Protocol Title:	Multinational randomized controlled cross-over trial comparing C-Brace to conventional knee ankle foot orthoses with respect to balance, fall risk and activities of daily living.
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	Name / Function	Date	Signature
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Approved and released by	Name / Function Dr. Andreas Hahn Corporate Vice President Clinical Research and Services	Date See digital signature	Signature

Clinical Investigation Plan (CIP)

Multinational randomized controlled cross-over trial comparing C-Brace to conventional knee ankle foot orthoses with respect to balance, fall risk and activities of daily living.

CONFIDENTIAL DOCUMENT

Document No. PS00120016A-001

REVISION RECORD		
Vers. No.	**Description**	**Valid from**
1.0	Creation of the clinical investigation plan	Signed release
2.0	Changes include minor changes to inclusion/exclusion criteria, addition of a second baseline to the study schedule, addition of US study sites, and other minor change for clarity.	Signed release
3.0	Changes include changes to the statistical analysis description and other minor changes for clarity	Signed release
4.0	Changes to address risks and effects of the COVID-19 pandemic including updated study timeline, adaptations to the study procedure (7.3.12), updated study flow chart (7.4), updated risk-benefit assessment (11), and COVID-19 Risk Factors Assessment and patient re-consent (17.3).	Signed release
5.0	Inclusion of Austria as new participating country, updated study flowchart	Signed release

REVISION RECORD		
Vers. No.	**Description**	**Valid from**
6.0	Changes to the statistical analysis and other minor changes for clarity. Moved primary safety endpoint to a secondary endpoint. Removed adaptive study design and amended planned interim analysis.	Signed release
7.0	Updated enrollment number to account for screen failures and to reflect expansion to allow additional enrollments.	Signed release

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Place, Date, Dr. Andreas Kranzl

Table of Contents

1 Study Overview

Sponsor	Otto Bock Healthcare Products GmbH
Short Study Title	Clinical trial comparing C-Brace to KAFO/SCO
Objective	To evaluate effectiveness and benefits in patients with lower limb impairment in activities of daily living comparing the C-Brace microprocessor – controlled stance and swing orthosis to standard of care use of knee ankle foot orthosis/stance control orthoses
Design	Prospective international multicenter open-labeled randomized controlled cross-over trial
Devices	C-Brace, KAFOs, SCOs
Primary Efficacy End-point	Improvement of static and dynamic balance by using C-Brace compared to KAFO /SCO
Secondary Endpoints	1. To evaluate the effect of the C-Brace compared to KAFO/SCO on gait, balance, plain level walking, walking during more challenging tasks and divided attention tasks during walking. 2. To assess and compare the safe use of the C-Brace compared to KAFO/SCO in regards to falls: frequency of falls, severity of falls, fall-related injuries, fear of falling and related treatment efforts. 3. Evaluation of patient`s confidence in performing various ambulatory activities without falling using C-Brace compared to KAFO/SCO. 4. Assessment of quality of life and re-integration to normal living using C-Brace compared to KAFO/SCO. 5. Assessment of disability and impact on productivity. 6. Assessment of patient´s C-Brace satisfaction and usage habits compared to KAFO/SCO 7. Reduced probability of falling more than once by using C-Brace compared to KAFO / SCO

Clinical Follow-up	Screening, 2 baselines, visit 1 after 3 months usage of device 1 at home, visit 2 after 3 months usage of device 2 at home
No of patients	At least 56 randomized
Inclusion criteria	• Patient has been tested with the Trial Tool (DTO) and demonstrated the potential to utilize the C-Brace successfully • Patient has a BBS score < 45 • Lower limb functional impairment according to CE label wording • Prior active and compliant use of unilateral or bilateral KAFO or SCO in the past 3 months prior to enrollment in the study • Patient meets minimum physical requirements to be fitted with a C-Brace, such as muscle status, joint mobility, leg axis and proper control of the orthosis must be guaranteed. • The User must fulfill the physical and mental requirements for perceiving optical/acoustic signals and/or mechanical vibrations • The existing muscle strength of the hip extensors and flexors must permit the controlled swing-through of the limb (compensation using the hip is possible). • Patient´s commitment to use C-Brace 2 at least 1-2 hours per day 5 days per week- • Patient is ≥ 18 years old • Patient is willing and able to independently provide informed consent. • Person is willing to comply with study procedures
Exclusion criteria	• Patient who is not able to follow the entire study visits or is unwilling/unable to follow the instructions • Patient was not able to use DTO • Patient who is not using an orthosis at least 1 to 2 hours/

	day for 5 days per week • Patient with body weight > 125 kg (includes body weight and heaviest object (weight) carried) • Patient with Orthoprosthesis • Patient with flexion contracture in the knee and/or hip joint in excess of 10° • Patient with uncontrolled moderate to severe spasticity (relative contraindication moderate spasticity) • Leg length discrepancy in excess of 15 cm • Patient with unstable neurological or cardiovascular/pulmonary disease, cancer • Pregnancy • Patient using a C-Brace • Patient with known vertigo or with history of falls unrelated to orthosis use or unrelated to motor disability • Patient who has never been fitted an orthosis before • Patient is not able to answer the self-administered questionnaires independently; for patients with upper extremity impairment is it allowed to verbally answer the questions. • Patient participating already in a study during this study´s duration • Patient participated in earlier C-Brace studies
Estimated Time Course	Estimated study duration: First Patient In: 1 Mar 2019 Last Patient In: 31 Dec 2021 Last Patient Out: 31 Mar 2023
Principal Investigators	Site 1: Prof. Frank Braatz Site 2: Dr. Axel Ruetz Site 3: Dr. Bea Hemmen Site 4: PD Dr. Rüdiger Rupp

	Site 5: Jason Wening, CPO, FAAOP Site 6: Tom DiBello, LO, CO, FAAOP Site 7: Chris Toelle, LCO, ACM Site 8: Eric Weber, LCPO, FAAOP Site 9: Dr. Alexander Krebs
Clinical Site Locations	Site 1: Göttingen (D) Site 2: Koblenz (D) Site 3: Hoensbroek (NL) Site 4: Heidelberg (D) Site 5: Chicago, IL (USA) Site 6: Houston, TX (USA) Site 7: Sarasota, FL (USA) Site 8: Seattle, WA (USA) Site 9: Wien (AT)
Clinical Project Manager	Dr. Marten Jakob

2 Abbreviations

AE	Adverse Event
ABC	Activities-specific balance confidence scale
ADE	Adverse Device Effect
BBS	Berg Balance Scale
C-Brace	Axon Orthotic System
CRF	Case Report Form
CB2	C-Brace 2 (the New C-Brace)
CIP	Clinical Investigation Plan = Protocol
CPO	Certified Prosthetist/Orthotist
DGI	Dynamic Gait Index
DTO	Trial tool (Diagnostische Testorthese)
EC	Ethics Committee
GCP	Good Clinical Practice
ICF	Informed Consent Form
KAFO	Knee Ankle Foot Orthoses
PRO	Patient reported outcome
OPUS	Orthotic and Prosthetic User Survey
QUEST	Quebec User Evaluation of Satisfaction with Assistive Technology
RNL	Re-integration to normal living
SAE	Serious Adverse Event
SADE	Serious Adverse Device Effect
SAI	Stair Assessment Index
SCO	Stance Control Orthoses
SF-36	Medical Outcome Study Short Form
tbd	To be defined
WLQ	Work limitations questionnaires
US	United States
6MWT	6-Minute Walk Test

3 Background

The estimated incidence for people with lower limb weakness due to neurologic, neuromuscular or orthopedic impairment, such as lower motor neuron injury, spinal cord injury, multiple sclerosis, post-polio syndrome, stroke, arthritis or trauma requiring the use of an orthosis for walking is about 394.400 cases in Germany (1). It is estimated that approximately 0.01 % of those requiring an orthosis will benefit from a C-Brace. Distribution is comparable in other countries like the US.

People with lower limb weakness due to neurologic, neuromuscular or orthopedic impairment, such as lower motor neuron injury, spinal cord injury, multiple sclerosis, post-polio syndrome, stroke, arthritis or trauma may require the use of a knee-ankle-foot orthoses (KAFO) for walking. The conventional KAFO has a knee joint that can be "locked" in extension during ambulation, but this can cause abnormal gait patterns with hip hiking, circumduction and vaulting during walking (2). These gait deviations using conventional KAFOs may contribute to chronic pain, decreased mobility and a higher physiological energy cost (2,3)

Stance Control Orthoses (SCO) are usually knee ankle foot orthoses (KAFO) that have a built-in locking mechanism which locks the knee joint for the stance phase and unlocks it for the swing phase of gait. The stance-control knee-ankle-foot orthosis (SCO) has addressed some of these issues by mechanically locking the orthotic knee joint during the stance phase of gait while allowing free knee flexion during swing.

These devices have been shown to improve gait kinematics and gait speed on level ground in compared to the use of KAFOs (2,4). Due to the method needed to engage the knee lock for stance, however, users have reported increased mental effort to use these devices, specifically to disengage the knee for initiation of swing (5). Success in using SCOs has been limited by balancing the need to resist flexion in stance and providing a lightweight and small device. The challenges that remain for the SCO are to control the knee in flexion, missing knee flexion under load and extension phases and to switch smoothly between the phases (6).

Current evidence finds that the benefit of KAFO use is for home mobility, general exercise and standing (7) and that, in general, most patients feel that the difficulties and inconvenience encountered with the orthoses and the modest increase in function do not warrant their acceptance for regular, daily use in functional activities (7). However, walking provides exercise to promote musculoskeletal and mental health benefits to counteract the effects of long-term wheelchair use. It may also increase functional independence, community participation and re-integration back to normal life and work.

On the other hand, there is low knowledge about disability and the impact on work background as well as re-integration into work.

A KAFO orthotic device that can provide mechanical support while allowing greater control in swing and stance phases of gait may increase the user's ability to walk with decreased metabolic cost and mental effort to allow increase functional mobility and participation in daily activities allowing a self-administered life.

The C-Brace orthotic system is designed with custom thigh and calf shells connected by a monocentric knee joint with a microprocessor-controlled linear hydraulic damper. The orthotic knee is equipped with a sensor that detects the knee angle and knee angle velocity. The microprocessor controls extension and flexion dampening of the hydraulic knee joint separately by adjusting two valves with the help of servomotors and a planetary gear set. In this way, the entire gait cycle is controlled in real time. The C-Brace is a default-stance orthosis that switches into low flexion resistance for swing when a pre-set, customizable ankle moment is exceeded, while the knee is simultaneously extended, followed by significant knee flexion. It switches back to high flexion resistance for stance as early at the initiation of knee extension. The C-Brace offers controlled stance knee flexion, knee flexion during weight-bearing and dynamic control of the swing phase. Knee flexion during weight bearing makes it possible to reciprocally descend ramps and stairs and to sit down with both legs loaded. We hypothesize that the use of C Brace in comparison to conventional KAFO / SCO systems shall lead to a better balance associated with a reduced risk of falling, hence allowing better participation and an increase in quality of life.

C-Brace Clinical data

Title	Objective(s)	Comparator(s)	Patient number	Published
Prospective, pilot study to evaluate performance, patient benefits and acceptance of a new generation of C-Brace microprocessor-controlled stance and swing control orthosis– AOS	Safety and functionality of CB2	KAFO/SCO	8	Study final Dec 2018
Clinical Algorithm for Post-Stroke Gait Training with C-Brace	functionality	N/A	15	recruiting
Micro-processor controlled Knee-Ankle-	Metabolic, functionality, safety	SCO	18	Study final, publication

Foot Orthosis (C-Brace) vs. Stance-control Knee-Ankle-Foot Orthosis (SCO) and conventional Knee-Ankle-Foot Orthosis (KAFO): Functional Outcomes in Individuals with Lower Extremity Impairments due to Neurologic or Neuromuscular Disease, Orthopedic Disease or Trauma (RIC)				in preparation
A Prospective Registry of patients fitted with a microprocessor-controlled knee ankle foot orthosis	Functionality, safety	KAFO/SCO	150	recruiting

Table 1: Published and non-published clinical data on C-Brace

4 Rationale

The C-Brace microprocessor (MP) controlled hydraulic system is the next generation in the development of lower limb orthoses allowing more control during the swing and stance phases of gait. The device will provide better static and dynamic balance leading to a reduced risk of falling. Improvements may comprise stand to sit transfers, walking on uneven surfaces, slopes and stairs. Such functions may help to improve patients´ mobility, integration, participation and quality of life.

The study will specifically evaluate the potential of the C-Brace to improve the efficacy in daily life activities and benefits for individuals with lower extremity functional impairments as compared to SCOs and conventional KAFOs.

5 Investigational Device Information

Intervention: C-Brace

5.1 Manufacturer

Otto Bock Healthcare Products GmbH
Brehmstraße 16,
1110 Vienna

Austria

Version investigational device
Model number: 17KO1=*
Device name: 17KO1 C-Brace Gelenkeinheit / C-Brace joint unit
Investigational device comprises:

- Microprocessor controlled knee joint (model no. 17KO1)
- Custom made orthotic shells for each patient

C-Brace is a class I device according to 93/42/EEC Annex IX and according to Regulation (EU) 2017/745 Annex VIII
CE-mark was obtained 14 Jun 2018.

For further technical details about the product, product development and testing procedures please refer to the Investigator's brochure (IB).

5.2 Description of the investigational device

Intended use

The C-Brace microprocessor swing and stance control orthosis is used for patients with paresis or flaccid paralysis of the lower limbs (e.g. due to post-polio syndrome, traumatic paresis including paraplegia) requiring orthotic knee support.

Indications / Contraindications C-Brace

Suitable patients will fulfil the following criteria:

- Unilateral or bilateral lower limb paresis or flaccid paralysis e.g. due to post-polio syndrome, traumatic paresis including paraplegia.
- Physical prerequisites such as muscle status, joint mobility and possible axis deviations are crucial and proper control of the orthosis must be guaranteed.
- The user must fulfill the physical and mental requirements for perceiving optical/acoustic signals and/or mechanical vibrations
- The existing muscle strength of the hip extensors and flexors must permit the controlled swing through of the limb (compensation using the hip is possible).

