Postoperative Edema Management of Foot and Ankle Patients with Neuromuscular Electro-stimulation of the Peroneal Nerve using geko™

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Indication: Post-operative Edema

SPONSOR



Firstkind Ltd.
Hawk House, Peregrine Business Park, Gomm Road
High Wycombe, Buckinghamshire, HP13 7DL, UK

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Firstkind Ltd

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Version Control

Protocol Version No.	Date	Details of change made
1.0	25SEP2020	New Document
1.1	23OCT2020	Incorporating feedback from Tony Humphrey specifically on population criteria and endpoints
1.2	09DEC2020	Amendment to schematic and schedule of events Addition of bioimpedance of lower limb as edema measurement Addition of Appendices Incorporation of reviewer comments
1.3	21JAN21	Incorporation of reviewer comments
1.4	01JULY21	Addition of sections 4.3.1 and 4.3.2 Section 4.4 amended Table 1 correction of typographical errors List of Abbreviations updated Addition of section 7.9 Section 7.11 amended Section 9 amended Table of Contents updated
2.0	21DEC2021	Updated CPM-US contact details Addition of “Achilles tendon repair” to section 3.1 and Appendix 5 – Additional fitting instructions for patient. Creation of Appendix 6 geko fitting instructions (for investigator) Revised “ankle arthroscopy” to “ankle ligament reconstruction (open or arthroscopic)” in section 3.1
3.0	11APR2022	Removal of the following paragraph, which was carried over from a previous version of the protocol and is not applicable to the current version of the protocol. Note: The T device will run for 30 hours unless switched off, therefore, each device will deliver 24 hours continuous use and must be switched off after the 24 hours treatment period has ended. For 12 hours daily geko™ therapy, each device will deliver two doses of 12 hour continuous use and must be switched off after each 12 hour treatment period has ended. The device should be stored on the re-usable backing strip between doses and then disposed of following use of the second dose. Appendix 4 updated to reflect current version of US Instructions for Use
4.0	11MAY2022	Updated CPM-US contact details

5.0	18JAN2023	Section 3.1 – updated language to broaden inclusion of all foot and / or ankle surgeries. Section 7.8.3 – updated language referencing the value on the analyser machine to “resistance” instead of “bioimpedance”. Section 7.11 – clarify that a 12 hour break in dosing should follow the initial 24 hour dose. Removed Appendices 5 and 6 as updated versions were approved after v4.0 of the protocol was approved. Updated Chief Investigator on Protocol Approval Signatures page.

Sponsor Contacts

Firstkind Ltd

Hawk House, Peregrine Business Park

Gomm Road

High Wycombe

Buckinghamshire

HP13 7DL

UK

Clinical Project Manager – United States

Julie Cramer

e-mail: julie@clinicalresearchstrategies.com

Tel: (330) 507-0801

Clinical Project Manager – United Kingdom

Marie-Therese Targett

e-mail: marie-therese.targett@firstkindmedical.com

Tel: +44 (0) 7340 903 377

Clinical Research Associate - United Kingdom

Anne-Marie Piftor

e-mail: anne-marie.piftor@firstkindmedical.com

Tel: +44 (0) 1494 572 056

PROTOCOL APPROVAL SIGNATURES

We, the undersigned, have reviewed this protocol and agree that it contains all relevant information required to meet Good Clinical Practice (GCP) and all applicable regulatory guidelines and statutes.

Dr Kieron Day	Date

Head of Clinical Affairs
Firstkind Ltd
Hawk House, Peregrine Business Park
Gomm Road, High Wycombe,
Buckinghamshire, HP13 7DL, UK

Mr Shelain Patel FRCS	Date

Chief Investigator
Royal National Orthopaedic Hospital
Brockley HillStanmore
HA7 4LP

INVESTIGATOR SIGNATURE PAGE

I have read the protocol specified above and agree to participate in and comply with the procedures, as outlined herein for the conduct of this clinical study. I also agree to comply with the Independent Ethics Committee (IEC) / Investigational Review Board (IRB) requirements for testing on human patients. I agree to ensure that the requirements for obtaining informed consent are met.

Investigator's Signature	Date

Print Name

Abbreviations

ADE	Adverse Device Effect
ADL	Activities of Daily Living
AE	Adverse Event
ANOVA	Analysis of Variance
ASADE	Anticipated Serious Adverse Device Effect
BMI	Body Mass Index
CRF	Case Report Form
CRA	Clinical Research Associate
CRO	Clinical Research Organization
CV	Curriculum Vitae
DD	Device Deficiency
DVT	Deep Vein Thrombosis
eCRF	Electronic Case Report Form
EC	Ethics Committee
EDC	Electronic Data Capture
EOT	End of Treatment
F&A	Foot and Ankle
ICF	Informed Consent form
IEC	Independent Ethics Committee
ITT	Intent-to-Treat
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GP	General Practitioner
ICH	International Conference on Harmonization
ICMJE	International Committee of Medical Journal Editors
IPC	Intermittent Pneumatic Compression
IRB	Investigational Review Board
MOxFQ	Manchester-Oxford Foot Questionnaire (Foot & Ankle)
NA	Non-adherent
QoL	Quality of Life
PET	Polyethylene Terephthalate
PI	Principal Investigator
PP	Per Protocol
PROM	Patient Reported Outcome Measure
RV	Run-in Visit
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SC	Standard Care
SOP	Standard Operating Procedure

USADE	Unanticipated Serious Adverse Device Effect
VAS	Visual Analogue Scale
VTE	Venous Thromboembolism

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1. Introduction

1.1 Rationale

The geko™ device has a wide range of clinical applications including the post-operative management of edema.

Although many short-term acute studies have been completed using the device, little clinical data has been collected on the effect of geko™ use in current standard care pathways for edema management on patient outcomes during long term follow-up after surgery.

The multicentre randomized geko™ Foot and Ankle Trial will prospectively and systematically collect clinical data on patients randomized, on a 1:1 basis, to either standard care or standard care plus geko™ therapy to assess edema management and patient outcomes during a follow-up period of up to three months post-surgery.

1.2 geko™ Neuromuscular Stimulator

The innovative geko™ device, manufactured by Firstkind Ltd (High Wycombe, United Kingdom), is a small, self-adhesive, disposable, battery powered, neuromuscular electrostimulation device designed to increase blood circulation and is indicated for the prevention and treatment of edema, and the prevention of venous thromboembolism (VTE).

The device is made from mylar (polyethylene terephthalate (PET)) and the electronic circuit is enclosed in a fully insulated polypropylene protective casing, so there is no risk of shock to the patient. The geko™ device also has charge-balanced waveforms that yield no build-up of charge in the patient, therefore, provided the device is used in accordance with the instructions for use, galvanic effects such as electrical burns cannot occur. The device is powered by battery and is thus totally isolated from the mains electricity supply. The primary lithium coin cell battery powering the device is removable for disposal. See Figure 1 for an illustration of the device (front view)

