the obligations under a clinical study sponsored by Medtronic.
- Financial Disclosure
- Curriculum Vitae of investigators and key members of the investigation site team (as required by local law)
- Documentation of delegated tasks
- Documentation of study training

Medtronic will provide each study center with documentation of investigation site/investigator readiness; this letter must be received prior to subject enrollment.

15.2. Monitoring

Monitoring visits will be conducted onsite or remotely at the start, during and at the closure of the clinical

study in accordance with Medtronic SOPs and the Monitoring Plan. The sponsor will adhere to the monitoring plan which contains the strategy for frequency of monitoring visits and source data verification to be performed for this study. Medtronic is responsible for ensuring the proper conduct of this study in terms of adherence to applicable regulations, protocol compliance, and the validity and accuracy of the study data entered on eCRFs. The Principal Investigator and site personnel will provide the Medtronic monitor(s) with complete access to primary source data (e.g., paper and electronic hospital/clinical charts, appointment books, laboratory records) that support the data on the eCRFs as well as other documentation supporting the conduct of the study. Procedures for monitoring subject compliance will be documented in the monitoring plan.

During the site evaluation or **Site Qualification** process, Medtronic or Medtronic representatives will review the protocol and regulatory requirements with the investigator and/or clinical site personnel and will assess if the site meets pre-defined requirements, has the experience, the time and resources to conduct the study.

Site Initiation Visits will be conducted for sites participating in this trial for training to ensure that protocol-related activities will be conducted in compliance with this CIP.
Medtronic will provide clinical study training on the CIP, Informed Consent process, data collection tools, and regulations to the involvement of personnel conducting clinical study activities and investigator responsibilities.

During an **Interim Monitoring Visit**, the monitor will perform source data verification by review of original subject documents. To do this, the monitor must have direct access to original source documentation, certified copies of the original source must be provided, or supervised access in situations where direct access is not possible. It will be verified whether signed and dated Informed Consent/Assent Forms have been obtained from subjects and/or parent(s)/legal guardian before any clinical-study-related procedures are undertaken. In addition, the monitor will perform routine reviews of study-related regulatory documents and work to secure compliance should any deficiencies be observed

Close Out Visits: The Investigator Site File will be reviewed for completeness; however, verification of individual regulatory documents may also be confirmed if noted in prior monitoring visits reports and do not necessarily need to be re-reviewed during the Close-out Visit.

15.3. Data Management

Medtronic personnel will perform routine edit and consistency checks for items such as missing data or inconsistent data. Identified data inconsistencies will be resolved by use of data discrepancies; investigators and site personnel will review data discrepancies and respond to the discrepancies in a timely manner. The resolved discrepancy will become a part of the eCRF record for the subject.

The RDC system which is 21 CFR part 11 compliant controls user access and ensures data integrity. This system is a fully validated system. The RDC system maintains an audit trail of entries, changes or

corrections in eCRFs. User access will be granted to each individual based on his or her delegation of authority and completion of required training. If a person only authorized to complete eCRFs makes changes to an already signed eCRF, the system will require the Principal Investigator, or authorized sub-investigators, to re-sign the eCRF.

The Principal Investigator, or designated sub-investigators, is responsible for the data submitted and must review all data for accuracy and provide his/her approval of the eCRF and sign each form with an electronic signature.

15.4. Direct Access to Source Data/Documents

The investigator(s)/institution(s) will permit study-related monitoring, audits, IRB/EC/REB review, and regulatory inspection(s), providing direct access to original or certified copies of source data/documents.

Medtronic or third-party auditors representing Medtronic may perform Quality Assurance audits to verify the performance of the monitoring process and study conduct, and to ensure compliance with applicable regulations. Representatives for regulatory bodies may also perform site inspections related to this clinical study. The Principal Investigator, site personnel, and institution will provide auditors with direct access to primary source data and all study-related documentation.

Medtronic will investigate, and report suspected cases of fraud or misconduct as appropriate.

15.5. Confidentiality

All information and data sent to parties involved in study conduct concerning subjects or their participation in this study will be considered confidential. Study sites will assign a unique SID to each subject. Records of the subject/SID relationship will be maintained by the study site. The SID number is to be recorded on all study documents to link them to the subject's medical records at the study site. Confidentiality of data will be observed by all parties involved at all times throughout the clinical investigation. All data shall be secured against unauthorized access. The privacy of each subject and confidentiality of his/her information shall be preserved in reports and when publishing any data. In the US, "Protected Health Information" (PHI) will be maintained in compliance with the HIPAA of 1996. To maintain confidentiality, the subject's name or any other PHI should not be recorded on any study document other than the IC. This scenario will be covered in the IC. In the event a subject's name/PHI is included for any reason, it will be blinded as applicable. In the event of inability to blind the identification (e.g., digital media), it will be handled in a confidential manner by the authorized personnel. Data relating to the study might be made available to third parties (for example in case of an audit performed by RA), provided the data are treated as confidential and that the subject's privacy is guaranteed. No identifiable subject information will be published.

15.6. Liability

15.6.1. Financing and Insurance

Medtronic maintains appropriate clinical study liability insurance coverage as required under applicable laws and regulations and will comply with applicable local law and custom concerning specific insurance coverage. If required, a Clinical Trial insurance statement/certificate will be provided to the IRB/EC/REB and the Regulatory Authorities.

15.6.2. Center for Medicare and Medicaid Services (CMS) IDE Study Criteria

Medicare beneficiaries most likely will not be affected by the investigational device because the indications for the study are for the treatment of juvenile or adolescent idiopathic scoliosis. The study results are expected to be within the adolescent population. Adolescents covered by Medicaid may be included in the trial if they meet the indications.

15.7. CIP Amendments

Protocol amendments may be initiated by Medtronic to address changes to the conduct of the study.