Patients will not be suitable for using the system if they show the following:
Absolute contraindications:

- Flexion contracture in the knee and/or hip joint in excess of 10°
- Knee varus/valgus malposition in excess of 10°
- Severe spasticity

- Body weight over 125 kg / 275 IBs

Relative Contraindications

- Moderate spasticity

Technical description of the C-Brace

The C-Brace consists of individually manufactured orthotic shells, which interface with the thigh, shank and foot. The orthotic shells are made out of commonly used materials in orthotics.

The knee joint is controlled by a microprocessor controlled joint unit, while the ankle joint is designed according to the patient's needs. Elastic elements (such as the C-Brace carbon fiber spring) or state of the art orthotic joints can be used.

Figure 1 C-Brace existing of thigh, tibial and foot shell, mpKnee joint and medial follower.

Knee joint motion is controlled using a microprocessor-controlled joint (mpKnee joint) which consists of microprocessor-controlled hydraulic cylinders that can provide variable resistance. The microprocessor uses the signals from various sensors to adjust the joint behavior in real-time, according to situation (i.e. phase in gait cycle). For example, during stance phase of gait the knee joint provides high resistance to stabilize the patient. During swing phase, the knee joint switches to minimum resistance and is almost free (only inner friction of the system). At maximum resistance, joint motion is blocked. The joints are capable of providing any resistance between these extreme points. For further technical details about the mpKnee joint unit, please refer to chapter 5.2.1 Technical description of mpKnee Joint.

The patient has the possibility to turn the system on and off via a control panel. Furthermore, the patient gets information on the control panel about the battery status, if service is required (after a certain amount of cycles or if a problem with the sensor is

detected by the system) and about the Bluetooth status (see Figure 2: Control panel of C-Brace). Bluetooth can be initialized by the patient if he/she wants to use the Remote Control App. The App will be comparable to the one available for Ottobock's microprocessor controlled prosthetic knee and foot prostheses Genium, C-Leg and Meridium. The use and application of the control panel as well as the Remote Control App is described more detailed in the instruction for use.

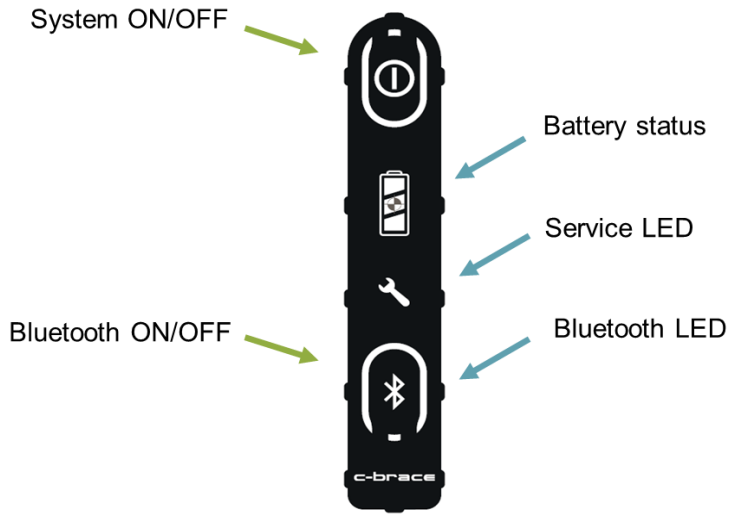

Figure 2: Control panel of C-Brace

5.2.1 Technical description of mpKnee joint

The knee joint for the Braces used in this study as shown in "Figure 3: Microprocessor controlled knee joint unit" is controlled by microprocessor controlled hydraulics. The knee joint can only dissipate energy and is not capable of energy storage. As the hydraulic unit has two valves, flexion and extension resistance can be controlled independently. This means that flexion resistance can be high but at the same time extension resistance can be low, which is a safety feature.

The unit has a modular design with electronic components connected with the proprietary AXON bus, with the exception of the hydraulic sensor.

The system control is based on signals from several sensors:

- 3D accelerometers and gyroscopes measure motion and orientation in space.
- A hydraulic force sensor measures the load that is transmitted by the Brace system.

- Knee angle is measured with a special sensor based on magnetic principles.

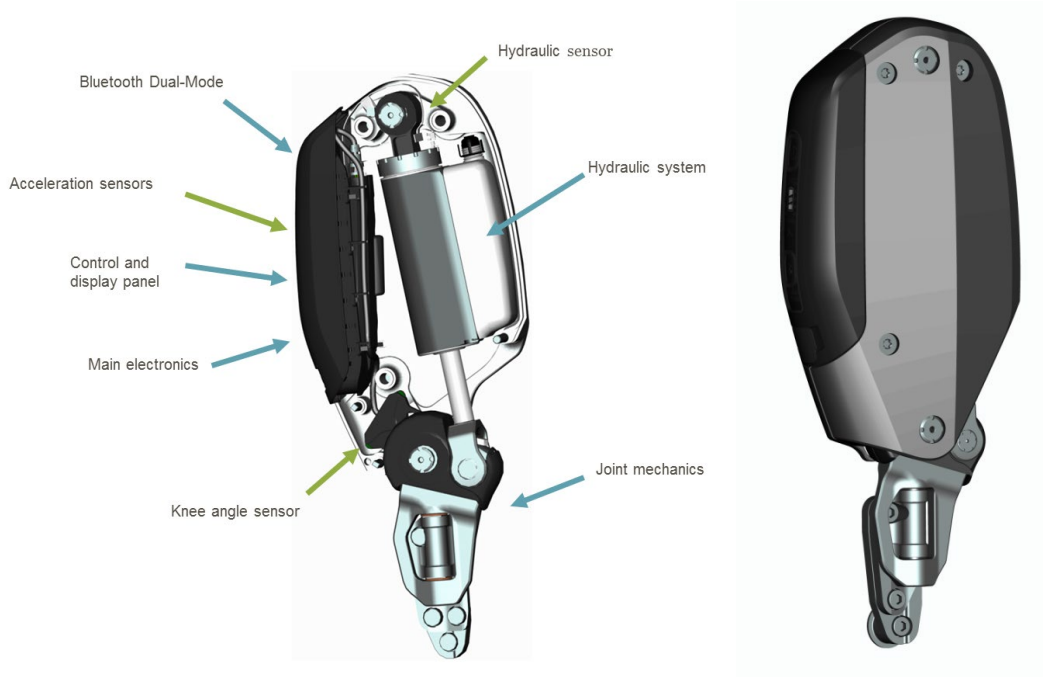

Figure 3: Microprocessor controlled knee joint unit

The control paradigm is mainly based on the evaluation of motion signals. Thus, it can provide optimum support in every phase of the gait cycle. In level walking, the system would behave in the different gait phases according to the following table:

Gait phase	Knee joint resistance	Effect on gait.
Heel strike	High flexion Low extension	Stance phase stability, stance phase flexion is possible
Mid stance (rollover)	High flexion Controlled extension	Stance phase stability Stance phase extension controlled for soft extension stop and improved propulsion
Toe off	Low flexion Low extension	Swing initiation, knee can bend Extension is free.
Swing phase flex-	Controlled flexion Low extension	Knee flexion angle can be controlled to achieve a physiological knee angle

ion		Extension is free.
Swing phase extension	High flexion Low extension	Flexion resistance is high to provide support in case of stumbling. Extension is free.
Terminal swing	High flexion Controlled extension	Flexion resistance is high to provide support in case of stumbling. Extension is controlled for soft extension stop.

Table 1: Description of the knee joint resistance depending on the gait phase and the respective effect on gait.

The system only activates swing initiation at toe off if a signal pattern that is typical for level walking is detected.

The control system is kept as simple as possible; it is principally based on posture control. This method has proven to be appropriate for the control of prosthetic knee joints (e.g. C-Leg 4). For safety reasons also load signals representing the knee moment are taken into account. Therefore, the knee joint does not switch to a low flexion resistance for swing initiation if a flexion moment is measured. Such “default stance” behavior of the system is inherently safe.

5.3 Necessary training and experience to use the investigational device (C-Brace)

5.3.1 Orthopedic technician

The orthopedic technician needs a C-Brace (C-Brace 2) certification.

5.3.2 Patient

The patient will be trained to put on C-Brace, to use the cockpit app and perform adjustments safe and routinely. Training will be performed by a certified CPO or physiotherapist.

Patient will be discharged with C-Brace only if he/she demonstrated that he/she was able to walk safely and is able to program the device. This will be assessed with a benchmark system within the adaption phase (see section 7.3.4).

5.4 Comparator Devices

The C-Brace will be compared with the standard SCOs or KAFOs, which have been prescribed in clinical routine to the patient. All CE registered SCOs or KAFOs are allowed.

5.5 Accommodation to the devices

During the phase of system setup, patients will receive appropriate accommodation support.

For details of accommodation support, please see section 7.3.4.

5.6 Specific medical or surgical procedure involved

Not applicable.

5.7 Receipt, distribution and usage

During screening, the site will test the patients regarding the ability to use C-Brace. During this testing procedure, the parameters will be documented and sent to Ottobock afterwards.

Final assembly of the patient-specific C-Brace orthosis will be performed either at Ottobock SE & Co. KGaA in Duderstadt, Germany or at the study site. In case, Ottobock is responsible for assembly, Ottobock will provide the study site with the assembled C-Brace orthoses. All orthoses will be labeled with a specific label “For clinical investigation only”. Shipment of the final assembled orthosis is done by Ottobock Duderstadt. In case assembly is done at the study site, Ottobock Duderstadt will provide the study site with sufficient mpKnee joints. The mpKnee joints will be labeled “For clinical investigation only”. Traceability of all investigational devices is ensured by maintaining a device accountability log.

If study patients decide not to keep C-Brace for up to 24months after finishing the study, C-Brace needs to be sent back to Ottobock Duderstadt.

6 Study objectives and hypotheses

6.1 Objectives

6.1.1 Primary objective

Primary Efficacy Endpoint

Improvement of static and dynamic balance by using C-Brace compared to KAFO/SCO.

6.1.2 Secondary objectives

- To evaluate the effect of the C-Brace compared to KAFO/SCO on gait, balance, plain level walking, walking during more challenging tasks and divided attention tasks during walking.
- To assess and compare the safe use of the C-Brace compared to KAFO/SCO in regard to falls: frequency of falls, severity of falls, fall-related injuries, fear of falling and related treatment efforts.
- Evaluation of patient`s confidence in performing various ambulatory activities without falling using C-Brace compared to KAFO/SCO.
- Assessment of quality of life and re-integration to normal living using C-Brace compared to KAFO/SCO.
- Assessment of disability and impact on productivity.
- Assessment of patient´s C-Brace satisfaction and usage habits compared to KAFO/SCO.
- Reduced probability of falling more than once by using C-Brace compared to KAFO / SCO

6.1.3 Endpoints

Assessments will be taken at baseline with the patient's own orthotic device, after completing the first randomization phase and after completing the second randomization phase. Please refer to section 8 Outcome Measures.

6.2 Hypothesis

The primary hypothesis is that the microprocessor based C-Brace technology will help moderately active patients to improve balance compared to a non-microprocessor controlled KAFO/SCO.

As a consequence, the C-Brace should help reduce the risk of falling/falls in these patients and eventually make them more independent in their daily life activities including their job and improve their quality of life, which represents the secondary hypothesis of the is study.

7 Study design

This is a prospective international multicenter randomized controlled cross-over open-labeled trial.

The study will have multiple sites in the United States, Germany, Netherlands and Austria. In total 56 patients will be recruited. Patients can be enrolled in a competitive manner without any allocation.

7.1 Experimental plan

After obtaining informed consent, patients will be screened. Patients fulfilling inclusion/exclusion criteria will be enrolled in the study. After screening, a first baseline assessment will be conducted. Within maximum 48 hours, a second set of baseline data will be collected. Afterwards the participants will be randomly assigned to be fitted either with C-Brace or maintain his/her KAFO/SCO. The randomization procedure will be concealed and assigned off-site. After fitting, an accommodation period follows that will last up to 14 days prior home use. The first follow-up data collection will occur after 3 months after the initial home use period. Afterwards, the patients will cross over to KAFO/SCO or C-Brace, respectively. The participants who were fitted with C-Brace will cross over to KAFO/SCO and vice versa. Another accommodation phase will be offered for both C-Brace and KAFO/SCO wearers to ensure that the patient can properly use both devices before the cross-over home use period. The second follow-up data collection will occur after 3-months of home use. At the end of the study, the patients can choose to keep C-Brace until reimbursement or return to their original KAFO/SCO.

7.2 Measures taken to minimize bias

The research center will delegate the role of assessor to one trained employee. The assessor will be responsible for evaluating functionality of participants in the performance-based tests in all phases of the study. During all performance tests, patients will be instructed to refrain from giving any comments. The certified prosthetist (CPO) and physical therapist cannot be blinded.

7.3 Study visits and procedures

7.3.1 Patient enrollment

This study will enroll up to 150 eligible patients. At least 56 subjects passing screening will be randomized. Dropouts shall be replaced, a dropout rate of 20% is assumed. Recruitment planning shall be done in accordance with the capabilities of the centers. Competitive recruitment shall be allowed. All means to increase recruitment shall be taken.

Treatment failures: C-Brace must be fitted according to Ottobock instructions. During study visits, the C-Brace fitting quality will be checked; poor fitting quality needs to be corrected and may be reported as adverse event (AE) or adverse device effect (ADE). For definitions, please refer to section 12.2.

Patients who do not comply with using the C-Brace at least 1-2 hours per day 5 days per week will be included in the intention to treat analysis only; however, they will be excluded from the per-protocol analysis.

Potential patients will be called by the participating sites and pre-screened for study eligibility. In addition, patients contacting the sites or visiting them on a routine basis can be also pre-screened.

7.3.2 Screening and baseline procedures

Pre-screening prior to informed consent may be done with chart reviews or following standard of care assessments to determine if subjects may be potential candidates for the study. Assessments performed exclusively to determine eligibility for this study would be done only after informed consent has been obtained.

Assessments performed for clinical routine and documented in patient´s records may be used for baseline even if they have been done prior to informed consent being obtained.

A screening log will be tracked. Screening failures will be documented.

If the patient enrollment and screening is done at a location separate from the orthotic clinic (e.g. rehabilitation clinic), remote screening including a video of the performance of the BBS will be done at the orthotic clinic to reduce patients' travel efforts to the investigator. Patients must give their informed consent before entering this remote screening procedure.