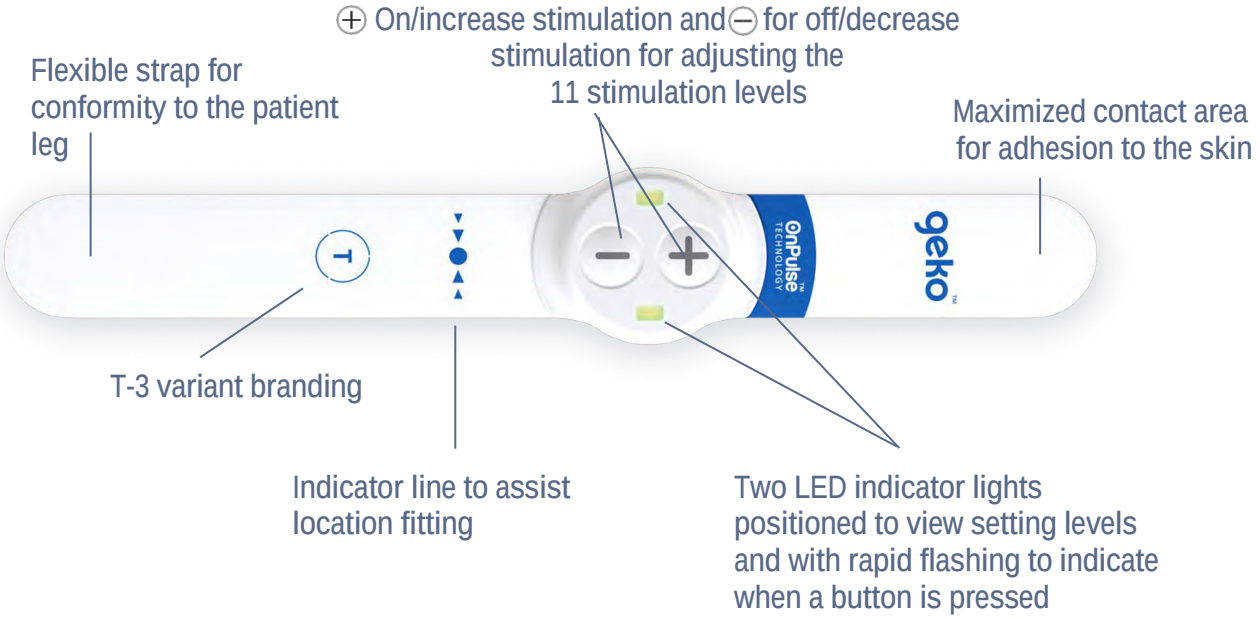


Figure 1: The geko™ T-3 device variant (front view)

The geko™ device utilizes an electronically conductive skin adhesive solid hydrogel layer that adheres to the skin and when applied externally to the leg on the lateral/posterior aspect of the knee, the device will stimulate the common peroneal nerve prior to its deep-superficial branch bifurcation. Figure 2 shows an illustration of the device (rear view) with electrodes.

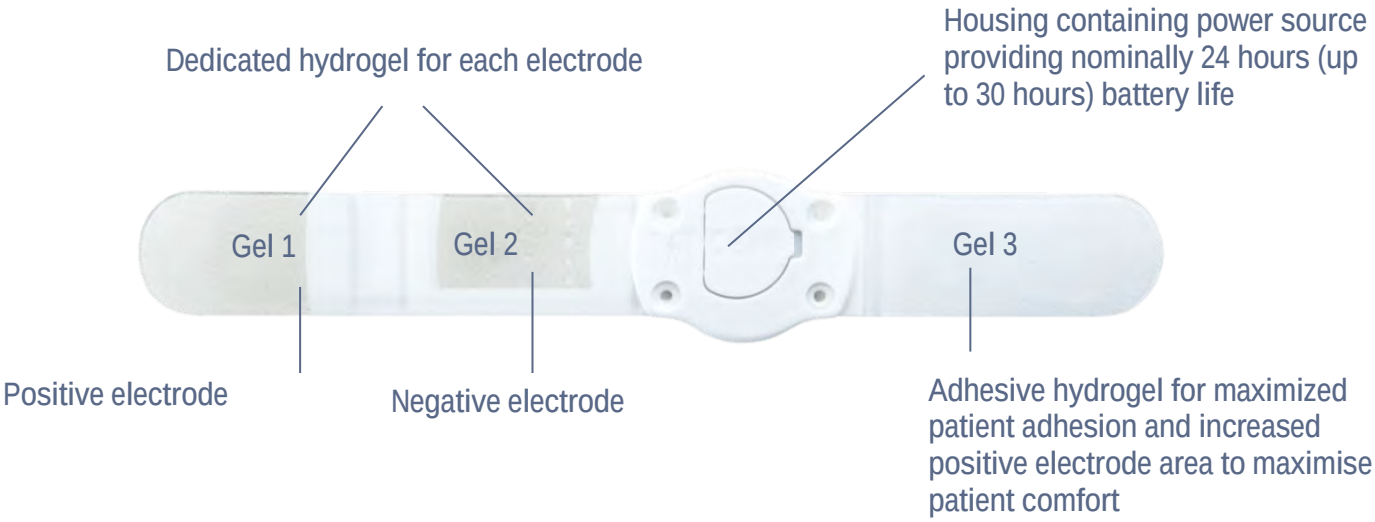


Figure 2: The geko™ T-3 device variant (rear view) with adhesive hydrogel layers and electrodes.

Subsequently, two separate and opposing complexes of muscles in the anterior and lateral muscle compartments of the lower limb will be stimulated by the device, eliciting a near-

isometric contraction of the lower leg muscles and activating the venous muscle pumps of the leg and foot, so increasing blood flow in the lower limb, which will boost venous return and increase blood circulation. Neither normal movement of the limb nor patient mobility are affected by the device. Stimulation of the nerve requires less current and is considerably more comfortable than directly stimulating the muscle as in other forms of mechanical stimulation such as intermittent pneumatic compression (IPC), and achieves the same degree of muscle contraction, while utilizing considerably less electrical power. Please see Figure 3 for an illustration of the device fitted to the lower leg.



Figure 3: Administering non-invasive neuromuscular electrical stimulation via the geko™ device applied at the peroneal nerve.

The geko™ device has up to eleven stimulation levels to balance maximal effect of stimulation with patient comfort. The optimal stimulation level, which may vary between patients, is achieved when a stimulus results in a visible dorsi-flexion of the foot.

1.3 Summary of Clinical Studies

The geko™ device has been tested clinically to evaluate its safety and efficacy in human use. These studies did not give rise to any safety concerns for the geko™ device.

As previously described the geko™ device is indicated for the prevention and reduction of edema formation.

Clinically, edema is described as an abnormal build-up of interstitial fluid in the body that is enough to produce palpable swelling[1] and it remains an issue for patients post-surgery as it represent one of the main clinical reasons for delayed discharge and or rehabilitation.

The formation of edema post-operatively is widely accepted to lead to pain and to exacerbate loss of muscle function. Increased rates of wound dehiscence and infection are also associated with post-operative edema which can impede oxygen delivery to the wound site and inhibit healing[2], negatively impacting patient length of stay, surgical outcomes and healthcare costs[3].

Edema formation can be the result of direct surgical trauma, however, decreased mobility immediately post-operatively can lead to a reduction in venous return, preventing the movement of fluid from tissues back into blood vessels[2]. This creates an imbalance between capillary filtration and lymph drainage, leading to edema formation. By activating the venous muscle pumps of the leg and foot, the geko™ device increases blood flow boosting venous return, resulting in increased blood circulation[4]. The pressure difference between the capillaries and the surrounding tissue will decrease, thus transferring tissue fluid back into the veins and lymph vessels[5]. This can prevent edema build-up, but equally enable edema clearance by local reabsorption of excess interstitial fluid into the vasculature and lymphatic systems[6].

To date, little clinical data has been collected on the effect of geko™ use in current standard care pathways for edema management on patient outcomes following surgery. However, several clinical studies have been carried out supporting the effectiveness of the geko™ device to reduce edema in patients including both pre and post-operative patients.

The results from a randomized controlled trial, comparing the effect of the geko™ device and TED stockings on post-operative edema in total hip replacement patients, reported the geko™ device to be significantly more effective than TED stockings at preventing the build-up of post-operative edema[6]. Furthermore, the results of this study suggest that the geko™ device was safe and well tolerated by patients. The positive patient tolerability data for the geko™ device is especially interesting given that patient compliance with compression stockings has been previously reported to be low owing to issues of discomfort, difficulty applying and appearance. In addition, the use of compression stockings is contra-indicated in patients cardiac failure, peripheral vascular insufficiency, and venous ulceration, which can limit their applicability, particularly in elderly populations who frequently have hip replacements procedures.