Protocol amendments must be approved by Medtronic and submitted to the IRBs/ECs and the governing regulatory authority (where required); protocol amendment approval and approval of any associated changes to the informed consent/assent document must be obtained prior to implementation of the amendment except:

- When necessary to eliminate an immediate/or apparent immediate hazard to participating subjects

15.8. Record Retention

All study-related documents must be retained for a period of at least 2 years after market-release in his/her region and after study closure (or longer if required by local law). Medtronic will inform the investigator/study site when these documents are no longer required to be retained.
No study document or image will be destroyed without prior written agreement between Medtronic and the investigator. The investigator should take measures to prevent accidental or premature destruction of documents. Should the investigator wish to assign the study records to another party or move them to another location, advance written notice must be given to Medtronic.
Medtronic will retain the study records according to Medtronic corporate policy and record retention schedule.

15.9. Publication and Use of Information

At a minimum, study data will be analyzed and results will be released on www.clinicaltrials.gov. Due to limited data availability, there is no intent to publish the available study results in a peer-reviewed journal.

Only with Medtronic's explicit and written permission, may investigators who gathered data for this study (i.e., enrolled subjects and complied with the protocol) write or contribute to the writing of abstracts and manuscripts based on the results of this study.

Before publication of any study-related data, the following guidelines will apply:

- Investigators are obligated to provide Medtronic with an opportunity to review any publication developed from data derived from this study.
- Medtronic will not financially compensate health care professionals (HCPs) or health care organizations (HCOs) for writing or editing activities on scientific publications related to research sponsored by Medtronic.

15.10. Suspension or Early Termination

15.10.1. Planned Study Closure

Study closure is defined as closure of a clinical study that occurs when Medtronic and/or regulatory requirements have been satisfied per the Clinical Investigation Plan and/or by a decision by Medtronic or regulatory authority, whichever occurs first. In all geographies, the study closure process is complete upon distribution of the Final Report or after final payments, whichever occurs last. For each center, Ethics Board approval renewals are required per local/country regulation until the study closure process is complete at that center.

15.10.2. Early Termination or Suspension

Medtronic reserves the right to suspend or terminate the study at any time. Reasons may include, but are not limited to, the following:

- Insufficient enrollment to complete the study within the expected timeframe
- Identification of unacceptable safety profile; suspicion of an unacceptable risk will result in a suspension, confirmation of an unacceptable risk will result in termination
- If a death occurs attributable to the Braive™ GMS, the study will be terminated
- Product performance/product supply issues
- IRB/EC/REB or governing regulatory authority (where applicable) suspension and/or termination of the study

Medtronic reserves the right to suspend or terminate the study at an individual site. Reasons may

include, but are not limited to, the following:

- Noncompliance with the protocol
- Serious or repeated deviations at the site
- Failure to implement required corrective and preventive actions
- Insufficient enrollment to complete the study within the expected timeframe
- Loss of appropriately trained site personnel

Investigators are required to notify the IRB/EC/REB of study suspension/termination. For European sites the Sponsor will notify the EC of study suspension/termination. Subjects will be notified by the investigator of suspension/termination due to unacceptable risk or of termination due to any other cause.

If, for any reason, Medtronic suspends or prematurely terminates the investigation at an individual investigation site, Medtronic shall inform the responsible regulatory authority as appropriate and ensure that the IRB/EC/REB is notified, either by the Principal Investigator or by Medtronic. If the suspension or premature termination was in the interest of safety, Medtronic shall inform all other Principal Investigators and investigational sites. The Principal Investigator or authorized designee shall promptly inform the enrolled subjects at his/her investigation site, if appropriate. In case of early investigation site suspension or termination subjects will be followed-up as per standard of care.

16. Records and Reports

16.1. Responsibilities of the Investigator

The investigator is responsible for the preparation, review, and signature (as applicable), and retention of the records listed as follows:

- All essential correspondence that pertains to the investigation
- Device use/disposition records
- Records of each subject's case history and exposure to the device. Case histories include the eCRFs and supporting data (source documentation), including, for example:
- Signed and dated consent/assent forms
- Medical records, including, for example, progress notes of the physicians, the subject's hospital chart(s) and the nurses' notes
- All adverse event/device deficiency information
- A record of the exposure of each subject to the BRAIVE system
- Documentation of any deviation from the CIP, including the date and the rationale for such deviation
- Signed Investigator Agreement, signed and dated curriculum vitae of the PI, sub-investigator(s) and key members, signed Delegated Task List
- The approved CIP, PI/ICF/Assent and any amendments
- Insurance certificate, where applicable

- Ethics Board approval documentation and voting list
- Sample eCRFs
- Regulatory authority notification and approval documentation
- List of Medtronic/monitor contacts
- List of investigation sites
- Training records
- Disclosure of conflict of interest
- Certification of adequacy of equipment
- Subject Identification & Enrollment Log
- Subject Screening Log
- Clinical investigation report including the statistical analysis

The investigator may withdraw from responsibility to maintain records by transferring custody to another person, who will accept responsibility for record and report maintenance. The investigator is responsible for the preparation, review, signature, and submission of the reports listed in Table 13 and Table 14. These are also subject to inspection by government agencies and must be retained. Reports will be submitted to regulatory authorities per local reporting requirements/regulations.

Table 13. Investigator records and reporting responsibilities applicable to the US

Investigator reports applicable to the US		
Report	**Submit To**	**Description/Constraints**
Withdrawal of Ethics Board approval	Medtronic	An investigator shall report to Medtronic, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation. *(21 CFR 812.150(a)(2)).*
Progress report	Medtronic and Ethics Board	An investigator shall submit progress reports on the investigation to Medtronic, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly. *(21 CFR 812.150(a)(3))*.