Two baseline assessments will be performed in order to generate a more confident baseline assessment. Both baseline assessments should be performed within 1 or 2 days. Only the first baseline measurement will be used for statistical analysis.

7.3.2.1 The screening procedures include:

- Informed consent
- Inclusion/Exclusion criteria
- Ability of the patient to sufficiently use C-Brace (via DTO testing)
- Berg Balance Scale
- Demographics: age, gender, ethnicity, weight, height, BMI

- General health information
- Functional muscle test (Janda) / Manual Muscle Testing (MMT)
- Sensitivity test (Rydel-Seiffer Test)
- Passive range of motion assessment (neutral zero method)
- Medical history: Joint replacement, current orthosis use, current use of assistive devices, fall history

7.3.2.2 The first baseline procedures include:

- Review patient's eligibility criteria
- Functional and self-reported baseline assessment (Full assessment of outcome measures)

Performance Assessment

Functional assessment will be done using the Berg Balance Scale, the 6-minute walk test, Dynamic Gait Index, and the Stair Assessment Index. If the first baseline procedure is performed within 24 hours of the screening, the results from the Berg Balance Scale testing, obtained during screening, may be used as first baseline value.

Self – administered Questionnaires:

Activity-specific Balance Confidence Scale, Reintegration to Normal Living index questionnaire, EQ-5D-5L, SF36, Work limitation questionnaire and the OPUS questionnaire. For a detailed description of administered questionnaires, please refer to section 8.2.

Note that screening and first baseline procedures may be combined in one visit.

For statistical analysis, only values from the first baseline will be used. Values from second baseline will be used only to support the values from the first baseline.

7.3.2.3 The second baseline procedures include:

- Functional baseline assessment (Performance assessment)

7.3.2.4 C-Brace potential

Testing C-Brace potential (DTO) with patients is done during screening to ensure the use is appropriate and possible. In the case, a patient cannot fulfill the test criteria; this will be handled as a screening failure.

7.3.3 Randomization

Patients are assigned to treatment groups by means of a state-of-the-art randomization procedure. For details on the randomization procedure, please refer to section 10.3.1.

7.3.4 Fitting and Accommodation

7.3.4.1 KAFO / SCO

Patients entering the study will use their existing fitted KAFO/SCO.

Up to 10 hours of accommodation support with a physical therapist/orthotist will be provided in-house after enrollment within 2 weeks. The progress of accommodation will be assessed and documented. Benchmarks will be used to check patients' ability to use their current orthosis. Two levels will be used for benchmarking:

- Level 1, the minimum requirement for all patients to use their current device should be demonstrated at two different points in time (see 7.3.4.3).
- Level 2 will be documented for patients with higher functional status, walking outdoors, over ground surfaces, steep ramps, slopes and climbing stairs with step-over-step pattern.

7.3.4.2 C-Brace

Up to 10 hours of accommodation support with a physical therapist/orthotist will be provided in-house after definitive fitting within 2 weeks. The progress of accommodation will be assessed and documented. Benchmarks will be used to check patient's readiness to be discharged with C-Brace.

- Level 1, the minimum requirement for all patients to use C-Brace should be demonstrated at two different points in time (see 7.3.4.3).
- Level 2 will be documented for patients with higher functional status, walking outdoors, over ground surfaces, steep ramps, slopes and climbing stairs with step-over-step pattern.

C Brace accommodation support shall follow standardized Ottobock procedures.

7.3.4.3 Benchmarks

Level 1 benchmarking requires independent donning/doffing of the orthosis, charging of the device (if applicable), transfers sit to stand / stand to sit, standing in the orthosis with or without assisted device for a minimum of 2 minutes, safe over ground ambulation, ambulatory turns, to perform a swing phase, walking ramps with a low gradient and climbing stairs with step-to pattern. CPO or physical therapist shall do benchmark assessment.

C-Brace and KAFO/SCO home use may only be permitted after successful Level 1 benchmark testing. C-Brace settings shall be documented by pdf-exports of the cockpit app and device read-out.

Both devices shall be fitted with a step-count transponder. After 14 days, the patient will remove the step-count transponder from the orthosis and will send it back to the study site in a prepared envelope which will be handed to the patient after passing the benchmark criteria (Level 1). After having received the step-count transponder, the site investigator(s) and the sponsor will analyze the daily step count of the patient.

7.3.5 Home use (both arms) / Follow-up phone calls

Patients will be followed up by phone calls after discharge with KAFO/SCO or C-Brace: End of month 1, end of month 2.

The purpose of these phone calls is to check if any notable adverse events, device malfunctions or falls have occurred. Patients should be reminded during this call on use requirements and on the minimum use time of the device to avoid non- or misuse. The phone call shall follow a detailed procedure (see Annex III), results will be documented in a CRF and shall be conducted by the investigator.

Patient is responsible to call the investigator in the case of malfunction, fall or other limiting event without any further delay.

A patient diary is to be documented by the patient to ensure proper collection of fall information and to bring it at each visit.

7.3.6 Study visit 1

After 3 months of C-Brace or KAFO/SCO home use, respectively, a full performance assessment using clinical tests and questionnaires, as defined in 8.2 will be performed.

During study visit 1, patients will perform the following clinical tests and will fill out the following questionnaires:

Clinical tests

- Berg Balance Scale
- Dynamic Gait Index (DGI)
- Stair Assessment Index (SAI)
- 6-minute walk test

Questionnaires

- Changes in current assistive devices
- Documentation of falls (Analysis of patient diary)
- Documentation of fear of falling
- Activity-specific balance confidence (ABC) Scale
- EQ-5D-5L
- Medical Outcomes Study Short Form (SF-36)
- Orthotics & Prosthetics User Survey (OPUS)
- Quebec User Evaluation of Satisfaction with Assistive Technology (QUEST)
- Reintegration to Normal Living (RNL) Index questionnaire
- Work limitations questionnaires WLQ-25

Device settings and step count shall be read out from C-Brace. An anamnestic interview is conducted to document possible changes in the medical history, specifically the use of assistive devices and to record AE´s, SAE`s and device malfunctions.

Study visit 1 has to be planned 3 months after patients have passed the benchmarking criteria and have been discharged to use the orthosis. To facilitate the appointments with the patients, a time frame of -1 to +2 weeks around the scheduled visit is allowed.

The following test sequence is recommended:

Test sequence
Documentation of falls Documentation of fear of falling Patient related outcome questions (only during study visit 2) Activity-specific balance confidence (ABC) Scale
Berg Balance Scale (BBS)
EQ-5D-5L Medical Outcomes Study Short Form (SF-36)
Dynamic Gait Index (DGI) **Stair Assessment Index (SAI)**
Orthotics & Prosthetics User Survey (OPUS) Quebec User Evaluation of Satisfaction with Assistive Technology (QUEST)
6-minute walk test

The clinical testing of the Berg Balance Scale and the Dynamic Gait Index is to be documented additionally by video. If possible, Stair Assessment Index and 6-minute walk test is also to be documented by video. Video files will be stored at the study site and transferred to the sponsor after completion of last-patient-last-visit milestone.

7.3.7 Cross –over process

Cross over of devices following procedure 7.3.4 Fitting and accommodation shall be performed.

7.3.8 Wash out phase

In the arm “C-Brace cross-over to KAFO/SCO”, a wash out phase of 4 weeks is implemented to take a possible carry over effect into account. For safety reasons, wash out phase will begin after patient reaches benchmark level 1.

In the arm KAFO/SCO crossover to C-Brace, no carry over effect is estimated, as it was not observed in previous studies.

7.3.9 Study visit 2

After 3 months of C-Brace or KAFO/SCO home use, full performance assessment using clinical tests and questionnaires, as defined in 8.2 will be performed.

Procedures will follow the description in section 7.3.6 Study visit 1. Two individual questions to evaluate patient-related outcomes (PRO) will also be asked.

7.3.10 Patient´s C-Brace use after study end

After the study documentation is completed, the individual study data can be used to support a reimbursement application according to local regulations for the time after the study. If such an application is filed, the device may remain with the patient until reimbursement is granted but for a maximum of 24 months.

Patients who finish the study on a KAFO/SCO but want to return on C-Brace will be re-trained.

Patients who prefer to use their original orthosis shall also be re-accommodated.

7.3.11 Transfer of patients to C-Brace registry for long term follow up

In the United States and Germany, a prospective registry with a 3-year observational period per patient is collecting data from clinical routine fitting.

Patients enrolled in a US or German study site can be transferred after study end and after signing an informed consent for the registry. In this case, patients should return to their original orthosis for at least 2 weeks before entering the registry.

7.3.12 Adaptations to the study procedure due to the COVID-19 pandemic

Due to the outbreak of the COVID-19 pandemic, patients' study visits were interrupted for the time of the lockdown. This had significant impact on the study procedure as well as on the patients' individual study duration.

The point of restarting patient assessments will be determined according to national, state and local regulations on COVID-19 containment. Starting dates may therefore be different per individual study site.

In order to get comparable results before and after the lockdown, a full performance assessment using clinical tests and questionnaires, as defined in 8.2 will be performed. After the performance assessment, patients will be re-assessed regarding the ability to reach benchmark Level 1 as described in section 7.3.4.3.

After successful Level 1 benchmark testing, patients will re-start the home-use phase in which they had been when the COVID-19 lockdown became effective. Home-use phase will be performed as described in section 7.3.5.

If patients were in the wash-out phase or before the start of a home-use phase, patients will start with the following home-use phase according to protocol after successful Level 1 benchmark testing.

Patients will receive a StepWatch as noted in the footnote to the Study Schedule in section 8.3.

A device read-out will be performed as described in section 8.2.2.4.

Patients will continue the study as outlined in 7.3.

In case of further lockdowns or in case local regulations prohibit patients' study visits, the study visits shall be re-organized and patients will continue with the study following the procedure described above.

Study Flow Chart

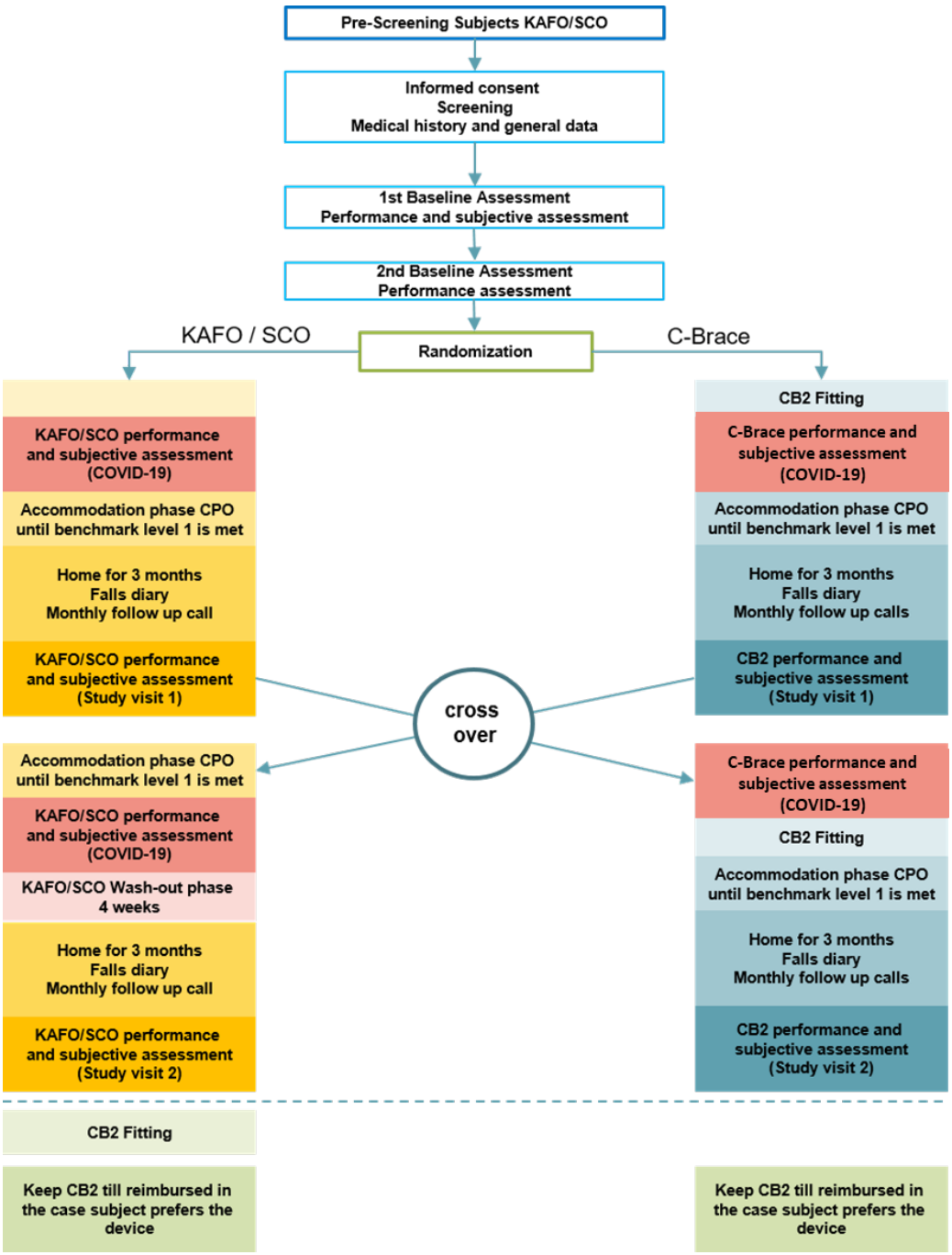

Figure 4: Study flow chart

8 Outcomes measures

8.1 General data collection

Due to the nature of the study, several non-validated, self-designed questionnaires (SDQ) will be used as case report forms (CRF) to collect the necessary data.

General patient and orthosis use data will include such information as:

- Patients' demography: patient age, gender, ethnicity, weight, height, BMI
- Patients' medical history: time since impairment, cause of limb impairment, limb(s) impaired, surgical history, comorbidities, medications, current orthosis fitting, use of aids, falls, duration of orthosis support since impairment, etc.

Data collection is completed by video documentation of the performance tests.