In a later pilot study, carried out in patients following referral to physiotherapy after a grade I or II ankle sprain, NMES delivered by the geko™ device in addition to standard care was found to reduce edema and was statistically significant when compared with standard care alone, as measured by volumetric displacement[7].

Additionally, data from a more recent study by Mahmood *et al* illustrates the effectiveness of the geko™ device in the management of pre-operative edema in ankle trauma patients. This was a prospective evaluation of 20 patients admitted for ankle fracture fixation with the application of the geko™ device to the skin just below the knee (intervention arm). Participants were matched for baseline demographics and injury descriptors to a historical operative cohort (control arm). The time until the swelling had settled to a level permitting surgery ("readiness for surgery") was recorded alongside patient tolerability and device acceptance. The mean time until swelling reduced to a level permitting surgery was 1.66 days (geko™) versus 3.66 days (control) (P=0.001). Overall, 60% of participants were ready for theatre after 2 days of treatment with the geko™ device compared with 27% in the control group (P<0.01).

These data suggest that the geko™ device is effective in reducing ankle edema and accelerating readiness for theatre and may therefore allow earlier surgery and reduced length of hospital stay in this patient group[8].

2 Study Objective

The objective of this study is to determine the clinical safety and performance (i.e. residual risks) of the geko™ device when used in conjunction with its approved labelling for edema reduction.

2.1 Endpoints

2.1.1 Primary Endpoint

Primary endpoint as follows:

- The primary objective of the study is to assess the effect of geko™ therapy on edema formation following foot and / or ankle surgery.

2.1.2 Secondary Endpoints

Assessment of the effect of geko™ therapy following foot and / or ankle surgery on the following secondary outcomes:

- Incidence of Adverse Events (AEs)
- Incidence of Device Deficiency (DD)
- Pain level via a visual analogue scale (VAS) score (see Appendix 1)
- Surgical wound healing status
- Analgesia intake
- Dosage of analgesia intake
- Patient reported outcomes via Manchester-Oxford Foot & Ankle Questionnaire (MOxFQ; see Appendix 2)
- Assessment of patient diary (patient reported daily geko™ usage and feedback / satisfaction with the geko™ device, see Appendix 3)

3 Study Design and Patient Pathway

This study is an open label, multi-center prospective randomized study. A schematic of the study design and patient pathway is presented in Figure 2. The study will be a multinational, multicenter study with study centers in the United Kingdom, the United States and the European Union. The study patient population will be randomized on a 1:1 basis into two groups. These groups are defined as Group A patients who receive geko™ therapy and SC i.e. the intervention group and Group B patients who receive Standard Care (SC) only i.e. no intervention. The two groups will be compared using an appropriate statistical measure.

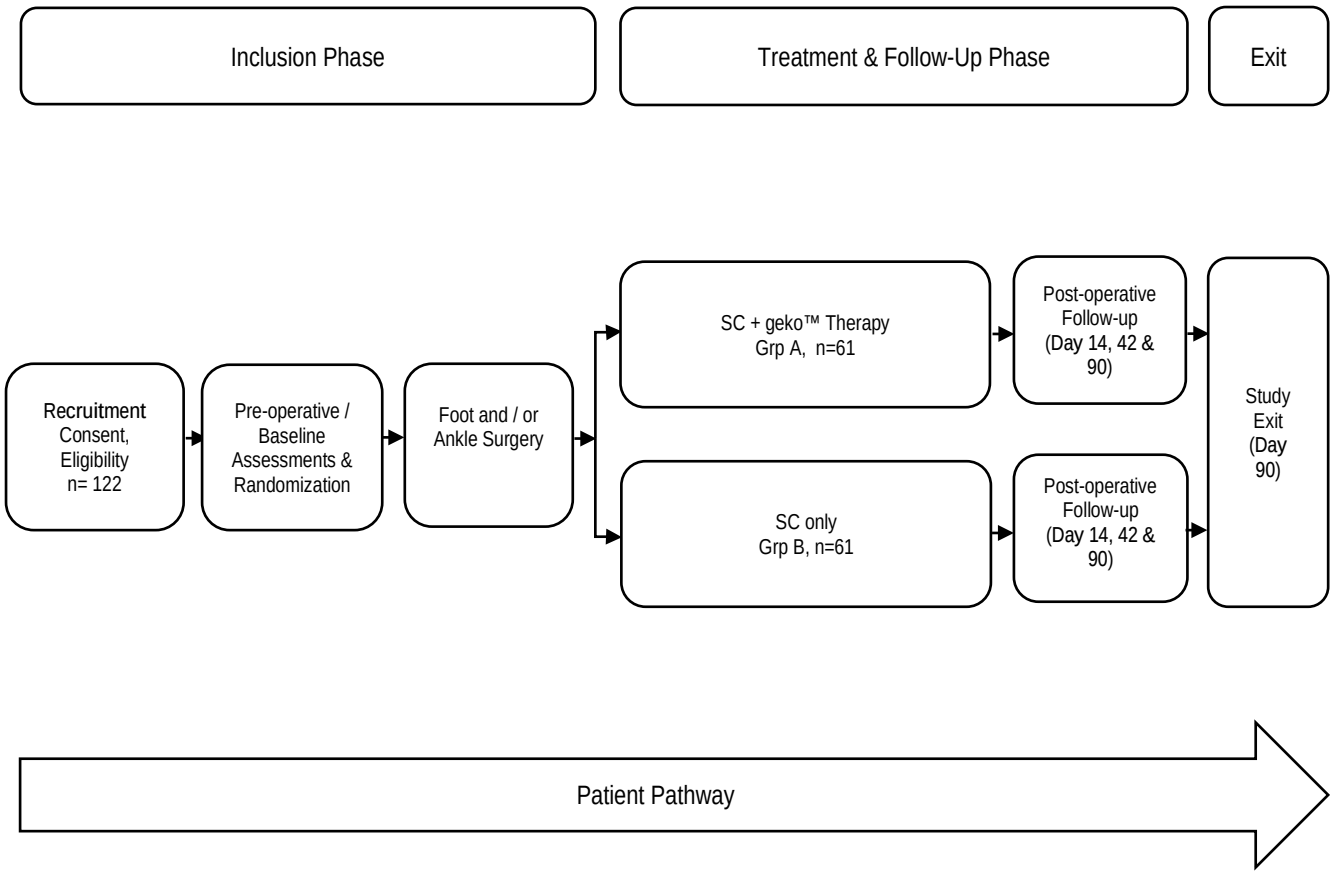


Figure 2: Schematic of Study Design and Patient Pathway.

3.1 Study Population

Participants who have been identified to receive foot and / or ankle surgery. Possible surgeries include, but are not limited to: -

- Forefoot surgery
  - Hallux valgus correction
  - 1st MTPJ Cheilectomy
  - 1st MTPJ fusion
  - Lesser Toe surgery

- Morton's neuroma

- Mid/hindfoot surgery: -
  - Ankle fusion
  - Ankle replacement
  - Ankle ligament reconstruction (open or arthroscopic)
  - Mid/Hindfoot fusion

- Achilles tendon repair

3.1.1 Number of Participants

Based on the mean and standard deviation difference between study arms in previous studies, 61 patients will be needed in each group, therefore a total of 122 patients will be randomized in the study.