Deviations	Medtronic and Ethics Board	An investigator shall notify Medtronic and the reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency. Such notice shall be given as soon as possible, but in no event later than 5 working days after the emergency occurred. Except in such an emergency, prior approval by Medtronic is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human subjects, FDA and IRB in accordance with 812.35(a) also is required. *(21 CFR 812.150(a)(4))*
Failure to obtain Assent/IC prior to investigational device use	Medtronic and Ethics Board	If an investigator uses a device without obtaining informed consent, the investigator shall report such use to Medtronic and the reviewing IRB within 5 working days after the use occurs. *(21 CFR 812.150(a)(5))*
Final report	Medtronic, Ethics Boards	An investigator shall, within 3 months after termination or completion of the investigation or the investigator's part of the investigation, submit a final report to Medtronic and the reviewing IRB. *(21 CFR 812.150(a)(6))*
Other	Ethics Board and FDA	An investigator shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation. *(21 CFR 812.150(a)(7))*

Table 14. Investigator records and reporting responsibilities applicable to Europe and Canada

Investigator reports applicable to Europe and Canada		
Report	**Submit To**	**Description/Constraints**
Withdrawal of Ethics Board approval	Medtronic	An investigator shall report to Medtronic if required by local law.
Progress Report	Medtronic and Ethics Board	Provide if required by local law or Ethics Board. *(ISO 14155)*

Deviations	Medtronic and Ethics Board	Any deviation from the CIP shall be recorded together with an explanation for the deviation. Deviations shall be reported to Medtronic who is responsible for analyzing them and assessing their significance. Note: When relevant, Ethics Boards or regulatory authorities should be informed. *(ISO 14155)*
Failure to obtain Assent/IC	Medtronic and Ethics Board	IC shall be obtained in writing and documented before a subject is enrolled into the clinical investigation. *(ISO 14155)*

16.2. Responsibilities of Medtronic

In conducting this study, Medtronic will have certain direct responsibilities and may delegate other responsibilities to consultants and/or contract research organizations; however, Medtronic remains ultimately responsible for the conduct of the study.

Medtronic will maintain the following records, including but not limited to:

- All essential correspondence related to the clinical study
- Signed Investigator Agreement
- Signed and dated current curriculum vitae for each investigator
- Records of device shipment and disposition (shipping receipts, material destruct records, etc.)
- Adverse event and device deficiency information
- Device complaint documentation
- All data forms, prepared and signed by the investigators, and received source documentation and core laboratory reports
- CIP, Report of Prior Investigations and subsequent amendments
- Site monitoring reports
- Financial disclosure information
- Study training records for site participants and internal study staff members
- Contact lists of all participating investigators/investigative sites, Ethics Board information, study monitors and Medtronic staff members; Medtronic will maintain these lists and provide updates to the necessary parties.
- Sample of device labeling attached to the BRAIVE system
- Insurance certificates
- Ethics Board approval documentation and voting list
- Regulatory authority notification and approval documentation
- Statistical analyses
- Clinical investigation report

Medtronic is responsible for the preparation of, the accuracy of the data contained in, the review of and

the submission of the reports listed in Table 15, Table 16 and Table 17.

Table 15. Medtronic records and reporting responsibilities applicable to the US

Medtronic reports for US		
Report	**Submit To**	**Description/Constraints**
Premature termination or suspension of the clinical investigation	Investigators, Ethics Board, and relevant authorities	Provide prompt notification of termination or suspension and reason(s). *(ISO 14155)*
Unanticipated Adverse Device Effect (UADE)	Investigators, Ethics Board, FDA, and relevant authorities	Notification within 10 working days after Medtronic first receives notice of the effect. *(21 CFR 812.150(b)(1))*
Withdrawal of Ethics Board approval	Investigators, Ethics Board, FDA, and relevant authorities	Notification within 5 working days after receipt of the withdrawal of approval. *(21 CFR 812.150(b)(2))*
Withdrawal of FDA approval	Investigators, Ethics Board, and relevant authorities	Notification within 5 working days after receipt of notice of the withdrawal of approval. *(21 CFR 812.150(b)(3))*
Investigator List	FDA	Submit at 6-month intervals, a current list of the names and addresses of all investigators participating in the investigation. *(21 CFR 812.150(b)(4))*
Progress Reports	Ethics Board and FDA	Progress reports will be submitted at least annually. *(21 CFR 812.150(b)(4)(5), 812.36(f)*
Recall and device disposition	Investigators, Ethics Board, relevant authorities, and FDA	Notification within 30 working days after the request is made and will include the reasons for any request that an investigator return, repair, or otherwise dispose of any devices. *(21 CFR 812.150(b)(6))*
Failure to obtain Assent/IC	FDA	Investigator's report will be submitted to FDA within five working days of notification. *(21 CFR 812.150(b)(8))*
Final Report	Investigators, Ethics Board, Regulatory authorities upon request, and FDA	Medtronic will notify FDA within 30 working days of the completion or termination of the investigation. A final report will be submitted to the FDA, investigators, and Ethics Boards within six months after completion or termination of this study. *(21 CFR 812.150(b)(7))*

Deviation	Investigators	Ensure that all deviations from the CIP are reviewed with the appropriate investigator(s), are reported on the case report forms and the final report of the clinical investigation. Site specific deviations will be submitted to investigators periodically. *(ISO 14155)*
Significant new information	Ethics Board and FDA	Ensure that the Ethics Boards and FDA are informed of significant new information about the clinical investigation *(ISO 14155)*

Table 16: Medtronic records and reporting responsibilities applicable to Canada

Medtronic reports for Canada		
Report	**Submit to**	**Description/Constraints**
Unanticipated Serious Adverse Device Effects (USADE)	Ethics Board, investigators, Relevant Authorities	Medtronic will notify investigators, Ethics Board and relevant authorities in all geographies as soon as possible, but not later than 10 calendar days after Medtronic first learns of the effect.
Serious Adverse Device Effects (SADE)	Relevant Authorities	Medtronic will notify relevant authorities as soon as possible, but not later than 10 calendar days after Medtronic first learns of the effect.
DD with SADE potential	Relevant Authorities	Medtronic will notify relevant authorities as soon as possible, but not later than 30 calendar days after Medtronic first learns of the effect.
Premature termination or suspension of the clinical investigation	Investigators, Ethics Board and Relevant authorities	Provide prompt notification of termination or suspension and reason(s). *(ISO14155)*
Withdrawal of Ethics Board approval	Investigators, Ethics Board, Relevant Authority	All applicable investigators will be notified only if required by local laws or by the Ethics Board.