8.2 Outcome measures

In terms of outcome measures, several questionnaires and performance-based measures will be used in the study.

8.2.1 Primary study objective

For the primary study objective, the static and dynamic balance will be assessed using the **Berg Balance Scale** (Version 2013) as **primary efficacy endpoint**. Measures will be performed and compared at first baseline, after 3 months with the current orthosis and after 3 months with C-Brace by a physician, orthotist or physical therapist when randomized to the first treatment group, and at baseline, after 3 months with C-Brace and after completion of 4 weeks wash out period and 3 months with the current orthosis, when randomized to the second treatment group.

The Berg Balance Scale is a 14-item scale designed to measure balance in adults in a clinical setting. When scoring, the lowest response category that applies should be recorded. In each item, points should be deducted if the time or distance requirements are not met, the patient's performance requires supervision, or the patient requires assistance from support or examiner.

The Berg Balance Scale was investigated in a variety of etiologies including patients suffering brain injury, spinal injuries, Parkinson`s Disease, stroke, osteoarthritis and vestibular disorders. It was also investigated in older adults and within geriatric care. The tool is recommended in intervention research studies. The minimal detectable change in elderly adults was determined to lie between 3.3 and 6.3. The BBS is associated with cut off scores in elderly adults with a score of 45 and lower indicating an in-

creased risk of falling (8) and a score below 40 being associated with almost 100% fall risk (9).

This investigation includes subjects with a BBS score < 45 and hence investigating subjects that are believed to be at an increased fall risk.

Administration and burden: Performance-based measure evaluated by physician, orthotist or physical therapist.

8.2.2 Secondary study objectives

8.2.2.1 Assessment of static and dynamic balance and functional mobility

Assessment of static and dynamic balance and functional mobility is performed by using the activities-specific balance confidence (ABC) scale, the dynamic gait index (DGI), 6-minute walk test, Stair Assessment Index (SAI) in patients using a C-Brace compared to KAFO/SCO.

- **Activity-specific balance confidence (ABC) Scale**

This test, along with a functional balance test, such as the Berg, will tell the clinician if their client is over- confident or under-confident about falling.

The ABC is one of several tools designed to measure an individual's confidence in his/her ability to perform daily activities. These tools were designed for use with older adults. The ABC was designed to include a wider continuum of activity difficulty and more detailed item descriptors than the Falls Efficacy Scale (FES). Fear of falling is important to assess because it is a likely confounder in measuring postural performance. Deterioration in balance may result from activity restriction mediated by the fear of falling.

Administration and Burden**:** Patient self-administered; 5-10 min

- **Dynamic gait index (DGI)**

The Dynamic Gait Assessment is an 8-item test used to assess balance during walking tasks. It has a maximum score of 24 with each item being scored 0-3. It may be performed with or without an assistive device; however, individuals lose a point on all items requiring a device.

Administration and burden: Performance-based measure evaluated by physician, orthotist or physical therapist.

- **6-minute walk test**

The 6-minute walk test is performed as an objective evaluation of functional exercise capacity. The 6-minute walk test is easy to administer, well tolerated, and typically reflective of activities of daily living. The test measures the distance that the patient can walk on a flat, hard surface, indoors, in a period of 6 minutes. The walk test is patient self-paced and assesses the level of functional capacity. Patients are allowed to stop and rest during the test, however, the timer does not stop. If the patient is unable to complete the time, the time stopped is noted and reason for stopping prematurely is recorded.

Administration and burden: Performance-based measure evaluated by physician, orthotist or physical therapist.

- **Stair Assessment Index (SAI)**

The Stair Assessment Index (10) is a 14-point ordinal scale (from 0 to 13) used to assess different gait patterns during ascent or descent of stairs. It was developed to detect differences in function with different knee units for transfemoral prosthetics. Stair ascent and stair descent pattern will be assessed separately.

8.2.2.2 Measurement of safety and falls

Patients will keep a patient diary in each home use period.

To measure the safe use of C-Brace compared to KAFO/SCO, documentation will be done in the diary and information will be transferred to the CRF during study visits and phone calls.

- **Falls**

Principal investigator or his delegates interview patients every month for occurrence of falls, respectively occurrence of AEs/SAEs on the phone respectively ask for falls in study visits.

In the case falling occurs, the following information is obtained from the patient and documented in the CRF per fall:

Mild fall: no injury, bruising, abrasions, hematoma without physician / out-patient consultation

Moderate fall: bruising, sprains, cuts, abrasions, or a reduction in physical function for at least three days, or if the participant sought out-patient medical help (11)

Serious fall: fracture or admission to hospital or if any wounds needed stitches (sutures) (11)

What was the consequence of the fall:

Diagnosis, office-based physician, ambulance visit, radiology, therapy, length of hospital stay, follow up visits.

Frequency of falls are documented as well.

- **Patient reported outcomes questions regarding to fear of falling**

One question will address patients' fear to experience a fall indoor and a second one to fall outdoor. The rating will be done on an 11-item scale (0 = no fear to 10 = max. fear). In addition to each question, patients will be asked to explain in their own words the scenario of falling.

Administration and Burden**:** Patient self-administered; 1 min.

If an AE/SAE occurs, it will be processed as described in section 12.3.

- **Probability of falling more than once when using C-Brace compared to KAFO / SCO**

The probability to fall more than once using C-Brace will be calculated and compared to the probability to fall more than once using KAFO / SCO. For details of the statistical analysis, see section 10.3.

8.2.2.3 Quality of Life and Re-integration to normal living

Measurement of quality of life and re-integration to normal living using C-Brace compared to KAFO/SCO will be done using RNL index, EQ-5D-5L, WLQ-25, OPUS, SF-36, QUEST, and PROs.

- **Reintegration to Normal Living (RNL) Index questionnaire**.

The reintegration to normal living will be measured using the Reintegration to Normal Living (RNL) Index questionnaire.

A measure of community reintegration, which covers areas such as participation in recreational and social activities, movement within the community and the degree of comfort the individual has in his/her role in the family and with other relationships.

11 items measuring satisfaction regarding perceived physical functioning, and social and emotional life.

Internal consistency from a sample of persons with acute mobility impairments (including persons with spinal cord injury), yielded a Cronbach α = .91. The RNL Index has been found to have good construct validity (12).

Scoring: There are different scoring algorithms for this measure. There is a 1) visual analog scale ranging from 0 to 10; 2) a three-point scoring system; and 3) a four-point scoring system. Regardless of the scoring system used, higher scores represent higher levels of participation.

Administration and Burden**:** Patient self-administered; 30 min.

The RNL was developed by Wood-Dauphinee, Opzoomer, Williams, Marchand, and Spitzer in 1988 (12).

The RNL has been tested for use with individuals with stroke, malignant tumors, degenerative heart disease, central nervous system disorders, arthritis, fractures and amputations; spinal cord injury; traumatic brain injury; rheumatoid arthritis; subarachnoid hemorrhage; hip fracture; physical disability; and community-dwelling elderly (13).

- **EQ-5D-5L**

The EQ-5D-5L is a standardized measure of health status developed by the EuroQol group, applicable to a wide range of health conditions and treatments and has widespread currency outside the profession. It is often referred to as a quality of life questionnaire.

The EQ-5D-5L, is a very simple measure, which patients complete at the start and end of treatment. Its name means 'EuroQol – 5 Dimensions – 5 Levels' and comprises five dimensions of health: mobility, ability to self-care, ability to undertake usual activities, pain and discomfort, and anxiety and depression. There are five options (levels) under each domain.

Administration and Burden**:** Patient self-administered; 10 min.

- **Work limitations questionnaires WLQ-25**

The Work Limitations Questionnaire (WLQ-25) was developed by Lerner and colleagues (14). It is one of the most commonly used questionnaires to evaluate at-work disability and productivity loss. It contains 25 items arranged under four subscales addressing four dimensions of job demands namely: time demands, physical demands, mental/interpersonal demands, and output demands. The time demands subscale contains five items on punctuality, pacing, and productivity. The physical demands subscale has six items covering static positioning, moving around, lifting, repetitive movements, posture, and use of tools. The mental or interpersonal demands subscale contains nine items that assess concentration and on-the-job social interactions. The output demands subscale contains five items determining the volume and quality of work (14).

- **Orthotics & Prosthetics User Survey (OPUS)**

The Orthotic and Prosthetics User Survey (15) is a self-report questionnaire, which is designed to evaluate the outcome of orthotic and prosthetic services. Three of the five domains will be administered: lower limb functional measure, health-related quality of life and satisfaction with device. The domains of upper limb functional measure and satisfaction with service are not applicable in this study.

Administration and Burden**:** Patient self-administered; 15 min.

- **Medical Outcomes Study Short Form (SF-36)**

The SF-36 is a 36-item scale constructed to survey health status and quality of life. The SF-36 assesses eight health concepts: limitations in physical activities because of health problems; limitations in social activities because of physical or emotional problems; limitations in usual role activities because of physical health problems); bodily pain; general mental health (psychological distress and well-being); limitations in usual role activities because of emotional problems; vitality (energy and fatigue); and general health perceptions. The standard form of the instruments asks patients to reply to questions according to how they have felt over the previous week. The items use Likert-type scales, some with 5 or 6 points and others with 2 or 3 points. Sample items include "How much bodily pain have you had during the past 4 weeks", and "How much of the time during the past 4 weeks have you felt so down in the dumps nothing could cheer you up?" The SF-36 has been widely used and has excellent psychometrics.

More information on Version 2 can be found on the SF-36 website: http://www.sf-36.org/tools/sf36html

Administration and Burden**:** Patient self-administered; 10 min.

- **Quebec User Evaluation on Satisfaction with Assistive Technology (QUEST)**

The QUEST 2.0 evaluates a patient's satisfaction with various assistive technologies. The 12-item instrument is used to assess satisfaction with a specific assistive device; eight of these items assess characteristics of that assistive device in terms of the following dimensions: dimensions (size), weight, adjustments; safety, durability, simplicity of use, comfort, and effectiveness.

The remaining four items assess service and include service delivery, repairs and service of the device, professionalism of service, follow-up service.

Patients are asked to rate their satisfaction for the device on a five-point scale that ranges from "not satisfied" at all to "very satisfied".
Finally, patients are asked to choose the three most important items related to the assistive device in question.

Administration and Burden**:** Patient self-administered; 10 min.

- **Patient-Related Outcome Questions**

Patients will be asked how the specific orthoses affected activities they enjoy and their quality of life (5 levels each, 2 questions). In addition to that, patients are asked to provide in a free text field information on these two topics.

Administration and Burden**:** Patient self-administered; 4 min.

8.2.2.4 Device Read Outs

- Setup App:

A pdf-export and storage of the data file will be done at definitive fitting, every time a change in the settings is done and at the follow up visits.

- Step Count

A step count transponder will be fixed on C-Brace and on KAFO/SCO before starting the home use phase. It will be read out after each observational period (14 days).

For details on the procedures, please refer to section 23.1 (Appendix I).

8.2.2.5 General statement to self-administered patient questionnaires

The patient fills in the questionnaires after instruction of the investigator. If a patient has an upper extremity impairment which does not allow him/her to fill in the questions, it is allowed that he/she answers orally and data entry will be performed by the investigator, the CPO or PT. The patient is placed in a separate room. After filing out the investigator checks the questionnaires for completeness only. Questionnaires are available in English and German. If translation into another language is necessary, this will be done by an official translator.

8.3 Study schedule

Visit	IC	Inclusion/ Exclusion	Medical History	BBS	DGI	SAI	6MWT	Step count	ABC	2PRO	WLQ	RNL	EQ-5D	SF-36	OPUS	QUEST	C-Brace Set-tings	Fall history / Fear of falling	Patient Diary	AE/SAE/DD
Screening	x	x	x	x																x
1st baseline				x	x	x	x		x		x	x	x	x	x	x		x		x
2nd baseline				x	x	x	x													x
C-Brace Fitting[1]																	x			x
Training/ benchmarks(1)								x[2]											x	x
Phone call (1)																			x	x
Phone call (2)																			x	x
Additional Study visit (COVID-19)			x	x	x	x	x		x		x	x	x	x	x	x	x[3]	x	x	x
Additional Training/ benchmarks (COVID-19)								x[2]												x
Study visit (1)			x	x	x	x	x		x		x	x	x	x	x	x	x[3]	x	x	x
Training/ benchmarks (2)								x[2]												x
Phone call (3)																			x	x
Phone call (4)																			x	x
Additional Study visit (COVID-19)[4]			x	x	x	x	x		x		x	x	x	x	x	x	x[3]	x	x	x
Additional Training/ benchmarks (COVID-19)[4]								x[2]												x
Study visit (2)			x	x	x	x	x		x	x	x	x	x	x	x	x	x[3]	x	x	x

[1]Order shown for subjects randomized to start with C-Brace for whom casting is done after screening. C-Brace fitting to be done after Study Visit (1) for subjects starting with existing orthoses.
[2]StepWatch affixed to either existing orthosis or C-Brace after benchmarks during training are achieved.
[3]For subjects randomized to C-Brace only.
[4]For subjects restarting after cross-over

9 Patient population

9.1 Number of patients to enroll

Up to 150 patients fulfilling the inclusion and exclusion criteria will be enrolled in the study. At least 56 subjects passing screening will be randomized. All sites are allowed to recruit patients competitively according to their possibilities. Patient screening and enrollment will be performed in close collaboration with the sponsor to avoid over-recruitment.

Potential patients will be called by the participating centers and may be pre-screened for study eligibility. In addition, patients contacting the centers or visiting them on a routine basis can be also pre-screened.

Once a potential participant using a unilateral KAFO or SCO has been identified, study clinician may contact the potential patient or study staff will contact the potential patient on behalf of the principal investigator, starting with a letter followed by a phone call to the potential patient.

A screening log will be tracked.

9.2 Duration individual patient's participation

Each patient should be observed 8-9 months depending on which orthosis is used before the crossover.

9.3 Inclusion and Exclusion Criteria:

Patients must meet all of the inclusion and must not meet any of the exclusion criteria to be registered to the study.
Study treatment may not begin until a patient is registered.