3.1.2 Inclusion Criteria

The inclusion criteria of the study are:

- Aged ≥ 18 years
- Intact healthy skin at the site of geko™ device application.
- Patients that have been listed for foot and / or ankle surgery
- Patient understands and is willing to participate in the study and can comply with study procedures
- Patient is willing and able to give written informed consent

3.1.3 Exclusion Criteria

The exclusion criteria of the study are:

- Pregnant
- Use of any other neuro-modulation device.
- Trauma to the lower limbs that would prevent geko™ from stimulating the common peroneal nerve.
- No response to geko™ therapy i.e. no involuntary rhythmic upward and outward movement of the foot (dorsiflexion) at the maximum tolerable device setting
- Participation in any other clinical study that may interfere with the outcome of either study

4 Study Schedule

Data will be entered into the Case Report Forms (CRFs) using a specific Foot and Ankle Study Electronic Data Capture (EDC) system. Participant data will be collected at recruitment, the pre-surgery assessment (baseline, immediately post-surgery and at patient follow-up visits which will take place at two weeks (day 14 ± 2 days), 6 weeks (day 42 ± 6 days) and 3 months (day 90 ± 2 days) post-surgery.

Procedures / assessments should take place in the following order:

4.1 Recruitment

- Obtain written informed consent
- Assessment of response to geko™ therapy
- Confirm patient eligibility as per inclusion / exclusion criteria (sections 3.1.2 & 3.1.3)

4.2 Pre-surgery Assessments (Baseline)

- Record demographic data
- Record relevant medical history
- Record BMI (derived from height & weight measurements)
- Date of surgery
- Record type of surgical procedure e.g. Hallux valgus correction, ankle fusion
- Record surgical laterality
- Record medication including type & dose of analgesia
- Pain status (VAS score)
- MOxFQ Assessment
- Leg Edema Assessment (both legs)
    - Pitting Edema
    - Figure-of-Eight Edema Measure
    - Bioimpedance Method
- geko™ device training & instructions by member of healthcare team (geko™ arm only)
- Assess for any AEs
- Randomization

4.3 Post-operative Procedures and Assessments

4.3.1 Assessments and Procedures Immediately after Surgery

- Application of geko™ therapy (geko™ arm only; see section 4.4)
- Dispense geko™ devices and patient diary (geko™ arm only)
- Record changes in medication including analgesia
- Assess for any AEs
- Assess for DDs (geko™ arm only)

4.3.2 Follow-up Assessments and Procedures (day 14 ± 2 days, day 42 ± 6 days and day 90 post-surgery)

- Record changes in medication including analgesia
- Pain status (VAS score)
- Record current status of surgical wound
    - Wound healing status

- Wound surface if not healed
- Wound exudate
- Type of exudate
- Wound odor
- Wound infection

- MOxFQ Assessment
- Leg Edema Assessment (to be performed on both legs)
  - Pitting Edema
  - Figure-of-Eight Edema Measure
  - Bioimpedance Method
- Collect and sign completed patient diary (geko™ arm only: first follow-up visit only
- Assess for any AEs
- Assess for DDs (geko™ arm only; first follow-up visit only)

4.4 Application of geko™ Therapy

Patients assigned to the geko™ arm will receive geko™ therapy as follows:

- geko™ therapy will be applied immediately post-surgery on the operated leg and administered for 24 hours..
- geko™ therapy will then be administered for 12hrs / day until the patient returns for their first post-operative follow-up visit (Day 14 ± 2 days post-surgery)

The rationale is to mitigate post-operative edema build-up during the first 24 hours after surgery. geko™ therapy should be delivered to the patient at a setting which gives full dorsiflexion, thus maximizing activation of the venous muscle pumps of the calf and foot and increasing blood circulation in the veins, arteries and microcirculation of the operated leg and around the surgical site.

Prior to discharge, patients will be provided with enough devices for daily treatment (12 hrs/day) to last until day 14 post-surgery or their first post-surgery follow-up visit (whichever occurs first).

Patients will also be provided with a patient diary, to record their daily geko™ usage and feedback / satisfaction with the geko™ device.

Once the final follow-up has been completed, the patient's participation will end, and the patient will be exited from the study. A schedule of events can be found in Table 1.

Procedure / Assessment	Recruit-ment	Pre-surgery Assess-ments (Baseline)	Post-surgery geko™ Therapy	Post-surgery Follow-up 1 (Day 14)	Post-surgery Follow-up 2 (Day 42)	Post-surgery Follow-up 3 & Exit (Day 90)
Informed Consent Confirmation of Eligibility	X					
Assessment of response to geko™ therapy	X					
Confirmation of Eligibility	X					
Demographics (date of birth, age, gender)		X				
Medical History		X				
BMI derived from height & weight measurements		X				
Surgical Procedure		X				
Surgical Laterality		X				
Medication		X	X	X	X	X
Pain status (VAS score)		X		X	X	X
MOxFQ		X		X	X	X
Pitting Edema (both legs)		X		X	X	X
Edema Figure-of-Eight (both legs)		X		X	X	X
Edema Bioimpedance (both legs)		X		X	X	X
Randomization		X				
geko™ Device Training & Instructions		X				
Dispense geko™ devices and patient diary (geko™ arm only)			X			
Application of geko™						

Procedure / Assessment	Recruit-ment	Pre-surgery Assess-ments (Baseline)	Post-surgery geko™ Therapy	Post-surgery Follow-up 1 (Day 14)	Post-surgery Follow-up 2 (Day 42)	Post-surgery Follow-up 3 & Exit (Day 90)
Therapy (geko™ arm only; see section 4.4)			X			
Collect and sign participant diary (geko™ group only)				X		
Surgical Wound Status				X	X	X
Assess for AEs		X	X	X	X	X
Assess for DDs			X	X		

Table 1: Schedule of Events

4.5 Unscheduled Visits

Unscheduled visits may be required in addition to the visits detailed above.
The details of these unscheduled visits will be recorded in the patient's medical records / source documents and on the appropriate eCRF in EDC.

4.6 Missed Visits

If a patient misses a visit, the site is to make every effort to have the patient return as soon as possible to make up the visit. Once the patient is seen, he / she is to return to his / her original visit schedule.

5 Participant Completion and Withdrawal

5.1 Participant Completion

Participants will have completed the study once all protocol related activities have been completed.

5.2 Premature Withdrawal / Discontinuation from the Study

Participants will be advised that they are free to withdraw from the study at any time for any reason or, if necessary, the Investigator may withdraw a subject from the study to protect the subject's health. The Investigator may withdraw a subject from the study if it is considered that the scientific, and therefore, ethical standards of the study are compromised. Participants may also be withdrawn for not complying with study procedures. The reasons for withdrawal will be fully recorded in the study specific EDC.

Before a patient is identified as lost-to-follow up, the site should make all reasonable efforts to contact the patient. These attempts must be documented and should include at a minimum one phone call and one letter/email.

5.3 Screen Failures

A patient who has signed a consent form, has been assigned a patient number, but is not randomized is classified as a screen failure. The patient will be exited from the study and the reason for screen failure will be recorded in EDC on the appropriate eCRF. An example of a screen failure would be a patient who does not respond to geko™ therapy i.e. shows no involuntary rhythmic upward and outward movement of the foot (dorsiflexion) at the maximum tolerable device setting at any of the three device fitting locations.

6 Study Treatments

6.1 Method for Assigning Eligible Patients to Treatment

Eligible patients will be assigned to one of the following two treatment groups, based on the randomization schedule:

- Group A: Intervention Group: SC plus daily treatment with the geko™ T-3 device or variant
- Group B: No Intervention Group: SC only

6.2 Description of the Investigational Device

The geko™ device is CE marked (GB12/87339; SGS, United Kingdom Ltd) and has regulatory approval for use in a human patient population for multiple indications in numerous countries. The geko™ device is made from mylar (polyethylene terephthalate (PET)), it is enclosed in a polypropylene casing and a hydrogel layer will adhere the device to the skin. In this study the geko™ T-3 device or variant will be used please refer to Appendices 4 & 5 for Instructions for Use and Fitting Instructions).