Medtronic reports for Canada		
Report	**Submit to**	**Description/Constraints**
Withdrawal of Regulatory Authority approval	Investigators, Ethics Board, and Regulatory Authority	Investigators and Ethics Boards will be notified only if required by local laws or by the Ethics Board.
Progress Reports	Ethics Board and Regulatory Authority	This will be submitted to the Ethics Board and/or Regulatory Authority if required.
Recall and device disposition	Regulatory Authority	Notification within 24 hours of a decision to recall.
Final Report	Investigators, Ethics Board, and Regulatory Authority (if required)	The investigator shall have the opportunity to review and comment on the final report. If a clinical investigator does not agree with the final report, his/her comments shall be communicated to the other investigator(s). The coordinating investigators shall sign the report. *(ISO 14155)*
Deviation	Investigators	Ensure that all deviations from the CIP are reviewed with the appropriate clinical investigator(s), are reported on the CRFs and the final report of the clinical investigation. Study site specific study deviations will be submitted to investigators periodically. *(ISO 14155)*
Significant new information	Ethics Board and Regulatory Authority	Ensure that the Ethics Boards and Regulatory Authorities (where applicable) are informed of significant new information about the clinical investigation *(ISO 14155)*

Table 17: Medtronic records and reporting responsibilities applicable to Europe

Medtronic reports for Europe		
Report	**Submit To**	**Description/Constraints**
Unanticipated Serious Adverse Device Effects (USADE)	Ethics Board, investigators, Competent Authorities	Medtronic will notify investigators, Ethics Board and competent authorities in all geographies as soon as possible, but not later than 10 working days after Medtronic first learns of the effect.

Serious Adverse Event (SAE)	Ethics Board, Competent Authorities	Submit to Ethics Board per local reporting requirement. Submit to Competent Authority per local reporting requirement.
Serious Adverse Device Effects (SADE)	Ethics Board, Competent Authorities	Submit to Ethics Board per local requirement *(ISO 14155).* Submit to regulatory authority as per local competent authority reporting timelines.
Device Deficiency that might have led to a SADE	Ethics Board, Competent Authorities	Submit to Ethics Board per local requirement. Submit to regulatory authority as per local competent authority requirement.
Premature termination or suspension of the clinical investigation	Investigators, Ethics Board, Relevant Authority	Provide prompt notification of termination or suspension and reason(s). *(ISO 14155)*
Withdrawal of Ethics Board approval	Investigators, Ethics Board, Relevant Authority	All applicable investigators will be notified only if required by local laws or by the Ethics Board.
Withdrawal of Competent Authority approval	Investigators, Ethics Board, and Regulatory Authority	Investigators and Ethics Boards will be notified only if required by local laws or by the Ethics Board.
Progress Reports	Ethics Board, Regulatory Authority (if required)	This will be submitted to the Ethics Board and/or Regulatory Authority if required.
Final Report	Investigators, Ethics Board, and Regulatory Authority (if required)	The investigator shall have the opportunity to review and comment on the final report. If a clinical investigator does not agree with the final report, his/her comments shall be communicated to the other investigator(s). The coordinating investigators shall sign the report. *(ISO 14155)*
Deviation	Investigators	Ensure that all deviations from the CIP are reviewed with the appropriate clinical investigator(s), are reported on the case report forms and the final report of the clinical investigation. Site specific deviations will be submitted to

Significant new information	Ethics Board and Regulatory Authority	Ensure that the Ethics Boards and Regulatory Authorities (if applicable) are informed of significant new information about the clinical investigation *(ISO 14155)*

16.3. Final Report

Medtronic will provide a final written report of the study results according to applicable regulations, and will include at a minimum:

- Identification of the device(s)
- Description of the methodology and design of the clinical investigation
- Summary of the deviations from the CIP
- Statistical analysis of the study data
- Critical appraisal of the aims of the study

Medtronic will submit this final report to the PIs for review and shall document and disseminate discrepant comments to all study PIs. The Coordinating Investigators will provide their signatures, indicating their agreement with the content of the final report.

All required study reports will be submitted to regulatory authorities and Ethics Boards per local reporting requirements/regulations.

17. Contact Information

17.1. Sponsor contact information

Detailed sponsor contact information not outlined in the Clinical Investigational Plan will be provided under a separate cover.

17.2. Participating Investigators and Investigation Sites

A complete list of names, addresses, professional positions and emergency contact details of the clinical investigators and clinical investigation sites will be distributed under a separate cover.

17.3. Reviewing Institutional Review Board

A complete list of names and addresses of each reviewing Institutional Review Board will be provided under a separate cover.

18. History

Version	Summary of changes	Author(s)/Title
1.0	Not Applicable, New Document	[redacted] Clinical Study Manager
2.0	• Separated safety objective from primary objective • Updated PedsQL Term and definition throughout document • Adapted SRS-22r to SRS-22 to capture medication use • Removed 24 months from safety objective and safety endpoint • Updated all secondary endpoints from "Changes in" to "Assessment of change from baseline" and added at all available follow-ups to integrate follow-up until skeletal maturity. • Removed changes in shoulder imbalance from secondary endpoints • Neurological status collection adapted from all follow-ups to preoperative and discharge • Removed 12 months and 24 months from the adverse event and reoperation secondary endpoint • Updated reference to Appendix E: Medtronic Reusable Instruments and Accessories for Use with Braive™ Growth Modulation System - Instructions for Use • Added Appendix F: Medtronic Navigated Manual Reusable Instruments for Use with the StealthStation™ System for Braive™ Growth Modulation System – Instructions for Use **Exclusion criteria:** • Added "Concurrent participation in another clinical study that may add additional safety risks and/or confound study results* *Subjects in concurrent studies can only be enrolled with permission from Medtronic. Please contact Medtronic's study manager to determine if the subject can be enrolled in the BRAIVE IDE Study." **Study Design:** • Added that clinical assessments and radiological evaluation will be completed biannually until the subject is skeletally mature. **Sample Size**	[redacted], Clinical Study Manager