9.3.1 Inclusion criteria

- Patient has been tested with the Trial Tool (DTO) and demonstrated the potential to utilize the C-Brace successfully (see section benchmarks: independent donning/doffing of the orthosis, charging of the device, transfers sit to stand/stand to sit, standing in the orthosis with or without assisted device for a minimum of 2 minutes, safe over ground ambulation, ambulatory turns and to perform a swing phase).
- Patient has a BBS score < 45
- Lower limb functional impairment according to CE label wording
- Prior active and compliant use of unilateral or bilateral KAFO or SCO in the past 3 months prior to enrollment in the study
- Patient meets minimum physical requirements to be fitted with a C-Brace, such as muscle status, joint mobility, leg axis and proper control of the orthosis must be guaranteed.

- The User must fulfill the physical and mental requirements for perceiving optical/acoustic signals and/or mechanical vibrations
- The existing muscle strength of the hip extensors and flexors must permit the controlled swing-through of the limb (compensation using the hip is possible).
- Patient´s commitment to use C-Brace 2 at least 1-2 hours per day 5 days per week-
- Patient is ≥ 18 years old
- Patient is willing and able to independently provide informed consent.
- Person is willing to comply with study procedures

9.3.2 Exclusion criteria

- Patient who is not able to follow the entire study visits or is unwilling/unable to follow the instructions
- Patient was not able to use DTO
- Patient who is not using an orthosis at least 1 to 2 hours/ day for 5 days per week
- Patient with body weight > 125 kg (includes body weight and heaviest object (weight) carried)
- Patient with Orthoprosthesis
- Patient with flexion contracture in the knee and/or hip joint in excess of 10°
- Patient with uncontrolled moderate to severe spasticity (relative contraindication moderate spasticity)
- Leg length discrepancy in excess of 15 com
- Patient with unstable neurological or cardiovascular/pulmonary disease, cancer
- Pregnancy
- Patient using a C-Brace
- Patient with known vertigo or with history of falls unrelated to orthosis use or unrelated to motor disability
- Patient who has never been fitted an orthosis before
- Patient is not able to answer the self-administered questionnaires independently; for patients with upper extremity impairment is it allowed to verbally answer the questions.
- Patient participating already in a clinical study during this study´s duration
- Patient participated in earlier C-Brace studies

Additional determination of exclusion criteria for Austrian centers:
Pregnant and nursing women are NOT allowed to participate in this study.
Women of childbearing age are only allowed to participate in this study, if they have confirmed that they are not pregnant before the study (according to a pregnancy test). They will be asked to perform pregnancy tests once a month during the study. Female patients will be asked to inform the investi-

gator immediately, if they become pregnant during the study, or suspect that they are pregnant. Their participation in the study will be terminated under these circumstances.

9.3.3 Drop out or early termination of the study

Patients can withdraw from the study at any time and for any reason. This decision has no impact on the patient's medical care. In case of early termination, the investigator must document the reasons as completely as possible. The investigator can temporarily or permanently discontinue the patient's study participation for any reasons that are in the patient's best interest, particularly in cases of serious adverse events. If a patient is lost to follow-up, the investigator will use all available means to get into contact with him or her. After three weekly telephone reminders, the patient will be recorded as lost to follow-up.
The investigator will fill in the reason for the drop out or early termination of follow-up in the case report form. Patient who drop out of the study may not keep the C-Brace up to 24 months as described in section 7.3.10.

Dropouts will be replaced until the milestone last patient in was reached.

10 Statistics

The goal of this study is to assess the improvement of static and dynamic balance by using C-Brace compared to KAFO/SCO which should in consequence help reduce the risk of falling/falls in these patients.

10.1 Sample size calculation

The sample size calculation is based on the hypothesis as described in 6.2 and crossover study design as described in 7. The number of recruited patients however will be larger than what would be needed to fulfill the requirements of the primary efficacy endpoint in order to achieve a higher power for any tests performed on secondary objectives and to improve the likelihood that the random allocation of patients results in similar baseline characteristics in the compared group.

Sample size calculation was performed with G*Power 3.1.9.7 or manually as described.

10.1.1 Primary efficacy endpoint

The efficacy of the microprocessor based C-Brace technology compared to a non-microprocessor controlled KAFO/SCO will be determined through the detection of a statistically significant improvement of the Berg Balance Scale.

One null-hypothesis will be tested in the confirmatory analysis:

H_0: ΔBerg Balance Scale $<= 0$
H_1: ΔBerg Balance Scale > 0

Sample size calculations are based on a mean group difference $\Delta = 6.6429$ between the C-Brace technology compared to a non-microprocessor controlled KAFO/SCO and a standard deviation $\sigma = 4.9085$ of this difference.

The estimations of the parameters come from paired observations in the RIC study combined with the paired observations of 4 patients from the Wien/Goettingen study (RIC combination study). In total, 14 patients in the RIC combination study were considered to determine the estimates. All the included patients displayed a Berg Balance Scale of less than 45.

To test the hypothesis of an expected effect in one direction a one-tailed paired t-test will be used.

At an α level of 0.05 and a power of 0.8, a total of 6.4557 of patients are needed as calculated from the t-distribution. Under the assumption of a dropout rate of 20% a total of 9 patients would need to be recruited.

10.1.2 Secondary endpoints

An improvement in patients balance is hypothesized to aid the patients in their daily life and potentially influence some of the other outcome measures collected in this study. These measures will be explored without a strict expectation for the magnitude of expected change. Due to the expected nature of the distribution of the number of falls or rather the proportion of patients to fall more than once with the device C-Brace, these measurements would require the largest sample size in order to detect significant improvements at a reasonable power level.

If the probability to fall more than once with the device C-Brace is significantly lower than the probability to fall more than once with the device KAFO/SCO it could be used as a supporting argument to relevance of a potentially identified improvement in the primary efficacy endpoint. Previous observations on the RIC combination data however revealed a low expectancy of the probabilities to fall more than once with either KAFO/SCO and C-Brace device during the observed time span. A probability to fall more than once of $p_{KAFO/SCO} = 0.1333$ with the device C-Brace and a probability to fall more

than once of $p_{C-Brace} = 0$ for the device KAFO/SCO was recorded for 15 paired observations in the RIC combination study.

The sample size needed to detect a difference of $p_{diff} = p_{KAFO/SCO} - p_{C-Brace} = 0.1333$ for the paired proportions with on the basis of one-sided McNemar's Z-test without continuity correction is calculated as

$$n = \left(\frac{z_{1-\alpha}\sqrt{p_{disc}} + z_{1-\beta}\sqrt{p_{disc} - p_{diff}^2}}{p_{diff}} \right)^2$$

where $p_{disc} = p_{KAFO/SCO} + p_{C-Brace} = 0.1333$

At a significance level of 0.05 and a power of 0.8, a total of 44.2386 of patients would be needed. Under the assumption of a dropout rate of 20% a total of 56 patients would need to be recruited. We recognize that the inclusion of a continuity correction may be more appropriate given the small proportion to fall more than once with either type of device and that a shift in the expected proportions away from zero would drastically increase the number of patients needed to detect the difference to show a significant difference. Regardless the merit of the observing these proportions at a higher absolute occurrence will yield a sound basis for future studies. For this reason, the number of patients to be included in the study is based on this value.

10.2 Management of missing, unused or spurious data

If data are missing, illegible or incoherent, requests for further information will be sent to the investigator in question. Although every effort will be made to ensure that each patient's data is complete, some patients may not have data on one or more measures.

For the intention-to treat analysis the missing data will be imputed. The imputation method will depend on whether the missing data are at baseline or follow-up visit as well as the reason for the missing data as further described below.

Missing baseline data for patients will be imputed. For missing data in any of the measurements which are taken again at the second baseline, these values might be used in place of the first baseline measurement. Evaluation whether other missing baseline data might not be missing at random, will be done by exploring patterns of missing data within different measurements and patients for which data was collected.

Strong evidence for missing data patterns within measurements of secondary interest may lead to the exclusion of such measurements for any supportive analysis and will be documented in the study

report accordingly. In case such a pattern is observed within the measurement of primary interest may lead to the study being declared invalid in regard to the analysis planned for it.

Appropriate data management as defined in the protocol should reduce the chance of this being the case. Strong evidence for missing data patterns within patients of specific characteristics will be evaluated and might be indicative of a serious limitation to the study and could potentially lead to the study being declared invalid. Previous studies on the topic have not shown this to be very likely in the patients that fulfill the inclusion criteria of the study. Where data is assumed to be missing at random multiple imputation and a sensitivity analyses will be used.

In order to perform a sensitivity analysis, patients who terminated treatment early, will be imputed using multiple imputation methods in order to substitute missing values. Here, multiple copies of the original dataset will be generated by replacing missing values using e.g. a multivariate normal distribution. Each of these complete sets will be analyzed as complete sets and the corresponding parameter and standard error estimates will be combined with taking the uncertainty of the imputation process into account.

For the patients missing follow-up data, proportions of missingness, type of missing measurements, patient characteristics and baseline value levels will be explored in order to detect patterns of missing data. If data is assumed to be missing at random the following imputation strategy will be used.

A linear mixed effects model with the outcome measure as dependent variable will be fitted to the data. This model will use the treatment group and period as fixed factor and the first baseline measure as covariate. Random patient effects will be introduced for the intercepts and thus taking the correlation within patients into account. The analysis implicitly uses a weighted average to estimate the outcome measures, with estimations coming from the complete observations and from the observations with missing values.

Missing data for study patients at follow-up on C-Brace, KAFO/SCO or both because they 1) died, 2) are lost to follow-up (LTFU), 3) withdrew from the study or were withdrawn from the study by the investigator, 4) miss the follow-up visit or 5) do not complete the outcome measure at follow-up, will be imputed by using a mixed model with a random intercept for patient and treatment group as predictor variables.

The details of the imputations methods applied will be documented in the study report.

10.3 Planned statistical analysis

In general, the most suitable statistical analysis consistent with the form of data will be used and the underlying assumptions of the statistical method will be verified through appropriate pre-tests.

The analysis will be performed on the intention-to-treat (ITT) population and then on the per-protocol (PP) population. The ITT population is defined as all the patients randomized into their randomization group, regardless of the treatment received or their outcome in the study. The PP population is defined as all the patients in the ITT population without any major protocol deviations

For the outcomes measures being evaluated, three assessments are undertaken:

after base line measurements with original orthosis (first baseline measurement)

after first follow up measurement with the C-Brace or original orthosis

after second follow-up measurement with the C-Brace or original orthosis

Quantitative variables will be summarized using standard descriptive statistics (average, standard deviation, median, minimum and maximum, first and third quartile). Qualitative variables will be described using group sizes and frequencies. When relevant, 95%confidence intervals will be given.

Patient characteristics at enrolment will be presented and compared in each group to ensure the groups are initially comparable. The features of any patients lost to follow-up will be studied and influence the imputation strategy as described in 10.2.

Patient profile plots for the outcome measures in both treatment groups for all three assessments will be viewed, showing imputed values. Furthermore, the group means in each treatment group will be evaluated. Outcome measures will be visualized for the crossover periods in scatter plots of first follow up measurement against second follow-up measurement in both treatment groups i.e. period vs period plots.

10.3.1 General patient and orthosis use data

Assessments will be displayed in summary tables.

10.3.2 Primary efficacy outcome

One null-hypothesis as outlined in section 10.1 will be tested in the confirmatory analysis.
Absolute values and changes from first baseline and follow ups respectively will be presented for the Berg Balance Scale after 3 months of treatment using descriptive summary statistics for each treatment period. Moreover, percentage changes from baseline and follow ups respectively will be displayed.
The confirmatory inferential statistical evaluation of the primary outcome measure will be based on a linear mixed effects model with the Berg Balance Scale as dependent variable. This model will use the treatment group and period as fixed factor and the first baseline Berg Balance Scale as covariate. Random patient effects will be introduced for the intercepts and thus taking the correlation within patients into account.

The confirmatory analysis of the primary efficacy endpoint will be done for the intention-to-treat population. Additional efficacy analyses will be conducted for the per-protocol population. The p-values of these analyses will be interpreted in the exploratory sense only.

10.3.1 Secondary outcome analysis

Analyses for the secondary outcome measures will be performed for the intention-to-treat population as well as for the per-protocol population. All inferential analyses for the secondary efficacy variables will be interpreted in the exploratory sense. All secondary outcome measures will be evaluated by using descriptive statistics primarily, absolute values at each time point and if appropriate changes from first baseline and follow ups respectively. These analyses will be performed in a similar way as the primary efficacy outcome using a linear mixed effects model when appropriate.
Additional attention will be paid to the exploration of the measurements of safety and falls. The number of Falls is expected to be reduced in general by using a C-Brace, but the extent of a possible reduction remains uncertain. Therefore, frequency of falls, severity of falls, fall-related injuries, fear of falling and related treatment efforts will be explored in rigorously in order to formulate appropriate hypothesis for future research.
In the past the reduced probability of falling more than once by using C-Brace compared to KAFO / SCO showed the most promise as a reliable measure to compare the two device types, since it was less sensitive to outliers e.g. patients with a high number of falls on either device as compared to the total number of falls. However, sample sizes in prior research were relatively small and estimations for potential differences remain uncertain, albeit of great clinical interest.
Therefore, we explore whether a reduction in the probability of falling more than once using the C-Brace can be detected by a McNemar Test for paired proportions. This test will likely be underpowered in comparison to the expected best-case scenario used in the sample size calculation and will be reported accordingly.

10.3.2 Randomization procedure

Randomization will be performed by site in random permutated blocks of 6 by allocation order. A randomization sequence will be produced and integrated into the electronic case report form to define the randomized treatment order (X or Y device) and provide the investigator with this information during the enrolment visit.

10.4 Interim analysis

An interim analysis will be performed after at least 35 patients have completed the study. After the interim analysis, it will be decided whether: 1) the sample size must be increased 2) the study will be

stopped early for futility, or 3) interim hypothesis testing will be done for the primary objective and select secondary objectives.