6.3 Participant Investigational Device Use

Each geko™ device will be used to deliver two 12 hr doses to be used on separate days. Patients randomized to the geko™ arm will be provided with enough geko™ devices to last until their first post-surgery follow-up visit (approximately 14 days post-surgery) and will be trained in the use of the geko™ device by a member of their healthcare team. Instructions for Use will also be provided (refer to Section 7.9 geko™ Device Training & Instructions)

Patients randomized to the geko™ will also be provided with a patient diary on which their geko™ usage and feedback / satisfaction with the geko™ device will be recorded. Patients should bring the diary with them to the first follow-up visit at which the diaries will be verified and signed by a member of the healthcare team.

6.4 Labelling

The study supplies will be labelled in accordance with all applicable regulatory requirements.

6.5 Device Storage, Handling and Application

The investigational devices will be supplied in single use labelled packages. The whole device with the battery in place can be disposed of in domestic waste. Details on application of the geko™ device and Instructions for Use are available in Appendices 4 & 5.

6.6 Product Accountability

The Investigator or designee will verify the contents of each shipment against the shipping documents. Verification of investigational device receipt will be documented according to Sponsor's requirements.

Accountability and Dispensing Logs will be provided to the site for use by the Investigator to maintain current and accurate inventory records (batch, expiry, and quantity) covering the receipt, dispensing and the destruction of the investigational product.

At the conclusion of the study the Investigator must agree to return or dispose of all investigational products as instructed by the Sponsor.

7 Description of Protocol Procedures and Assessments

7.1 Informed Consent

The Investigator or suitably qualified designee will obtain written informed consent for this study from all patients before the performance of any protocol-specific procedure.

In obtaining and documenting informed consent the Investigator must comply with applicable regulatory requirements, local standard operating procedures and must adhere to Good Clinical Practice (GCP).

The investigator will explain to each patient the nature of the study, its purpose, the procedures involved, the expected duration, the potential risks and benefits and any discomfort it may entail. Each patient will be informed that participation in the study is voluntary and that he / she may withdraw from the study at any time and that withdrawal of consent will not affect his / her subsequent medical assistance and treatment. The patient must be informed that his / her medical records may be examined by authorized individuals other than their treating physician. All patients for the study will be provided with a participant information sheet and a consent form describing the study and providing enough information for the patient to make an informed decision about their participation in the study. The patient must be given ample time to decide whether to participate in the study or not. The formal consent of a patient, using the approved consent form, must be obtained before the patient is submitted to any study procedure. The

patient should read and consider the statement before signing and dating the informed consent form and should be given a copy of the signed document. The consent form must also be signed and dated by the Investigator (or designee) and it will be retained as part of the study records. The patient's medical record should clearly indicate that the patient is participating in this study.

7.2 Assessment of Eligibility

The Investigator must assess a patient's continued suitability and eligibility for the study, especially with regards to the Inclusion and Exclusion criteria of this Protocol described in Sections 3.1.2 and 3.1.3.

7.3 Demographics

For the purposes of this study, demographic information will include:

- Dates of Informed Consent Form signature
- Date of birth
- Patient Age
- Gender

7.4 Medical History

Medical history will be documented at Baseline and will include:

- Patient height, weight and BMI (derived from the height and weight measurements)
- Surgical procedure patient listed for
- Side of body being operated on (right / left)
- And the following relevant medical histories:
    - Any cardiovascular disease
    - Hypertension
    - Cardiac insufficiency
    - Coronary heart disease
    - Peripheral vascular disease
    - Any metabolic disorders
        - Type 1 diabetes mellitus
        - Type 2 diabetes mellitus
        - Hyperuricemia
    - Any rheumatic or immunological diseases
    - Any malignant skin disease
    - Any infectious disease

7.5 Medications

All relevant medications including analgesia used will be recorded in the source documents and on the appropriate page of the eCRF.
For each medication the following will be documented:

- Medication / treatment name (generic name may be used if trade name is unknown)
- Dose, unit, and frequency of dosing (individual dosages, not total daily dose)
- Route of dosing
- Indication for use
- Start date
- Stop date (if applicable)

7.6 Pain Assessment Using Visual Analogue Scale (VAS)

The Visual Analogue Scale (VAS) is a commonly used pain assessment tool. Patients will be using the VAS instrument to indicate their perceived current pain status.
They will be asked to mark using a pen, the point that best represented the intensity of their pain on a horizontal line (100mm in length) anchored by the word descriptors at each end, "no pain" on the left side and "worst pain possible" on the right side of the line.

The VAS score is determined by measuring in millimeters from the left-hand end of the line to the point indicated by the patient. This value in millimeters will then be entered into EDC.

7.7 Manchester-Oxford Foot Questionnaire – Foot & Ankle (MOxFQ)

The MOxFQ (Foot & Ankle) is a 16-item Patient Reported Outcome (PRO) developed and validated for use in clinical studies involving foot / ankle surgery. This self-administered PROM assesses how foot / ankle problems impair health-related quality of life can be completed before and after surgery.

The questionnaires (and instructions for completing them) will be provided to all participants for completion at their baseline and follow-up assessments.

7.8 Edema Assessment

Leg edema will be assessed on both the involved limb and the un-involved limb, using the following methods:

7.8.1 Pitting Edema

Assessment - Press firmly with your thumb for at least 2 seconds:

- Over the dorsum of the foot
- Behind the medial malleolus
- Lower calf above the medial malleolus

Pit depth and the time needed for the skin to return to its original appearance (recovery time) should be recorded in EDC as per the grading scale below

The grading of edema is determined by pit depth (measured visually) and recovery time from grade 0-4. The scale is used to rate the severity and the scores are as follows:

- Grade 0: No clinical edema
- Grade 1: Slight pitting (2 mm depth) with no visible distortion that rebounds immediately.
- Grade 2: Somewhat deeper pit (4 mm) with no readily detectable distortion that rebounds in less than 15 seconds
- Grade 3: Noticeably deep pit (6 mm) with the dependent extremity full and swollen that takes up to 30 seconds to rebound
- Grade 4: Very deep pit (8 mm) with the dependent extremity grossly distorted that takes more than 30 seconds to rebound

7.8.2 Figure-of-Eight Method for Measuring Ankle Joint Swelling

Swelling at the ankle will be measured using the Figure-of-Eight Method.
Using a tension-controlled measuring tape with the ankle in neutral position of eversion-inversion in 90° of dorsiflexion, the following bony landmarks should be connected by doing a figure-of-eight.

- The patient should be supine both feet extended beyond the end of the examination table to the level of midcalf
- Start midway between tibialis anterior tendon and lateral malleolus
- Draw tape medially across instep just distal to navicular tuberosity
- Pull tape across arch to base of 5th metatarsal, then across tibialis anterior tendon
- Then pull tape around ankle joint, just distal to tip of medial malleolus
- Take tape across Achilles tendon, just distal to lateral malleolus and return tape to starting point.
- Measurement in centimeters should be repeated 3 times on the involved limb and the un-involved limb and the average calculated for each limb to minimize variation. Each measurement should be within 1cm of each other.
  Using the average measurement, calculate the ratio as follows:

  Involved limb = X cm
  Un-involved limb = Z cm
  Ratio X cm / Z cm

Please note for comparison between repeated measurements , it is important to standardize the position of the foot and mark the anatomical landmarks on the foot used for the measurements with an indelible pen. This will also minimize variation between visits.