	• Adapted “40 patients” to “25 patients” • Adapted “up to 15 sites” to “up to 10 sites” **Statistics:** • Added that overcorrection will be counted as failure **Purpose:** • Removed reference to HDE **Duration:** • Adapted “24 months” to “until skeletal maturity, with an expected study duration of 7 years” **Rational:** • Added “Bracing does not correct the curve; rather it is intended to halt the progression of the curve. Bracing is considered successful if the curve progresses less than 5 degrees was added to the rationale” • Removed “There are no VBT devices approved for this pediatric use globally” **Product receipt and tracking:** • Removed duplicate sentence from product receipt and tracking • 8.1 Study population: Removed “current standard of care” **Subject enrollment:** • Removed “the investigator” **Schedule of events:** • Added biannually until skeletal maturity to schedule of events Updated footnotes to match changes • Pulmonary function (spirometry) adapted from all follow-ups to preoperative and discharge • Removed surgery indication from pre-op to match schedule of events • Rephrased what is required when a subject gets enrolled but not implanted in surgery section **All sections that cover enrollment:** • Adapted to “All parents or legal guardians must sign the ICF and all subjects need to sign the Assent form prior to	

	performing any study specific procedure" **Radiological effectiveness endpoints:** • Updated all radiological effectiveness endpoints from "Changes in" to "Assessment of change from baseline" and added at all available follow-ups to integrate follow-up until skeletal maturity. **Subject Withdrawal or Discontinuation:** • Compliance language for follow-up updated to "Compliance with the required follow-up schedule is essential" and adapted language to subjects should not be lost-to-follow-up • Withdrawal of consent: Added after undergoing the Braive Procedure **Potential Risks:** • Examples of potential risks were removed from the potential risks section as all risks are covered in the separate risk analysis **Reporting Adverse Events to Medtronic:** • Corrected table number to 11-4 for reporting AEs to Medtronic **Statistical Design and Methods:** • Removed reference to the 40 patients from sample size section • Removed: "The primary analysis will be based on the first 25 patients who are treated with the Braive™ system and have reached to 12-month follow up visit" **Liability:** • Updated Center for Medicare and Medicaid Services (CMS) IDE Study Criteria section	
3.0	• Updated biannual follow-up to "annual follow-up until skeletal maturity" after 24 months throughout the document • Added to skeletal maturity "(defined as Risser 5)" throughout the document	[redacted], Clinical Study Manager
4.0	**Overall:** • Juvenile added as inclusion criteria and in title • ISO14155:2011 updated to latest version of ISO14155 throughout document	[redacted], Clinical Study Manager [redacted],

	• Study purpose updated to establish probable benefit and evaluate the safety and preliminary effectiveness of the Braive™ GMS when used in the treatment of JIS and AIS. • Local sponsor – Europe updated to Local sponsor – EU Legal Representative • Lead Principal Investigators added • Cobb angle designation updated to remove "major" • Primary objective and primary endpoint updated from 12 months to 24 months • Safety objective updated to "secondary spinal surgery defined as treatment failure up to 24 months postoperatively." • Safety endpoint updated to secondary spinal surgery defined as treatment failure up to 24 months postoperatively • Updated "patient(s)" to "subject(s)" where appropriate • Removed full titles of Appendices where appropriate throughout document, added statements that they will be provided separate from the CIP • Deleted list of Appendices and all Appendix numbers throughout the document **Synopsis:** • Prospective, multi-center, single arm added to study type • External Organizations added • Indications updated: investigational in US and CA, CE marked in EU (within approved indication) • Investigation Purpose updated for HDE study • Sample size updated to include maximum number of subjects per site • Primary endpoint, safety endpoint and secondary endpoint updated to 24 months **Secondary Endpoints** • Updated endpoints to remove "Assessment of" • Updated secondary endpoint from 12 to 24 months post-operative • Updated definition for individual success • Added endpoint for change in shoulder imbalance • Updated the language and added levels to define total vertical thoracic spine height and total vertical spine height. • Updated neurological status collection timepoint from baseline and discharge to all available postoperative timepoints	Sr. Clinical Research Specialist

	• Updated adverse events to device and procedure related adverse events up to 24 months • Updated "reoperations/revisions/removals" to "secondary spinal surgeries" and added timeframe (24 months) **Study Design** • Added percent of total population each site can enroll with explanation of limiting subjects per site in order to mitigate bias • Updated rationale about outcome of bracing • Added definition of completion of the clinical study • Added reasoning for not implementing a control group **Product Description** • Updated Table 4: Braive Instrument Set CFNs to include CE Mark CFN • Added Table 5: Braive Licensing Disc • Added indications: investigational in US and CA, CE marked in EU (within approved indication) **Route of Administration** • Added Navigated Surgical Technique **Packaging** • Updated "unopened" to "intact" • Added statement that CE marked devices will be labelled in respective local language **Intended Population** • Added JIS • Deleted Risser score of 0-2 **Equipment** • Added statement that sites will be able to choose whether to implant the system non-navigated or navigated following the respective surgical techniques	

	• Added name of software company **Product Receipt and Tracking** • Added sites as responsible for maintaining device accountability logs • Added navigated instruments and BRAIVE licensing Disc Added record maintenance requirement for CE marked devices **Product Return** • Added statement that investigational components where the packaging is not intact should be returned or disposed of appropriately • Added Braive Instrument Set and applicable geographies to unused investigational device return **Exclusion Criteria** • Updated pregnancy exclusion criteria to add "within first 12-months of the study" • Removed "pulmonary issue" • Updated "significant respiratory problems" to "severe chronic lung disease (e.g. asthma, bronchiectasis)" • Reformatted sentence structure for poor bone quality exclusion criteria **Schedule of Events** • Updated table number to Table 6 • Updated Neurological Status in Table 6 to include 3, 6, 12, 18, 24 months and annually • Moved Spirometry in Table 6 from discharge to 3 months • Updated "Adverse Events" to "Adverse Events and device deficiencies" in Table 6 and footnote • Updated footnote to "probable benefit" and 24 months • Added O-Arm, StealthStation and Intraoperative image in Table 6 and footnote **Enrollment**	