The interim analysis will be performed for the primary endpoint (BBS). A statistical power calculation will be performed based on the observed intraindividual changes (IIC) between C-Brace and KAFO arms. The following rules will be applied:

1. If the power based on observed mean and standard deviation for the BBS IIC for the intended target of 56 subjects is less than 0.9, the proposed sample size for the study may be increased.
2. If the observed mean IIC is less than 3, the study may be stopped for futility, since this difference is of no clinical relevance.
3. If the power based on observed mean and standard deviation for the BBS IIC with the interim analysis cohort of at least 35 subjects is greater than 0.95, hypothesis testing will be performed at the alpha = 0.02 level to determine statistical significance. In this case, the primary objective will be analyzed at the 0.03 level for the final analysis of the full study cohort at the completion of the study to maintain an overall Type I error rate of 5%. If the power is less than 0.95, hypothesis testing will only be performed at the conclusion of the study and statistical significance determined using alpha = 0.05.

Conditional hypothesis testing may be performed for select secondary objectives using the same method described in rule 3 above.

11 Risk and benefit of the investigation device and clinical investigation

C-Brace is a CE-marked class I medical device. Risk analysis has been conducted and identified risks such as blocking of flexion in knee joints when descending stairs or ramps, unintentional locking during sitting, flexion resistance is not reduced when walking on level ground (swing phase), insufficient extension of knee joint in the stance phase, insufficient extension of the orthosis during standing up. All those identified risk could lead to a fall. After implementation of appropriate measures, the risk analysis concluded that the remaining risks are either acceptable or ALARP (as low as reasonably practicable).

In this clinical study, patients will be randomly assigned to two treatment groups. Treatment group 1 will start with 3 months usage of the patients' KAFO or SCO. The patients will then move to a 3-month period of C-Brace use. Treatment group 2 will start with 3 months of C-Brace use and will then enter into a 4-week washout period before moving to a 3-month period of KAFO/SCO use. This randomization will not add any additional risks to the patients since both groups will use both devices for the same period.

Patients enrolled in the study will enter with their current orthosis (KAFO/SCO). Before performing the clinical tests, patients will receive up to 10h of accommodation training and will be benchmarked according to their ability to use their orthosis. When entering the C-Brace group, patients will again receive up to 10h of accommodation support and an assessment. Patients enrolled in the study who will start with C-Brace, will receive accommodation support and assessment. When switching back to their regular orthosis (KAFO/SCO) they will again receive accommodation and assessment. Therefore, the risks due to switching of the devices in the clinical study are mitigated.

The expected benefit of C-Brace to the patients participating in this study will be comparable to the ones published on C-Brace. The literature published on C-Brace suggests that microprocessor controlled SSCOs offer benefits during walking on level ground, stairs and ramps when compared to conventional KAFOs such as locked KAFOs and SCOs. Biomechanical analysis showed that more physiological swing and stance phase during level walking is possible with C-Brace (Schmalz 2016). Walking on ramps and stairs was also more physiological allowing step-over-step descent. The load on the contralateral limb was reduced. C-Brace also resulted in improved safety and reduction in difficulty of performing activities of daily living (Pröbsting 2016). Subjects report of 91% of the ADLs being safer and 76% of the ADLs less difficult to perform with C-Brace in comparison to their previous orthosis. Greatest functional gain was achieved in the categories Family and Social Life and Sports and Leisure activities. Significant improvements were achieved in the domains of ambulation, paretic limb health, well-being and disturbing sounds of the orthosis.

The new version of C-Brace is smaller and reduced in weight. Furthermore, due to an improved sensor system in the joint unit, sensor at the ankle become obsolete and therefore the design of the orthotic shells can be better adapted to the individual anatomy. Therefore, the benefits of the new C-Brace should be better or at least in the range of those reported for the original C-Brace. The sensor technology that does not require an ankle sensor is already applied in the C-Leg 4. First clinical results showed high satisfaction (94% of users reported to be either satisfied or very satisfied) and 72% of users reported better or much better swing initiation compared to their previous prosthesis (Kraft 2015, Wismer 2016).

Therefore, it can be concluded that the risks associated with the use of the device are acceptable when weights against the benefits that this research can generate in terms of further development of C-Brace to the subjects and patient population in general.

Risk-benefit assessment of the clinical investigation during the COVID-19 pandemic situation

In this clinical study, patients are asked to visit the study site for 6 visits, as well as for additional visits if required by the site for the purpose of fitting of assistive devices (KAFO/SCO or C-Brace). In most likely all cases, patients will have to travel to get to the respective study site.

All patient appointments will be done in accordance with the effective national, state and local regulations on contact and /or travel restrictions due to the COVID-19 pandemic. Whenever possible, the number of appointments at the study site will be reduced and patient assessments will be managed over the phone (unless the patient needs assistance with their medical device).

Prior to arriving to the first visit since the start of the COVID-19 pandemic, a risk factors assessment shall be conducted in accordance with the procedures valid in the sites in order to decide whether the patient should attend the next visit at the site (i.e. to continue in the study for patients already enrolled or to attend an enrollment visit for patients interested in participating in the study).

During patient visits, every effort will be taken to minimize a potential infection risk by:

- limiting the number of staff to a minimum,
- providing sufficient protection material to the patients as well as to the staff (gloves, coats, face masks, hand hygiene practices, cleaning of assistive devices and surfaces, and other precautions that will be taken before and after every patient visit),
- minimizing the length of stay necessary for the patients and
- maximizing the distance between patients and staff as much as possible.

In case of increasing health risk or for any other reason, all enrolled subjects may withdraw from the study at any time.

Therefore, it can be concluded that, given that all mitigation measures described above are taken, the risks associated with a study visit during the COVID-19 pandemic are acceptable when weighed against the benefits that this research can generate for the individual and the population in general.

If the study is still running after the COVID-19 pandemic situation, some of the precautions will not be necessary anymore. In this case, potential subjects will be invited to attend an information meeting with the Principal Investigator (PI). If the subject is considered by the PI to be eligible for participation in the study, he/she will be fully informed about the study and given sufficient time to consider and given an opportunity to ask questions or to discuss participation with his/her general practitioner or therapist. Subjects who wish to enter the trial will then sign the consent form and subsequently be enrolled.

12 Management of adverse events

12.1 Description of possible adverse events & adverse device effects

Falls are expected to be reduced in general using a C-Brace, however in patients with limb impairment falls might occur.

12.2 Definitions

The investigator is responsible for recording all AEs diagnosed in the frame of study visits, reported by the participant or communicated to the investigator by a third person during the study period.

Adverse Event

An AE is (acc. to ISO 14155-2020) any untoward medical occurrence, unintended disease or injury, or untoward clinical sign (including abnormal laboratory findings) in patients, users or other persons, whether or not related to the investigational medical device

A Serious Adverse Event (SAE) is an Adverse Event that (acc. to ISO 14155-2020):

1. led to a death;
2. led to a serious deterioration in the health of the patient that
   - results in a life-threatening illness or injury;
   - results in a permanent impairment of a body structure or a body function;
   - requires hospitalization or prolongation of existing hospitalization;
   - results in medical or surgical intervention to prevent permanent impairment to body structure or a body function; or led to
3. fetal distress, fetal death or a congenital abnormality or birth defect. (Ref ISO/DIS 14155-2020)

Adverse Device Effects (ADE): adverse event related to the use of an investigational medical device. This includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device, as well as, any event resulting from use error or from intentional misuse of the investigational medical device (Ref ISO/DIS 14155-2020).

Serious Adverse Device Effect (SADE): adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event. (Ref ISO/DIS 14155-2020)

Unanticipated Serious Adverse Device Effect (USADE): serious adverse device effect, which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report (Ref ISO/DIS 14155-2020).

Device deficiency represents 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 (Ref ISO/DIS 14155-2020).

12.2.1 Additional national definitions

Germany

Notwithstanding the definitions in ISO/DIS 14155-2020, the following definitions apply according to Medizinprodukte Sicherheitsplanverordnung (MPSV) and have to be used for categorization of AEs and SAEs in Germany:

According to §2 (5) MPSV a serious adverse event is "... any unintentional event occurring in a clinical trial or performance evaluation subject to authorization which has led, could have led or could lead directly or indirectly to the death or serious deterioration of the state of health of a subject, user or other person without taking into account whether the event was caused by the medical device; the foregoing applies mutatis mutandis to serious adverse events that have occurred in a clinical trial or performance evaluation for which an exemption from the licensing requirement pursuant to § 20 (1) sentence 2 of the “Medizinproduktegesetz" has been granted.
According to §2 (1) MPSV an event is "... a malfunction, a failure, a change in features or performance or an improper labelling or instructions for use of a medical device, which has led, could have led or could lead directly or indirectly to the death or serious deterioration of the state of health of a patient, user or other person; a malfunction is also considered to be a lack of fitness for use, which causes misuse.".

Netherlands

Definitions for AE/SAE in the Netherlands follow the definitions in MEDDEV 2.7/3 rev.3 which are in line with the definitions in ISO 14155 2020. Therefore, no national definitions for AE/SAE are necessary.

United States of America

Definitions for AE/SAE in the US follow the definitions in ISO 14155. Therefore, no national definitions for AE/SAE are necessary.

Austria
Notwithstanding the definitions of ISO14155-2020, the following definition applies according to the Austrian "Medizinproduktegesetz":
Austria §2(17) MPG: Adverse Device Effect ("Nebenwirkung") is any undesirable clinical event occurring under and related to the normal conditions of use of a medical device, i.e., a device-related adverse event.

12.3 Documentation of Adverse Events / Serious Adverse Events

All AEs are to be recorded once only on the appropriate AE pages in the CRF. The investigator should complete all the details requested including dates of onset, severity, corrective therapies given, outcome and opinion as to whether the AE is likely to be device-related. Each event should be recorded separately.
In the case of a SAE, the investigator must complete, sign and date the SAE pages from the CRF, check that the data are consistent, and send a copy without any further delay to the contact specified below:

Ottobock SE & Co. KGaA, Max-Näder-Str. 15, 37115 Duderstadt
Fax: +49 5527 848-83402

Where additional follow-up information is required, this should be completed on a SAE follow-up form, a copy sent to the Sponsor and the original placed in the SAE section of the CRF.

12.4 Reporting of Adverse Events / Adverse Device Effects

During the entire patient follow-up period, any AE or ADE that occurs to a person during the study period must be followed until it resolves or is deemed permanent. Any AE or ADE, regardless of whether it is related to the study, must be documented. Any SAE (device/procedure-related or not device/procedure-related) must be reported to the sponsor on the form provided for this purpose in the case report form without any further delay from the moment of occurrence (or as soon as the investigator becomes aware of it). The initial report may be followed by relevant additional information within 7 days.

In the case of SAE and SADE, sponsor and investigator together complete the reporting forms for Ethics Committee(s) and competent authority. Both sponsor and investigator evaluate the causal rela-

tionship between the AE and investigational device and if different note this on the form. After signing the forms, either sponsor or investigator forwards it to the Ethics Committee and regulatory authority, if applicable. In case of multicenter and/or multinational studies, the sponsor has responsibility to inform other centers and relevant Ethics Committees / authorities.

12.4.1 Additional national requirements for reporting of adverse events

Germany

Notwithstanding the definitions in ISO/DIS 14155-2011, the following definitions apply according to Medizinprodukte Sicherheitsplanverordnung (MPSV) and have to be used for reporting AEs and SAEs in Germany:
After the sponsor has received a notification of an SAE that cannot be ruled out as being related to the medical device under investigation, a reference product or the therapeutic or diagnostic measures applied in the clinical trial or the other conditions for conducting the clinical trial, this must be reported to the responsible competent authority (BfArM) without further delay. The following form must be used for this purpose:

https://www.bfarm.de/SharedDocs/Formulare/DE/Medizinprodukte/Meldeformular_Klinische-Pruef_SAE.html

All other SAEs for which a connection with the medical device under investigation, a reference product or the therapeutic or diagnostic measures applied in the clinical trial or the other conditions for conducting the clinical trial can be ruled out must be reported to the competent authority (BfArM) on a quarterly basis. The following form must be used for this purpose:

http://ec.europa.eu/DocsRoom/documents/16477/attachments/2/translations

If an SAE occurs in the context of a clinical study with a CE-certified medical device in which a connection with the test product cannot be ruled out, this must be reported immediately to the competent authority (BfArM) as an "incident" in accordance with Sections §3 and §5 MPSV as soon as it becomes known. If a serious undesirable event also constitutes an incident, the sponsor may also fulfil its obligation to report the incident by submitting an SAE report in accordance with §3 (5) MPSV. In the report it must be made clear that the obligation to report an incident in accordance with §3 (1) MPSV is also fulfilled.

Netherlands

The sponsor must immediately inform the Inspectorate (within two working days and not later than four calendar days) of SAEs which indicate an inevitable risk of death, serious injuries or serious illness, and requiring prompt remedial action for patients.

This includes SAEs that result in (temporary) suspension of inclusion of patients in the clinical investigation, discontinuation of the clinical investigation (temporarily or otherwise), or modification of the medical device.

Events that were reasonably foreseeable and are described as such in the Protocol and the patient information ("calculated risks") are excluded from the above requirements, insofar as they do not lead to the (temporary) suspension or discontinuation of the clinical investigation or to modification of the medical device.

MEDDEV 2.7/3 stipulates that all other reportable events (see section 4 of MEDDEV 2.7/3) must be reported within no more than seven days. The Inspectorate applies a less intensive term in this respect. SAEs that do not fall under item 2 above may be reported quarterly in their totality to the Inspectorate by means of the reporting table, which can be found on the website of the European Commission.

Austria

The sponsor of a clinical investigation has to fully record all serious adverse events and notify them immediately to the BASG and to all other competent authorities in those member states of the EEA in which the clinical investigation is being performed.

Note:

- Where a medical condition is already established prior to the initiation of a clinical investigation and surgery has been scheduled to amend it, the definition of an adverse event according to MPG is not fulfilled and reporting to the BASG as SAE is not required. If the medical condition arises during the conduct of the clinical investigation, then SAE reporting to the BASG is required
- If a hospitalization preceded or was already planned prior to the initiation of a clinical investigation the definition of adverse event according to MPG is not fulfilled, no reporting as SAE is required. However, if unplanned hospitalization occurs during the conduct of the clinical investigation, SAE reporting to the BASG is required - whether or not causality has been established with the investigated device.

SAE and SADE that result in immediate risk of death, serious injury or illness will be reported without delay, at least within 2 calendar days to EK and BASG. All other SAEs and SADEs will be reported by sponsor within 7 days.

All incidents (Zwischenfall) will be reported by sponsor to competent authority (BASG) and ethics committee as specified in MPG §70(1) MPG.