7.8.3 Bioelectrical Impedance Assessment for Swelling

Swelling should be further quantified by measuring bioimpedance of the lower limbs. All measurements will be taken using and RJL Systems Quantum Legacy Bioelectrical Impedance Analyzer (Clinton Township, MI, USA) and recorded in Ohms as outlined below. Full details of how the procedure is carried out should be referred to and can be found in the separate manual provided.

- The patient should be supine for at least 10 minutes before measurements are recorded
- Start with the uninvolved limb i.e. the limb that was not operated on
- Place electrodes on the patient as shown in Figure 2 below:
    - 20cm proximal to the superior patellar pole over the midline of the thigh
    - 10cm proximal to the to the superior patellar pole over the midline of the thigh
    - On a point midway between the medial and lateral malleolus
    - 10cm distal to the midway point between the malleoli and the 2nd ray on the dorsum of the foot
- Attach electrode leads to the bioimpedance analyser as shown
- Turn the bioimpedance analyser on, wait for approximately 5 seconds and record the resistance value
- Repeat as above on the involved limb i.e. the operated leg



Figure 4: Placement of electrodes for bioelectrical impedance assessment

Swelling / edema is calculated as percentage difference in the involved limb to the uninvolved limb using the following formula:

[1 – (resistance of involved limb) / (resistance of uninvolved limb)] * 100

Normalizing to the uninvolved limb, allows for the accurate measurement of changes in fluid status between the limbs.

7.9 Randomization

Participants will be allocated to treatment groups using a validated variable randomization algorithm in the study specific EDC.

7.10 geko™ Device Training & Instructions (geko™ arm only)

Patients randomized to the geko™ arm, will be trained in the use of the geko™ device by a member of their healthcare team and be provided with Instructions to take home. Patients will also be instructed to hand in their patient diary at their first follow-up visit for verification and signature by a member of their healthcare team (see section 6.2)

7.11 Application of geko™ Therapy (geko™ arm only)

The geko™ T device has 11 stimulation settings designed to balance the degree of activation of the venous muscle pumps of the calf and foot together with patient comfort. The optimal setting will vary between patients and is achieved when the setting selected is enough, to simultaneously activate the calf and foot muscle pumps thus initiating dorsiflexion i.e. an involuntary upward outward movement of the foot whilst remaining comfortable for the patient.

In order to mitigate post-operative edema build-up during the first 24 hours post-surgery, geko™ therapy should be delivered to the patient at a setting which gives full dorsiflexion i.e. upward outward movement of the foot once a second, thus maximising activation of the venous muscle pumps of the calf and foot and increasing blood circulation in the veins, arteries and microcirculation of the operated leg and around the surgical site.

- The geko™ T device should be fitted on the operated leg as per the fitting instructions outlined in Appendix 4 and geko™ therapy should be delivered for the first 24 hours post-surgery. A 12 hour break should follow before applying the second geko™ device.

- geko™ therapy will then be applied for 12hrs / day for 14 days or until the patient returns for their first post-operative follow-up visit (Day 14 ± 2 days post-surgery) whichever comes first.

- There are three possible fitting locations that will give successful activation of the peroneal nerve and initiate dorsiflexion. If fitting at the primary location on the fibular head does not initiate dorsiflexion, the alternative fitting locations should be tried (refer to Appendix 5)

- Once the correct fitting location has been identified draw around the device with a permanent surgical marker. This will aid fitting of the device for the daily treatments when the patient is at home

- The maximum stimulation setting resulting in dorsiflexion that can be comfortably tolerated by the patient should be selected. It is anticipated that the patient will tolerate a higher stimulation setting initially, as analgesia will be in place following surgery

- As the effects of analgesia administered at surgery reduce, the stimulation setting may need to be adjusted to maintain a balance between the degree of activation of the calf and foot venous muscle pumps with patient comfort.

Note: if the stimulation setting is lowered, the setting selected must remain enough, to cause dorsiflexion of the foot on the operated leg.

Please ask the patient to ensure that during the daily 12 hr treatment periods, stimulation is resulting in dorsiflexion.

7.12 Surgical Wound Status

The following assessments of the surgical wound will be completed at all post-surgery follow-up visits (day 14 ± 2 days, day 42 ± 6 days & day 90 ± 2 days)

7.12.1 Wound Healing Status

At each follow-up visit, the PI or designee will assess the wound as follows:

- Healed - skin is intact
- Progressing – wound is progressing towards healing
- Static – wound is neither healing nor deteriorating
- Deteriorating – wound is deteriorating (e.g. increasing in size, exudate or odor; surrounding skin is deteriorating)
- Severe - is infected or with other complications which may require hospitalization and/or surgical intervention

7.12.2 Wound Surface (if not healed)

- None
- Necrosis
- Fibrin
- Granulation
- Slough

7.12.3 Wound Exudate (if not healed)

- None
- Low

- Moderate
- High

7.12.4 Wound Odor (if not healed)

- Yes or No

7.12.5 Wound Infection (if not healed)

- No
- Yes- mild infection
- Yes- moderate infection
- Yes- severe infection

7.12.6 Recording of Device Usage

Patients randomized to the geko™ will also be provided with a patient diary on which their geko™ device usage and feedback / satisfaction with the geko™ device will be recorded. Patients should bring the diary with them to the first follow-up visit at which the diaries will be verified and signed by a member of the healthcare team.

8 Statistical Analysis

8.1 General Statistical Considerations

This section presents general information concerning the statistical analyses which will be performed in this study, including for example, information about sample size, patient groups, endpoints, and the analysis methods and statistical tests to be performed.

8.2 Sample Size Determination and Rationale

Base on the mean and standard deviation difference between study arms in previous studies[7,9], 50 patients would be needed in each group for a power of 95% and type I error (alpha) of 0.05.

Calculation based on the formula:

$n = f(\alpha/2, \beta) \times 2 \times \sigma 2 / (\mu 1 - \mu 2)^2$

where μ1 and μ2 are the mean outcome in the control and experimental group respectively, σ is the standard deviation, and

$f(\alpha, \beta) = [\Phi^{-1}(\alpha) + \Phi^{-1}(\beta)]^2$

Φ^{-1} is the cumulative distribution function of a standardized normal deviate.

Assuming 15% of patients are lost to follow-up and 6% of patients do not respond to geko™ stimulation 61 patients will be recruited into each arm of the trial. A total of 122 patients will be recruited.

8.3 Randomization

This is a multi-center randomized clinical study. Participants will be allocated to treatment groups using a validated variable randomization algorithm in the study specific EDC.

8.4 Description of Study Endpoints

8.4.1 Primary Endpoints

Primary endpoint as follows:

- The primary objective of the study is to assess the effect of geko™ therapy on edema formation following foot and / or ankle surgery.

Shapiro-Wilk test shall be used to test whether there is a significant ($p<0.05$) departure from normal distribution in either group. Although at $n=122$ this test is not especially sensitive, it will pick up any pronounced skews or kurtoses. In the absence of any such pronounced effect in the underlying population, Central Limit Theorem determines that means sampled from that population will be normally distributed in any case.

In the event of a non-normal distribution as determined above, Mann-Whitney test shall be used to test the difference between groups. Otherwise, un-paired Student's t-test shall be used. In either case, $p<0.05$ shall be deemed significant.

8.4.2 Secondary Endpoints

The secondary efficacy endpoints are:

- Incidence of Adverse Events (AEs)
- Incidence of Device Deficiency (DD)
- Pain level via a visual analogue scale (VAS) score (See Appendix 1)
- Surgical wound healing status
- Analgesia intake
- Dosage analgesia intake
- Patient reported outcomes via Manchester-Oxford Foot & Ankle Questionnaire (MOxFQ, see Appendix 2)
- Assessment of patient diary (patient reported daily geko™ usage and feedback / satisfaction with the geko™ device

Secondary endpoint data from the study will be summarized descriptively. Continuous parameters may include mean, standard deviation, median, minimum, and maximum. Categorical variables may include frequency counts and percentages. Outcomes may also be

summarized descriptively by product variant and surgical location. In situations where direct comparisons are made between study data and historic or published data an appropriate statistical method will be selected on a case-by-case basis e.g. Student's t-Test for continuous variables, or Fisher's Exact test for categorical variables.