	• Deleted procedures • Updated "Sample" to "The" Informed Consent and Assent forms • Added (enrollment log) **Pre-op** • Added left hand X-ray **Surgery** • Added O-Arm 3D projection images and StealthStation Images • Added Intraoperative images **Discharge Assessment** • Removed "Pulmonary Function (Spirometry) • Added "Study Deviations" **Post-operative Assessment at 3 months** • New section; Split Post-operative Assessment at 3 months and Post-operative Assessment at 6, 12, 18, 24 months and annually into separate sections Added Neurological Status and Spirometry **Post-operative Assessment at 6, 12, 18, 24 months and annually** • Removed "Study Deviations" from section title • Added Neurological Status • Removed "Pulmonary Function (Spirometry)" **O-Arm and StealthStation Image Acquisition** • New section **Intraoperative Image Acquisition** • New section	

	Subject Consent • Added the latest version of ISO 14155 • IRB/EC/REB full spelling replaced with acronyms • Informed consent process updated from "source" to state must be documented in "subject's medical records" • Added statement that signed copies of the ICF and assent form will also be provided to parent(s)/legal guardians • Removed "local law" **Secondary effectiveness endpoints** • New section **Radiological effectiveness endpoints** • Removed "Assessment of" from each endpoint • Added "except at 24 months" to "Change from baseline in Cobb angle at all available postoperative timepoints" **Individual subject success** • New section **Safety Endpoint** • Safety endpoint updated to "any secondary spinal surgery defined as treatment failure up to 24 months postoperatively." **Adverse Events** • Updated reference to Table 7 • Updated CEC responsibility **Neurological Status** • Updated timepoints for neurological status evaluation • Updated scale for evaluating neurological status • Added definition for neurological change and success for neurological status	

Overcorrection

- Removed overcorrection of 20 degrees or more being considered clinically significant
- Added meaning of negative cobb angle

Types of Subsequent Spinal Surgical Interventions

- Updated definitions for revisions, removals, reoperations, and other.
- Updated revisions to include two categories, preventative and non preventative
- Added statement "Any subsequent spinal surgical intervention will be adjudicated by CEC to determine whether it is true treatment failure"

Relatedness of Subsequent Spinal Surgical Interventions

- Added "Spinal' to section title
- Moved statement "A subsequent spinal surgical intervention determined as having "possible," "probable," or "causal" relationship to the Braive™ GMS will be conservatively considered as being "related."" for clarity

Recording Data

- Updated to "The investigator must ensure that the data reported in the eCRF and all other required study reports are accurate, complete and reported in a timely manner."

- Clarified discrepancies as "between eCRF and source documents" and need to be justified in "writing"
- Added statement that data collected during subject phone calls will be considered as source data
- Added information for completing remote visit source document worksheet
- Moved statement "The Principal Investigator or an individual delegated by the Principal Investigator on the Delegation of Authority Log is responsible for documenting and entering data for the study on the eCRFs." for clarity

	• Updated "persons" to "site study staff" **Deviation Handling** • Removed additional word, "study" • Updated pregnancy example • Added COVID-19 impact **Reporting requirements for study deviations** • Added "and Regulatory Authorities (if applicable)" • Added "Medtronic is responsible for reporting all study deviations to Regulatory Authorities as applicable." **Lost to follow up** • Added "When subjects are lost to follow-up the investigator will make efforts to confirm the vital status of the subject, as described in the informed consent." **Potential Risks** • Radiation exposure risks added to CIP to meet ISO requirements **Risk Minimization, Overall Mitigation Factors, During Surgery, During Post-operative Care, Oversight of Safety, Warning and Precautions** • New sections added. Risk assessment that existed under separate cover is now fully integrated into the CIP to meet ISO requirements **Potential Benefits** • Updated the primary benefits expected for the subjects treated with the Braive GMS • Added statement that information collected in this study may assist in the modification of the existing system, design of new products/therapies, and/or IFUs	

Risk-Benefit Rationale

- Updated risk-benefit rationale
- Added statement "All the risks with the device have been deemed acceptable and the benefits of participating in the study outweigh the risks."

Adverse Event Definitions/Classifications

- Removed reference to ISO14155:2011 throughout section
- Updated Adverse (AE) definition
- Removed "Device Related Adverse Event or" from Adverse Device Effect and added note
- Removed "Europe and Canada Reporting Only" from Device Deficiency and updated notes
- Updated definition and note for Serious Adverse Event (SAE)
- Updated name from "Serious, Device Related Adverse Event or Serious Adverse Device Effect" to Serious Adverse Effect (SADE)
- Split "Unanticipated Serious Adverse Device Effect (USADE)" from Unanticipated Adverse Device Effect (UADE) and updated the definition
- Added Serious Health Threat and definition
- Removed MEDDEV 2.7/3 reference from relatedness
- Added severity grading
- Updated descriptions of revision, removal, reoperation, other and added supplemental fixation

Reporting of Adverse Events

- Updated table number to Table 8 and added "Adverse" to title
- Updated Table 8 classification responsibilities and added expectedness

Not reportable events

- Changed "pre-planned surgical procedure" to "elective or preventative medical procedure"
- Removed "surgery", "endoscopy", "transfusion", and "elective" from examples

- Replaced "expected surgical events" with "Unavoidable Adverse Events (UAE)"
- Updated Table 11-3 to Table 9. Updated title, event descriptions, and time frames
- Added event description and timeframe for back pain and shoulder pain

Device Deficiencies

- Updated reference of Table 11-4 to Table 10

Reporting Adverse Events to Medtronic

- Updated reference to Table 11-4 to Table 10
- Removed reference to 24-month visit
- Removed reference to MDD 93/42/EEC and MEDDEV 2.7/3
- Removed statement "Adverse events will be followed until resolved or until study completion, whichever comes first."