13 Monitoring

The Clinical Project Manager will ensure proper monitoring of the study with special attention to verification of all clinical requirements, adherence to protocol, good clinical practices and compliance with applicable government and institutional regulations.

Authorized, qualified representatives of the sponsor or authorized, qualified staff of a CRO commissioned by the sponsor will visit the investigational site in regular intervals to verify the adherence to the clinical investigation plan and local legal requirements, to perform source data verification and to assist the investigator in his study related activities.

The monitor will at least document protocol deviations to informed consent procedures, SAE reporting within required timelines and investigational product handling in the Protocol Deviations Log. The Protocol Deviations Log will be consecutively completed during the ongoing trial as an appendix to the Monitoring Visit Report. Protocol deviations detected by data management should be notified to the sponsor and to the monitor. The monitor or the data management will notify the investigator of deviations in writing.

The following visits are planned: site qualification and feasibility, site initiation, routine visits and closeout visit. More details are given in the Monitoring Plan.

Monitor is responsible for reviewing the data for completeness and clarity. The details are provided in the Monitoring Plan. The investigator(s) commits to allowing audits to be performed by the sponsor and to potential inspections being performed by competent authorities. All data, documents and reports can be suspect to audits and regulatory inspections.

13.1 Direct Access to Source Data/Documents

The investigator will permit study-related monitoring, audits, EC review and regulatory inspections and provide access to primary data (i.e. source data) which supports the data on the CRFs for the study, e.g. general practice charts, hospital notes, appointment books, original laboratory records to sponsor, authorized representatives of the sponsor such as study monitors and auditors, and appropriate regulatory authorities.

Any party with access to study records shall take all reasonable precautions consistent with applicable regulatory requirements to maintain the confidentiality of patient identifying information and sponsor's confidential and/or proprietary information.

13.2 Source Documents and Source Data

Source documents are defined as printed, optical or electronic documents containing source data (e.g. hospital records, laboratory notes, device accountability records, photographic negatives, radiographs, records kept at the investigation site, at the laboratories and at the medico-technical departments involved in the clinical investigation) (ISO 14155:2020).

The eCRF is used as source data.

14 Data management

Data collection

A web-based standardized electronic case report form (eCRF) (eClinicalOS IBM 2.0) and a paper-based CRF will be used to document the patients' data during the course of the study. Both CRFs are designed to accommodate the specific features of the study design. All data obtained after the patient has given informed consent must be recorded in the CRFs. The investigator will assure that all data are entered promptly, completely, and accurately according to the CRF instructions, and conform to source documents. Data for all patients screened for study inclusion have to be documented on a respective form.

The eCRF and a paper-based CRF are used as source data.

Case Report Forms (CRFs) must be completed after every visit for each patient enrolled into the study within 4 weeks.

Only investigators and authorized designees are allowed to make entries in the CRF. This will be regulated by appropriate reading and writing access. Completed CRFs per visit, must be electronically signed by the investigator or authorized designee. Any change or addition will be recorded by an audit trail system.

All forms must be filled out completely; data are checked electronically for consistency and plausibility.

It is the investigators' obligation to assure documentation of all relevant data in the patient's file, such as medical history, concomitant diseases, date of study enrolment, visit dates, results of examinations, administrations of medication, and AEs.

Worksheets are allowed as backup, information must be entered electronically.

Self-reported patient questionnaires are filled out by patient. Investigator checks when he receives the questionnaires back, if they are completed and refer to the patient to complete missing items if applicable.

Data management procedures

All data management activities will be conducted by the sponsor or a sponsor's designee following their SOPs. The database will be built by the sponsor or a sponsor's designee.

Details on data handling will be described in the Data Management Plan. The sponsor or the sponsor's designee will handle the data cleaning process, including logical check, and query processes. Computerized validation check programs on completeness, correctness, plausibility (such as range checks, crosschecks) will verify the data according to the Data Validation Plan. All identified discrepancies will be addressed to the investigator.

The database will be hard locked after all the changes following the data review meeting have been done and the database is considered complete and accurate. All changes will be tracked (audit trail).

15 Documentation and administration

15.1 Investigator's Brochure

The investigator shall be informed by means of the Investigator's Brochure on the preclinical and clinical state of knowledge concerning the Investigational Product. In so far as important new information arises, the information for the investigators will be updated on a regular basis.

15.2 Deviations from Clinical Study Protocol

A clinical study protocol deviation is any instance of failure to follow, intentionally or unintentionally, the requirements of the clinical study protocol (ISO 14155:2020).

Ottobock is responsible for analyzing deviations, assessing their significance, and identifying any additional corrective and/or preventive actions (e.g. amend the clinical study protocol, conduct additional training, etc.). Repetitive or serious investigator compliance issues may require initiation of a corrective action plan with the investigator, and in some cases, necessitate suspending site enrollment until the problem is resolved or ultimately terminating the investigator's participation in the study.

Major clinical study protocol deviations represent non-adherence to one or more inclusion and/or exclusion criteria or are considered to affect the safety and well-being of the patient. Major clinical

study protocol deviations increase the risk, decrease the benefit and/or affect the participant's rights, safety, and/or the integrity of the resultant data. They also may result from evidence of willful or knowing misconduct on the part of the investigator, or from ignorance of established research, medical, and ethical principles.

Examples for major deviations:

- Patients enrolled prior to EC notification of approval or after expiration of approval
- Enrollment of a patient outside the inclusion/exclusion criteria
- Use of an unapproved or expired informed consent form
- Inadequate/improper informed consent procedures
- Inclusion of patients who have not provided written consent
- Failure to maintain adequate patient records or proper study documentation

It is the responsibility of the Investigator not to deviate from the protocol approved by the EC, except as necessary to avoid an immediate hazard to the participant.

Procedure:

Should a deviation from the clinical study protocol be deemed crucial for the safety and well-being of a particular patient, such a departure will be instituted for that patient only. The Investigator should document in the patient's CRF and in the patient´s medical file the reason(s) for the deviation. Each participating center must adhere to the policies and guidelines established by their EC for the frequency and format of reporting clinical study protocol deviations.

Major clinical study protocol deviations are to be reported to the study Sponsor as soon as the Investigator or study personnel become aware of their occurrence.

Clinical study protocol deviations will be documented and reported at the time of continuing review report.

15.3 Amendments to the Clinical Study Protocol

All amendments to the clinical study protocol should be agreed between the Sponsor and the Investigator and be recorded with a justification for the amendment. The Investigator or the Sponsor will not implement any deviation from, or changes of, the clinical study protocol without mutual agreement and review/approval from the EC, and other agencies as required, of a proposed amendment. The only exceptions are where necessary to eliminate an immediate safety hazard to study patients,

or when the changes involve only administrative aspects of the clinical study (e.g. change in monitor(s), change of telephone number(s)).

The party initiating an amendment must confirm it clearly in writing and it must be signed and dated by the Sponsor, the Coordinating Investigator and the Principal Investigators. Clinical study protocol amendments will be submitted to the appropriate ECs and competent authorities in line with pertinent national regulatory requirements.

15.4 Final Report

After the statistical analysis, the final report for the study is prepared and has to be signed by the study coordinating investigator, the principal investigators and the sponsor.

16 Study Discontinuation

16.1 Investigational Site Termination

Otto Bock Healthcare Products GmbH reserves the right to terminate an investigational site for any of the following reasons:

- Failure to secure Informed Consent from a patient enrolled into the study
- Repeated protocol deviations
- Repeated failure to complete Case Record Forms on a timely basis
- The investigator requests discontinuation

If the study is prematurely terminated or suspended for any reason, study participants will be informed promptly and, where required by the applicable regulatory requirement(s), the relevant regulatory authority(ies) will be informed. The ethics committees will be informed promptly and provided with a detailed written explanation for the termination or suspension.

16.2 Premature discontinuation of the complete study

If the study is prematurely terminated or suspended, the Project Manager, on behalf of Otto Bock Healthcare Products GmbH, will inform promptly the investigator/institution, and, if applicable, the regulatory authority(ies) of the termination of suspension and the reason(s) for the termination or suspension. The ethics committees will be informed promptly and provided with a detailed written explanation for the termination or suspension by the Project Manager, on behalf of Otto Bock Healthcare Products GmbH, or by the investigator/institution, as specified by the applicable regulatory requirement(s).

Some of the reasons for premature termination of the study are:

- If the safety of the participants is jeopardized (eh. many falls and stumbles reported), and
- If the users cannot show "proficient use" of the intervention devices.

Please see section 18 for publication strategy after premature discontinuation.

16.3 Requirements for patient follow up

In case of premature discontinuation of the study, the study site will contact the patients enrolled in the study. The patients will return the C-Brace orthosis to the study center. To ensure a safe use of their current orthosis (KAFO/SCO), patients will get an accommodation support and will be assessed for their orthosis use by a CPO or PT. Since this orthosis represents their orthosis before entering in the study, no additional risk for the patient is assumed.
In case of premature discontinuation of the study, available study data can be used to support a reimbursement application according to local regulations for the time after the study. If such an application is filed, the device may remain with the patient until reimbursement is granted but for a maximum of 24 months. Patients will be re-trained or re-accommodated. All procedures described in section 7.3.10 will apply.

17 Ethical considerations

17.1 Independent ethics committee

In accordance with current laws of the countries where study will be conducted, the protocol will be submitted to the Research Ethics Committee for an opinion. The study will start once approved the study and authorities, if applicable. Any necessary extension or renewal of the ethics committee approval must be obtained. Change(s) to any aspect of the trial, such as modification(s) of the protocol, the written informed consent form, the written information provided to patients, and/or other procedures must be approved, in writing, by the ethics committee.

Ethics committee will be informed promptly of any new information that may adversely affect the safety of patients or the conduct of the trial. Similarly, any written summaries of the trial status will be reported to the ethics committee annually, or more frequently, if requested by the ethics committee. Upon completion of the trial, the ethics committee with be provided with a study report.

17.2 Ethical conduct of the study

The Guidelines of the World Medical Association Declaration of Helsinki, the Guidelines of GCP, and ISO 14155-2020 as well as the demands of national drug and data protection laws and other applicable regulatory requirements will be strictly followed

The investigator(s) must fulfill all requirements as stated in ISO 14155-1 and national law. He/she is responsible for the conduct of the clinical trial and is responsible for the clinical well-being of the patients involved. The investigator(s) is not allowed to deviate from the CIP. Request for changes needs to be first discussed with the sponsor who will if required request permission from the Ethics Committee. In case, deviation was not possible to omit (i.e. to protect rights, safety, well-being of patients), they need to be documented and reported.
The sponsor must fulfill the requirements and responsibilities as stated in ISO 14155-1 and national law.

17.3 Patient information and informed consent

The investigator is responsible for ensuring that no patient is patient to any study-related examination or activity before that patient and/or legal guardian has given informed consent. Written consent must be given by the patient, after the receipt of detailed information. The verbal explanation will cover all the elements specified in the written information provided for the patient.

The investigator will inform the patient of the aims, methods, anticipated benefits and potential hazards of the study including any discomfort it may entail. The patient must be given every opportunity to clarify any points he/she does not understand and if necessary, ask for more information. At the end of the interview, the patient may be given time to reflect if this is required, or more time for discussion with family, caregivers or their own General Practitioner. Patients and/or legal guardian will be required to sign and date the informed consent form. After all parties have signed and dated the informed consent, a copy will be given to the patients while the original will be kept and archived by the investigator.

It should be emphasized that the patient is at liberty to withdraw their consent to participate at any time, without penalty, loss of benefits or normal medical care to which the patient is otherwise entitled. Patients who refuse to give or withdraw written informed consent may not be included or continue in this study.

COVID-19 Risk Factors Assessment and patient re-consent
Prior to arriving to a study site for the first visit since the start of the COVID-19 pandemic (i.e. first visit at the site for patients not yet enrolled, or follow-up visit for patients already enrolled), an informed consent form will be sent to the patient per mail or email. After having received the informed consent form, the investigator will contact individual patient via phone to conduct the informed consent process. A patient who decides to continue in the study or remains interested in enrolling in the study will be asked to provide his/her consent verbally. Following verbal consent, the investigator will perform a risk assessment with the patient via phone. During this assessment the patient will be

asked about his/her exposure to COVID-19 (i.e. potential contact with infected subjects, potential COVID-19 test) along with other general health questions (i.e. age, lung disease, kidney disease, cancer, obesity) known to be placing the patient at an increased risk in accordance with those identified by the Robert Koch Institute (RKI) (Germany), , National Institute for Public Health and the Environment (The Netherlands), Federal Ministry Republic of Austria, Social Affairs, Health, Care and Consumer Protection (Austria). If no risk factors are identified and the patient is willing to continue or to enroll in the study, an appointment will be made for an on-site study visit. In case the investigator identifies one or more risk factors during the phone contact, the decision to continue or to enroll in the study will be deferred to the site Principal Investigator. At the on-site study visits, subjects enrolling or agreeing to continue with the study will physically sign the IRB-approved informed consent form.

17.4 Patient insurance

Ottobock has taken out patient insurance with Allianz Global Corporate & Specialty SE for all patients taking part in the trial under the policy number DEL007668190, NLL001051190 and ATL001224210.

All investigators shall receive a copy of the insurance certificate and the insurance conditions; the latter must be known to the patients and made available on request.

18 Disclosure of data and publication policy

The data generated in this study as well as the results of the study, are the property of the sponsor. The aim and contents of the clinical study, in addition to its results are to be treated as confidential by all persons involved in the clinical study.

No publication, disclosure, or any other use of the results of this study are allowed without prior written permission of the sponsor. Any publication is based on the final report approved by Ottobock. The investigator will receive a copy of the final report. Thereafter the manuscript for joint publication can be drafted. A joint publication of the results should be made in mutual agreement. All editorial decisions are taken jointly by Ottobock and the investigators. Ottobock is entitled to check a draft for publication latest 60 days before submission, and to advise within 60 days any necessary reasonable supplements.

Ottobock is entitled to utilize all relevant data of the study for registration purposes, worldwide scientific product documentation and for publication.

In case of a premature determination of the study, the publication strategy will be discussed and agreed between the sponsor and the investigators. Possibilities include i.e. to decide not to publish the study results.