9 Adverse Event, Adverse Device Event

The Investigator or designee will be responsible for detecting, documenting and reporting AEs and SAEs as detailed in this section of the protocol.

9.1 Definitions

9.1.1 Medical Device

Any instrument, apparatus, implement, machine, appliance, implant, software, material or other similar or related article

Intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the specific purposes(s) of

- Diagnosis, prevention, monitoring, treatments or alleviation of disease,
- Diagnosis, monitoring, treatment, alleviation of, or compensation for, an injury,
- Investigation, replacement, modification, or support of the anatomy or of a physiological process,
- Supporting or sustaining life,
- Control of conception,
- Disinfection of medical devices and

Which does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its intended function by such means

9.1.2 Adverse Event (AE)

Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the medical device.

This definition includes events related to the medical device or the comparator.

This definition includes events related to the procedures involved.

9.1.3 Serious Adverse Event (SAE)

An adverse event that led to:

- Death
- A serious deterioration in the health of the subject, that either resulted in:
  - A life-threatening illness or injury OR
  - A permanent impairment to a body structure or a body function OR
  - An in-patient or prolonged hospitalization OR
  - A medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function OR
  - A malignant tumor

- Fetal distress, fetal death or a congenital abnormality or birth defect

A planned hospitalization for a pre-existing condition, or a procedure required by the protocol is not considered a serious adverse event.

9.1.4 Adverse Device Effect (ADE)

An adverse event related to the use of a medical device. This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the medical device.
This definition includes any event resulting from the use error or from intentional misuse of the medical device.

9.1.5 Serious Adverse Device Effect (SADE)

Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event

9.1.6 Unanticipated Serious Adverse Device Effect (USADE)

A serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the Instructions for Use

9.1.7 Anticipated Serious Adverse Device Effect (ASADE)

A serious adverse device effect which by its nature, incidence, severity or outcome has been previously identified in the IFU

9.2 Recording and Reporting Adverse Events, Adverse Device Effects, Serious Adverse Events and Serious Adverse Device Effects:

Safety surveillance and reporting will be done for all subjects enrolled in this study.
Safety surveillance within this study and the safety reporting both performed by the Investigator, starts as soon as the subject is enrolled in this study (date of signature of the informed consent form). The safety surveillance and the safety reporting will continue until the last study visit has been performed or the subject is deceased, or the subject concludes his participation into the study.

- Serious Adverse Events and all Adverse Device Effects (serious or non-serious) are to be documented in EDC and reported to the Sponsor maximum 24 hours after becoming aware of the event.
- Non-serious events are to be documented in EDC and reported as soon as possible but not later than 72 hours after becoming aware.

Sponsor SAE Contact:
Kieron Day
Tel: +44 (0) 7921 106 253
e-mail: safety@firstkindmedical.com

Additional information may be requested by the Sponsor in order to support the reporting of AEs to regulatory authorities.

The Investigator must notify the EC / IRB, if appropriate, in accordance with national and local laws and regulations, of the AEs reported to the Sponsor

9.3 Device Deficiencies

A device deficiency is defined as an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. DDs include malfunctions, use errors, and inadequate labelling. Any DD should be documented in EDC & reported to the Sponsor as soon as possible but not later than 72 hours after becoming aware:

Sponsor DD Contact:
Kieron Day
Tel: +44 (0) 7921 106 253
E-mail: safety@firstkindmedical.com

Once the Investigator becomes aware of a device related adverse event, he/she must report this to the Sponsor, via the trial specific EDC system, within 24 hours.

10 Direct Access to Source Data / Documentation

Participants will be identified on eCRFs by a unique participant identification number and on source documents by name and date of birth. No personal identifier will be used in any publication or communication used to support this research study. The participant identification number will be used if it becomes necessary to identify data specific to a single participant.

The monitors, auditors, personnel authorized by the Sponsor, the local IRB/IEC, and regulatory agencies are eligible to review medical and research records related to this study as a part of their responsibility to protect human participants in clinical research and will be given direct access to source data and documentation (e.g., medical charts/records, printouts etc.) for source data verification, provided that participant confidentiality is maintained in accordance with local requirements. Access to electronic medical records may be governed by institution policy and each site will be required to ensure access while remaining compliant with institutional requirements.

11 Quality Control and Quality Assurance

11.1 Monitoring Requirements

In order to maintain knowledge of the progress of a study, the Sponsor's designated Clinical Research Associate (CRA)/monitor will remotely monitor data quality submitted by centers during the study as well as maintain frequent telephone and written communication. The Investigator will permit the Sponsor to monitor the study as frequently as is deemed necessary and provide access to medical records to ensure that data are being recorded adequately, that data are verifiable, and that protocol adherence is satisfactory.

The Investigator will permit representatives of the Sponsor and/or designated Contract Research Organization (CRO) to inspect all CRFs and corresponding study participant original medical records (source documents) at regular intervals throughout the study. Participant original medical records and other relevant data must be available to support all data recorded in the CRF. In addition to the original medical records, these data may include but is not limited to, study, laboratory and diagnostic reports, wound images and tracings etc.

Site inspections serve to verify strict adherence to the protocol and the accuracy of the data being entered on the CRFs, in accordance with applicable regulations. A Monitoring Log will be maintained at each study site which the monitor will sign, date and state the type of visit.

The Investigator should be aware that the study site and participant records might be inspected and audited by the Sponsor or representatives of Sponsor or relevant regulatory authorities.

11.2 Acceptability of Case Report Forms

A CRF must be completed for each participant who has signed an informed consent form on-line using the study specific Electronic Data Capture (EDC) system. All source documents and CRFs will be completed during or as soon as possible after the participant's visit. The Investigator will review CRFs to indicate that, to his/her knowledge, they are complete and accurate. CRFs will be reviewed by the Sponsor's CRA/ monitor, who will decide as to their acceptability. CRF data fields are specified in Appendix 7.

11.3 Modification of Protocol

A modification or alteration to this protocol may not be undertaken without first obtaining the concurrence of Sponsor. Both the Chief Investigator and the Sponsor representative must sign and date the amendment prior to implementation. In addition, the Chief Investigator must report all protocol amendments to, and receive all required approvals from, the Institutional Review Board/Independent Ethics Committee (IRB/IEC) PRIOR to implementation of any protocol amendment at the study center, with two exceptions:

- When necessary to eliminate apparent immediate hazard to the participant; or
- When the modification involves only logistics or administration.

If a protocol change is proposed for all participants, the following procedure for a protocol amendment will be followed. An amendment must be in writing and it must be dated by both the Sponsor and the Investigator. If necessary, the Sponsor will submit protocol amendments to the appropriate regulatory authorities and notify other Investigators using this protocol.

An amendment may also require modification of the informed consent form. The Investigator will provide an approval letter for the amendment and revised informed consent form, if applicable, to the Sponsor.

Any protocol amendments will be listed in the "Appendices" portion of the Table of Contents.

11.4 Reporting Protocol Deviations

The Investigator is obligated to follow the protocol without departure from the requirements written in the protocol. If the Investigator deviates from the protocol requirements, the Sponsor will make the determination as to whether the participant will continue in the study. The Sponsor also has the right to discontinue the participant for protocol deviations/violations. All protocol deviations must be documented in the CRFs via the study specific EDC system.