Pregnancy Reporting

- Updated to state "If the subject experiences untoward medical occurrences during pregnancy or at delivery, these should be recorded as an adverse event and reported."
- Added "If available, outcomes will be collected on both mother and child"

Death

- Added UADE
- Removed "If the cause of death is unknown, "death" may be reported as an adverse event."

Medical Monitor and Clinical Events Committee (CEC)

- Clarified role of CEC
- Deleted AE classification
- Updated classification for secondary spinal surgical interventions to include whether the event is a treatment failure

CRO / Core labs

	• New section **Sample Size** • Updated Table 13-2 to Table 12 • Updated calculations for sample sizes • Updated Table 12 with new calculations **Analysis Populations and/or Subset** • Updated safety failure to treatment failure **Analysis of Subgroups** • Removed the paragraph about the effect of investigational site on the primary outcome tested using an ANOVA model **Safety Analysis** • Removed "All the analyses will be conducted based on the CEC adjudication of relatedness and seriousness." **Secondary Safety Endpoint** • Updated "all adverse events" to "device or procedure-related adverse events up to 24 months." • Removed "from pre-op to post-op" from changes in Neurological Status • Updated "reoperations/revisions/removals" to "secondary spinal surgeries not defined as treatment failure up to 24 months" **Adverse Events** • Added procedure-related adverse events • Updated "revision, removal, reoperation" to "secondary spinal surgeries" • Updated "AEs related to the components of the surgical construct" to "device or procedure-related AEs and device or procedure-related SAEs"	

	Subsequent Spinal Surgical Interventions • Update "Subsequent spinal surgical interventions and safety failures at the index level(s)" to "Subsequent spinal surgical interventions including those that are defined as treatment and those that are not defined as treatment failures" **Statement of Compliance** • Removed reference to ISO14155:2011 and MDD 93/42/EEC **Medtronic Representative Role** • Added statement that Medtronic personnel may assist with collecting image data from the StealthStation and O-arm **Monitoring** • Added onsite or remotely **Record Retention** • Updated record retention requirements **Suspension or Early Termination** • Section split into Planned Study Closure and Early Termination or Suspension sections **Planned Study Closure** • New section **Early Termination or Suspension** • New section **Records and Reports** • New section, split responsibilities of investigators and Medtronic into two sections	

	Responsibilities of the Investigator • New section; details Investigator records and reporting responsibilities applicable to US and Europe • Added table 13 and 14 **Responsibilities of Medtronic** • New section; details Medtronic records and reporting responsibilities applicable to US and Europe • Added table 15 and 16 **Final Report** • Added section **Radiographic Review Core Lab, Software Development Lab,** and **Explant Analysis** • Removed sections, included under CRO / Core Labs section **Appendices** • Removed section, provided under separate covers	
5.0	**Overall** • Clarified which regulations and guidelines apply in the US, Europe and Canada. • Specified ISO14155:2020 version and Declaration of Helsinki 2013 version. • Corrected typo for Software Development Lab from Stirling to Sterling • Specified that the safety objective/endpoint is the primary safety objective/endpoint • Added Observational Radiographic Objectives/endpoints • Clarified that skeletally maturity as defined by Risser 5 will be assessed by the imaging vendor • Added intra-operative radiological assessment for Cobb angle to assess correction achieved on the table	[redacted] Clinical Study Manager

	• Updated in/exclusion criteria (detailed changes can be found in that specific section below) • Added Physical Assessment and unscheduled visit to schedule of events • Moved spirometry assessment from 3 Months FU to 12 Months FU visit since that is a more appropriate timepoint to assess this. • Clarified that eligibility report from imaging vendor must be received prior to surgery and extended the period for acquiring X-ray images from 6 weeks to 3 months prior to surgery since that is considered acceptable by the steering committee. • Added Observational radiographic endpoints to Statistics section and updated analysis population from Intention to Treat to primary analysis population. • Updated the wording radiological to radiographic assessment throughout for consistency. **Background** • Corrected '°' to degrees for consistency **Study Design** • Clarified that failed conservative treatment is per investigator's assessment. **Product description** • Updated table 4 to include commercially available Quick Connect Ratcheting Handle and Egg Handle • Generalized reference to IFUs instead of listing them all out. • Clarified that also intra-operative imaging will be shared with Sterling for the patients who give consent for this. Clarified requirements for product accountability, storage and return that is also applies for CE marked devices provided free of charge but that it does not apply for CE marked devices obtained via the commercial route. Added the requirement to collect received by name, date of return and returned by name (including reason for return)	

Subject enrollment

- Added the use of a subject screening log

In/Exclusion criteria

- Combined skeletally immature with Sanders Score inclusion criterium
- Clarified that failed conservative care is per investigator's assessment
- Clarified that Authorization to Use and Disclose Health Information only should be signed if applicable
- Updated exclusion criterium to indicate that the subject should not become pregnant within the first 24 months of the study instead of 12 months.
- Clarified that inadequate tissue coverage will be determined as per investigator's assessment
- Clarified that major psychiatric disorders/history of drug abuse patients are excluded if it interferes with the subject's ability to comply with the study instructions or might confound study interpretation and that DSM-5 can be used as a reference since it is not common in all regions to use this.

Diagnostic tests

- Added spirometry data collection requirements.

Radiographic assessment

- Clarified that images may be used for AE and DD analysis.
- Added O-arm 3D Projection Images, StealthStation DICOM, Intraoperative AP fluoroscopy since these are also collected and forwarded to the core lab.

O-arm and Stealth Station Image Acquisition and Intraoperative Image Acquisition

- Clarified secondary use of the images.