19 Retention of records

Essential clinical investigation documents, as defined in ISO 14155-2020, are to be retained by the investigator during the clinical investigation and for the period required by the applicable regulatory requirements or for at least 15 years after the premature termination or completion of the clinical investigation, whichever is the longer. However, the investigator should contact the sponsor prior to destruction of any records or reports pertaining to the clinical investigation in order to ensure they no longer need to be retained. In addition, the sponsor should be contacted if the investigator plans to leave the site so that arrangements can be made for transfer of records.

The medical files of study patients must be retained in accordance with local legislation and in accordance with the maximum period of time permitted by the hospital, institution or private practice.

Sponsor and principal investigator shall take measures to prevent accidental or premature destruction of these documents. The principal investigator or sponsor may transfer custody of records to another person/party and document the transfer at the investigation site or at the sponsor's facility.

20 Study timeline

First Patient first Visit planned: 1st Mar 2019.
Last Patient last Visit planned: 31 Dec 2022

Observational period per patient: 8 to 9 months depending which orthoses is used before cross-over
Given the impact of the COVID-19 pandemic, the observational period per patient may increase by additional 6 to 7 months.
Final report: 30 Jun 2023

21 Publication Plan

Please see section 18 for details regarding publication of study data.

22 References

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23 Appendix

23.1 Appendix I: Procedure for device read-outs

- Setup App

A pdf-export of the Setup App will be taken by the CPO at definitive fitting, every time a change in the settings is done and at the follow-up visits. The file shall be stored according to the following convention:

Exporting programming data from the C-Brace Setup-App

1. Launch the C-Brace Setup-App
2. Connect the mobile device and C-Brace via Bluetooth
3. Go to the menu and select “Data overview”
4. Choose the  icon to export the data
5. Use the following file name convention for the export file:

CB2-XX-ZZ-DDMMMYY

Where *XX-ZZ* is the Site ID and Patient ID and

DDMMMYY is the programming date

6. Download the data file and upload the file to the eCRF.

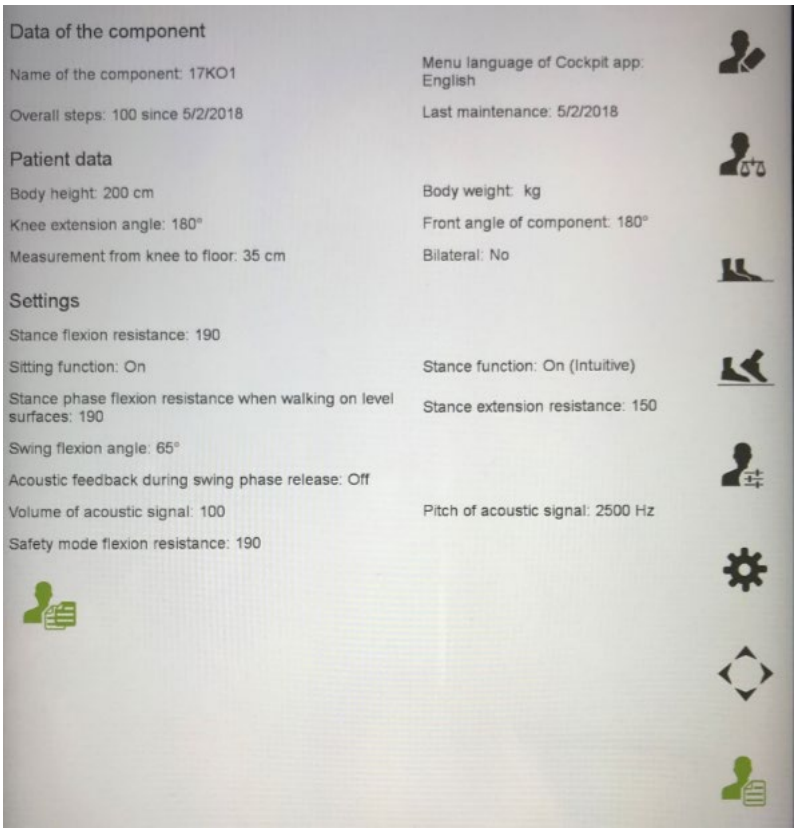

Figure 5: Screenshot of the C-Brace Setup App

- For C-Brace the following read – outs are collected from the SD-card of the joint unit at definitive fitting as well as at follow – up visits

- Steps with <1.5 km/h
- Steps between 1.5 and 2.5 km/h
- Steps between 2.5 and 3.5 km/h
- Steps between 3.5 and 4.5 km/h
- Steps between 4.5 and 5.5 km/h
- Steps faster than5.5 km/h
- Steps where the patient used stance phase flexion
- How often did the patient sit down respectively activated the sitting function?
- Time in stance/standing function
- Time in sit function
- Time in Freeze Mode
- Time in Training Mode

- Time in User-Defined Mode (MyMode)
- Time in Standby (C-Brace didn't move for >60s)
- Battery charging time
- Total Time of use (counts basically every after the fitting minus time of power-off)

- Step Count

A step count transponder will be fixed on C-Brace and on KAFO/SCO. It will be read out after each observational period.

23.2 Appendix II: Study Overview (German)

Sponsor	Otto Bock Healthcare Products GmbH
Studientitel kurz	Klinische Studie zum Vergleich C-Brace vs. KAFO/SCO
Studienziel	Evaluierung der Effektivität und des Patientennutzens bei Patienten mit Beeinträchtigung der unteren Extremität hinsichtlich der Aktivitäten des täglichen Lebens im Vergleich zwischen C-Brace, einer Mikroprozessorgesteuerten Stand- und Schwungphasen-kontrollierten Orthese und der Alltagsversorgung, einer KAFO/SCO
Design	Prospektive, internationale, multizentrische, offene, kontrollierte, randomisierte cross-over Studie
Prüfprodukte	C-Brace, KAFOs, SCOs
Primärer Wirksamkeits-endpunkt	Verbesserung der statischen und dynamischen Balance bei der Verwendung von C-Brace im Vergleich zu KAFO/SCO
Sekundäre Endpunkte	1. Evaluation des C-Brace Effekts auf das Gangbild, die Balance, das Gehen auf ebenem Untergrund, das Gehen während erschwerender Aufgaben, sowie während Aufmerksamkeitsaufgaben im Vergleich zu KAFO/SCO. 2. Bestimmung und Vergleich der sicheren Anwendung von C-Brace hinsichtlich der Parameter: Sturzhäufigkeit, Schwere der Stürze, Sturzassoziierte Verletzungen, Angst vor Stürzen und damit verbundener Behandlungsaufwand im Vergleich zu KAFO/SCO. 3. Bestimmung der Sicherheit der Patienten bei der Durchführung verschiedener ambulanter Aktivitäten unter der Verwendung von C-Brace im Vergleich zu KAFO/SCO. 4. Bestimmung der Lebensqualität und der Reintegration in normale Lebensumstände unter der Verwendung von C-Brace im Vergleich zu KAFO/SCO.

	5. Bestimmung des Umfangs der Behinderung und deren Einfluss auf die Produktivität. 6. Bestimmung der Patientenzufriedenheit und der Verwendungsgewohnheit von C-Brace im Vergleich zu KAFO/SCO. 7. Verringerte Sturzwahrscheinlichkeit bei der Verwendung von C-Brace im Vergleich zu KAFO /SCO
Klinische Nachverfolgung	Screening, Baseline 1 und 2, Visite 1 nach 3 Monaten Nutzungsdauer des ersten Prüfprodukts zu Hause, Visite 2 nach 3 Monaten Nutzungsdauer des zweiten Prüfprodukts zu Hause
Anzahl der Patienten	56
Einschlusskriterien	• Patient wurde mit der Diagnostischen Testorthese (DTO) getestet und zeigte erfolgreich das Potential, C-Brace nutzen zu können • Patient hat einen BBS Wert < 45 • Beeinträchtigung der unteren Extremität laut Indikation in der Gebrauchsanweisung • Vorangegangene aktive und verlässliche Nutzung einer unilateralen oder bilateralen Versorgung mit einer KAFO oder SCO in den letzten 3 Monaten vor Einschluss • Patient erfüllt die körperlichen Minimalvoraussetzungen für die C-Brace Versorgung, wie Muskelstatus, Gelenkmobilität, Beinachse und Kontrolle der Orthese • Der Nutzer erfüllt die körperlichen und geistigen Voraussetzungen, um optische, akustische Signale, sowie mechanische Vibrationen wahrzunehmen • Die bestehende Muskelkraft der Hüftflexoren und –extensoren muss die Auslösung der Schwungphase ermöglichen (Kompensation durch Verwendung der Hüfte ist erlaubt) • Patient erklärt sich bereit, C-Brace für mindestens 1-2

	Stunden pro Tag 5 Tage die Woche zu verwenden • Patient ist ≥18 Jahre alt • Patient ist fähig und willens, unabhängig sein Einverständnis zu geben • Person ist einverstanden, den Prozeduren innerhalb der klinischen Studie Folge zu leisten
Ausschlusskriterien	• Patient ist nicht in der Lage, alle Studienbesuche zu absolvieren oder ist unwillig/nicht in der Lage, den Anweisungen zu folgen • Patient war nicht in der Lage die DTO zu nutzen • Patient nutzt seine Orthese nicht für mindestens 1-2 Stunden pro Tag an 5 Tagen pro Woche • Patient mit einem Körpergewicht > 125 kg (eingeschlossen Körpergewicht + schwerstes getragenes Objekt) • Patient mit Orthoprothese • Patient mit Flexionskontraktur im Knie- oder Hüftgelenk > 10° • Patient mit unkontrollierter moderater bis schwerer Spastizität (moderate Spastizität ist relative Kontraindikation) • Beinlängendifferenz > 15cm • Patient mit instabiler neurologischer, kardiovaskulärer oder pulmonaler Erkrankung oder Krebserkrankung • Schwangerschaft • Patient nutzt bereits C-Brace • Patient mit bekanntem Schwindel (Vertigo) oder Sturzhistorie, welche nicht in Bezug zur Orthesennutzung oder motorischer Behinderung steht • Patient ist nicht mit einer Orthese versorgt • Patient ist unfähig, selbständig an ihn ausgehändigte

	Fragebögen zu beantworten; Patienten mit einer Beeinträchtigung der oberen Extremität dürfen verbal antworten • Patient nimmt während der geplanten Dauer der Studie an bereits einer weiteren klinischen Studie teil • Patient hat bereits an einer früheren C-Brace Studie teilgenommen
Geplanter Zeitverlauf	Geplante Studiendauer: First Patient In: 1 Mrz 2019 Last Patient In: 30 Dec 2021 Last Patient Out: 31 Mrz 2023
Prüfleiter	Zentrum 1: Prof. Frank Braatz Zentrum 2: Dr. Axel Ruetz Zentrum 3: Dr. Bea Hemmen Zentrum 4: PD Dr. Rüdiger Rupp Zentrum 5: Jason Wenig, CPO, FAAOP Zentrum 6: Tom DiBello, LO, CO, FAAOP Zentrum 7: Chris Toelle, LCO, ACM Zentrum 8: Eric Weber, LCPO, FAAOP Zentrum 9: Dr. Alexander Krebs Informationen zu zusätzlichen Prüfleitern in Addendum_CIPV5_SiteList_201217.
Studienzentren	Zentrum 1: Göttingen (D) Zentrum 2: Koblenz (D) Zentrum 3: Hoensbroek (NL) Zentrum 4: Heidelberg (D)

	Zentrum 5: Chicago, IL (USA) Zentrum 6: Houston, TX (USA) Zentrum 7: Sarasota, FL (USA) Zentrum 8: Seattle, WA (USA) Zentrum 9: Wien (AT) Informationen zu zusätzlichen Studienzentren in Addendum_CIPV5_SiteList_201217.
Klinischer Projektmanager	Dr. Marten Jakob

23.3 Appendix III: Example of the phone call protocol

PHONE CALL 1 (1 Month)

THIS PHONE CALL HAS TO BE DONE IN THE **END OF MONTH 1** AFTER ASSESSMENT OF READINESS!

- Please remind the patient about the **minimum time of use** (1-2 hours, 5 days per week) of the current orthosis.
- Ask the patient some questions about **adverse events (AE) and device deficiencies (DD)**.
- Remind the patient to call the investigator immediately in the case of malfunctions, falls or other limiting events.
- Remind the patient to **document any falls and near falls as well as unexpected behavior of the current orthosis in the patient diary** and to bring the diary at each visit.
- If you need more space for your documentation please use page 8-9.

Please specify the use of the current orthosis in day(s)/week and the hour(s)/day:

Which orthosis (es) have you been using? (Check all that apply)	|__| C-Brace	|__| KAFO
Time using the orthosis (es):	|__| day(s)/ week	|__| day(s)/ week
	|__|__| hour(s)/ day	|__|__| hour(s)/ day
Please specify, if the patient uses the current orthosis ≤ 1 hour/day or < 5 days a week: _____ _____ _____		

Did you have any health impairments in the past	|__| YES	|__| NO	If YES, number of events:	|__|__|__|

month? Ask for adverse events (untoward medical occurrence, unintended disease or injury, or untoward clinical sign whether or not related to the device)	If YES, please specify: Please complete an Adverse Event CRF for each reported AE.			
Did your current orthosis have any malfunctions or other problems in the <u>past month</u>? Ask for device deficiencies	|__| YES	|__| NO	If YES, number of events:	|__|__|__|
	If YES, please specify: Please complete an Adverse Event CRF for each reported DD.			

Have you felt unstable in the <u>past month</u>?	|__| Yes |__| No	
Did your orthosis prevent any falls in the <u>past month</u>?	|__| Yes |__| No	If YES: Number of events: |__|__|
Did you have any falls in the <u>past month</u>?	|__| Yes |__| No	If YES: Number of events: |__|__|

Did any falls require medical attention in the <u>past month</u>?	|__| Yes |__| No	If YES: Number of events: |__|__|
Did any falls cause permanent injury in the <u>past month</u>?	|__| Yes |__| No	If YES: Number of events: |__|__|
Did any falls result in missed work in the <u>past month</u>?	|__| Yes |__| No	If YES: Number of events: |__|__|

Date of signature	Name	Signature
|__|__||__|__||2|0|__|__| D D M M Y Y Y Y		