Assessment of Effectiveness

	• Added definition for clinically significant overcorrection • Specified that additional analysis will be performed by comparing the postop measurements with the measurements prior to discharge. In addition, for Cobb angle, the measurement prior to discharge will also be compared with the intra-operative measurement. These additional measurements of change are described in the Radiographic Evaluation Protocol. **Subsequent Spinal Surgical Intervention** • Clarified that subjects experiencing a treatment failure as assessed by the CEC will only be followed up for safety and radiographic imaging until skeletally mature since for the efficacy endpoints and neurological status the analysis will be carried forward. **Deviation handling** • Clarified that deviations for enrolled subject does not meet in/exclusion criteria only apply in case these criteria are assessed by the investigator and not the independent radiographic review core lab. **Reporting Adverse Events to Medtronic** Removed immediate (no later than 3 calendar days) ADE or Device Related AE reporting from investigator to Medtronic since there is no regulatory requirement to report it within these timelines so it will now be covered by timely reporting. **Analysis populations and/or subset** • Changed Intent to Treat population to Primary Analysis population • Clarified that for treatment failure subjects also the neurological status will be carried forward • Added stratification of primary endpoint based on degree of baseline curve flexibility	

	Medtronic representative role • Added assisting with device data collection and device and tissue explant retrieval activities. **Planned Study Closure** • Removed requirement to send initial study closure letter to initiate study closure since usually study closure is initiated by scheduling the close out visits. **Investigator and Medtronic records and reporting responsibilities** • Added requirements for Canada and updated European requirements in alignment with local regulations. • Site specific deviations will be reported to the investigators on a periodic basis instead of quarterly • Final report will be signed by the coordinating investigators instead of all investigators as required per ISO14155:2020 **Final Report** Final report will be signed by the coordinating investigators instead of lead principal investigators as required per ISO14155:2020	
6.0	**Overall** • Removed Oracle Clinical from Remote Data Capture System to not be too prescriptive. • Added secondary endpoint to assess TL/L cobb angle • Added observational radiographic endpoint to assess PT cobb angle • Added Main Thoracic to cobb angle for clarity considering we are now also assessing PT and TL/L cobb angles. • Removed intra-op cobb angle assessment since this will not be done as part of the study but only for future development purposes • Added that in case subjects do not undergo the Braive GMS procedure as defined in the CIP the Medtronic study manager should be contacted to determine whether subject should be exited or not. **Title page**	[redacted], Clinical Study Manager

	• Updated Medical expert contact details **Background** • Removed duplicate sentence **Primary safety objective** • Added clarification note that secondary spinal surgeries and subsequent spinal surgical interventions are used interchangeably. **Duration** • Updated enrollment period to approximately 18 months. **Product description** • Added BRAID Long • Added tensioner and threaded handle **In/Exclusion Criteria** • Clarified cobb angle to be main thoracic • Updated Consent/Assent language to indicate it should be obtained per local requirement • Added examples of spinal MRI abnormalities **Schedule of Events** • Removed O-arm 3D projection images **Enrollment and Subject Consent** • Updated consent/assent language to make it more general and to align with country regulations. **Neurological status** • Removed pin prick assessment from sensory function and corrected to T1-S1 assessment **Overcorrection** • Specified that clinically significant overcorrection must be reported as an ADE **Subsequent spinal surgical interventions** • Removed duplicate paragraphs/sections to make the	

	document leaner. • Updated definitions to make it more clear **Recording data** • Added that for instrument accountability the CRF will be the source. **AE/DD definitions/classification** • Added ISO14155:2020 references • Added Device and Procedure relatedness classification for CEC • Added date site became aware of the event as minimum requirement to be reported **DMC** • Frequency of meetings aligned with DMC charter **CRO/Core labs** • Clarified that Sterling Medical Devices is not part of the study but images from the subjects who give consent will be used for future software development **Statistical Design and Methods** Added that any additional interim analysis will be documented in the SAP	
7.0	**Overall** • Documentation of decision to discontinue the BRAIVE program. The CIP has been updated accordingly to reflect the changes. • Enrollment stopped when 10 subjects were enrolled. • Decision to not renew EC certification for the Braive GMS into the European Market. • Relevant changes from most recent Clinical Investigation Plan Medtronic template version E have been implemented in the applicable sections. • Removed external vendors: Explant and NAMSA **Study endpoints:** • Updated study purpose and endpoints due to discontinuation of the BRAIVE program. • Main focus on device/procedure safety: Updated primary endpoint “The primary safety endpoint is any secondary	[redacted] Clinical Study Manager

	spinal surgery defined as treatment failure up to 24 months postoperatively" to "device-related adverse events up to 24 month follow up". • Main Thoracic Cobb angle is a secondary endpoint • Instrumented Cobb Angle added as an endpoint (already collected in previous CIP version) • Removal of the following endpoints: Individual Subject Success, PedsQL, shoulder imbalance endpoint, T1-L1 length, disc wedging angle and Neurological status. **Schedule of Events** • Visits windows were widened to allow the investigators to plan the patient visits according to their growth. • Updated Neurological Status (collected at preop and discharge) • Updated pulmonary function (collected at preop) • Updated PedsQL (collected at preop) • Risser score: mandatory from 24 months onwards **Radiographic evaluation:** • Radiographic images will be evaluated by investigators. This is including radiographic endpoints assessment and Risser score evaluation (to assess skeletal maturity). • Radiographic measures will be performed according to site standard of care (except for Risser score). • Radiographic Core Lab had been used for eligibility assessment for all patients enrolled in the study. **Study committee/External organization** • Removal of CEC review because this committee was assessing secondary spinal surgeries for the primary safety endpoint analysis, which was modified. • Explant analysis: the decision has been made that explanted device will be analyzed following Medtronic processes. The Histology lab and Analysis lab for explanted devices have been removed. • Removal of DMC, instead, a steering committee and Medtronic medical advisor will monitor the safety of investigational treatment. • Removal of Sterling Medical Devices reference for the software development. • Removal of imaging core lab MMI: Pre-Op radiographic measurements have been performed by MMI for subject eligibility assessment. All other radiographic measurements	

	will be performed by the study site as site standard of care. **Statistical design and Methods:** • Adaptation of statistical analysis to updated endpoints • Adaptation of sample size due to enrollment stop • Removal of Per Protocol population analysis • Removal of subgroup analysis due to sample size **Others** • Unavoidable AE: Added non-serious Pneumothorax, Supplemental Oxygen, Blood loss less than 800cc as unavoidable AE. • Publication: due to limited data availability, publication strategy has been updated.	

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