12 Ethics and Regulatory Requirements

This study is to be conducted in accordance with the specifications of this protocol and in accordance with principles consistent with Declaration of Helsinki, Good Clinical Practice (GCP), ISO 14155:2020 and other currently applicable regulations.

No protocol changes will be implemented without the prior review and approval of the relevant IRB/IEC's, except where it may be necessary to eliminate an immediate hazard to a research participant (See Section 12.1).

Additionally, all study products used in this study are manufactured, handled and stored in accordance with applicable Good Manufacturing Practices (GMP) and the products provided for this study will be used only in accordance with this protocol.

12.1 Independent Ethics Committee (IEC) and / or Institution Review Committee (IRB)

This study will need IEC/IRB review. The Principal Investigator will provide the IEC/IRB with all appropriate materials as required by their IEC/IRB, including but not limited to the clinical study protocol, informed consent form, and any advertising materials. The study will not be initiated until the IRB/IEC provides written approval of the aforementioned documents and until approval documents have been obtained by the Principal Investigator and Sponsor or Sponsor designee. The Investigator will not participate in the decision. If the Investigator is an IEC/IRB member, documentation must be provided indicating recusal from the approval process. Appropriate reports on the progress of this study by the Principal Investigator will be made to the IEC/IRB as required by local and applicable government regulations and in agreement with policy established by the Sponsor. The Investigator is required to maintain an accurate and complete record of all written correspondence to and received from the IEC/IRB and must agree to share all such documents and reports with the Sponsor.

No changes from the final approved protocol will be initiated without the IEC/IRB's prior written approval or favorable opinion of a written amendment, except when necessary to eliminate immediate hazards to the participants or when the change involves only logistics or administration.

12.2 Investigator's Responsibilities

The Investigators are responsible for performing the study in full accordance with the specifications of this protocol and in accordance with principles consistent with Declaration of Helsinki (2013), Good Clinical Practice for Medical Devices (ISO 14155:2020) and other current applicable regulations. Information regarding any study centers participating in this study that cannot comply with these standards will be documented.

12.3 Participant Informed Consent Requirements

Written and oral information about the study in a language understandable by the patient will be given to all patients by the Investigator and/or designee. Written informed consent will be obtained from each patient before any procedures or assessments that would not otherwise be required for the care of the patient are done and after the aims, methods, anticipated benefits, potential hazards, and insurance arrangements in force are explained and the patient has been given sufficient time to ask questions and consider participation in the study. It will also be explained to the patients that they are free to refuse entry into the study and free to withdraw from the study at any time without prejudice to future treatment. It is permissible for a third person (e.g., a family member) to be present during the explanation of the study.

The written Informed Consent Form (ICF) is to follow Good Clinical Practice (GCP) guidelines. The Sponsor and / or designated Contract Research Organization (CRO) will approve the ICF and all amendments to the ICF prior to submission to the IRB/IEC. A copy of the ICF to be used will be submitted by the Investigator to the IRB/IEC for review and approval prior to the start of the study. Each study site must provide the Sponsor with an unsigned copy of IRB/IEC-approved ICF along with applicable documentation to support this approval. The original signed ICF is retained in the participant's study records, and a copy is provided to the participant. A second copy may be filed in the participant's medical record, if allowed by institutional policy.

13 Data Handling and Record Keeping

13.1 Recording and Collection of Data

The primary source document for this study will be the participant's medical record. If separate research records are maintained by the Investigator(s), the medical record and the research records will be considered the source documents for the purposes of auditing the study.

Applicable source data will be manually transcribed to approved CRFs. The Investigator is ultimately responsible for the accuracy of the data transcribed on the forms. All source documents and CRFs will be completed as soon as possible after the participant's visit.

The Principal Investigator (PI) will review CRFs to indicate that, to his/her knowledge, they are complete and accurate. If further changes are made after this, the PI will need to again sign the Investigator signature page. Designated source documents will be signed and dated by the appropriate study personnel. Investigators must agree to complete and maintain source

documents and CRFs for each participant in the study. All research data will be entered, either electronically or manually, into a computerized online database.

The PI will maintain a confidential list of study participants which will include each participant's study number, name, date of birth and unique hospital identification number if applicable. This list will be kept by the PI and will not be collected by Sponsor. A notation will be made in the participant's case history/medical chart that he/she is participating in a clinical study and has provided a signed and dated ICF. The PI must also maintain a separate screening log of all the patients screened for participation in the study; it should include gender; age; eligibility status; reason for ineligibility, if applicable; and study allocated participant number, if applicable.

13.2 Clinical Data Management

The Sponsor and/or designated CRO will be responsible for the processing and quality control of the data. Data management will be carried out as described in the Sponsor's or CROs standard operating procedures (SOPs) for clinical studies.

The handling of data, including data quality control, will comply with applicable regulatory guidelines and the Sponsor's SOPs as well as provisions of a study-specific Data Management Plan.

13.3 Archiving

All study documentation at the Study site and Sponsor site will be archived in accordance with Sponsor's quality standards and SOPs.

The Study site will maintain all research records, reports, and case history reports for a period of 15 years after study closure.

At the completion of the study, details of the archival process must be provided to the Sponsor. Study records are subject to inspection by applicable health and regulatory agencies at any time.

Records to be retained at the Study site include, but are not restricted to:

- Source data and the primary records upon which they are based (e.g., participant's progress notes, adverse event data, test results, and any other diagnostic procedures required to evaluate the progress of the study).
- Signed protocols and protocol amendments
- Product accountability records
- Study personnel signature log
- Monitoring logs
- Correspondence to and from the Sponsor, designee and IRB/IEC
- Principal Investigator and co-Investigator(s) Curriculum Vitae (CVs)
- Signed ICFs

- SAE reports
- IRB/ICE approval letters and correspondence if applicable
- Other documents pertaining to the conduct of the study

These documents must be maintained and kept on file by the Study site so that the conduct of the study can be fully documented and monitored.

14 References

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Appendices

Appendix 1: Visual Analogue Scale (VAS) Score

Participant ID: _____

Visit-ID: _____

To be completed by the Patient

Please mark the point on the line which best represents your current level of pain.



_____

To be completed by the Investigator

Distance from no pain point to the line marked by the participant in mm – please measure and enter below

_____mm

Date completed (dd/mm/yyyy): _____

Initials of person completing: _____

Signature of person completing: _____

Appendix 2: Manchester-Oxford Foot & Ankle Questionnaire (Foot & Ankle)

Manchester-Oxford Foot Questionnaire (MOxFQ)

Prior to completing the Questionnaire please complete the following:-

Today's Date:

				2	0		
D	D	M	M	Y	Y	Y	Y

On which side of your body is the affected joint, **for which you are receiving/have received treatment**.

Left ❑
Right ❑
Both ❑

If you said 'both', please complete the <u>first</u> questionnaire thinking about the <u>right side</u>. A second questionnaire, for the left side, will follow.

Circle as appropriate **Right / Left** Please tick (✓) one box for <u>each</u> statement.

1.	**<u>During the past 4 weeks</u> this has applied to me:**				
	I have pain in my foot/ankle				
None of the time	Rarely	Some of the time	Most of the time	All of the time	
☐	☐	☐	☐	☐	

2.	**<u>During the past 4 weeks</u> this has applied to me:**				
	I avoid walking long distances because of pain in my foot/ankle				
None of the time	Rarely	Some of the time	Most of the time	All of the time	
☐	☐	☐	☐	☐	

3.	**<u>During the past 4 weeks</u> this has applied to me:**				
	I change the way I walk due to pain in my foot/ankle				
None of the time	Rarely	Some of the time	Most of the time	All of the time	
☐	☐	☐	☐	☐	

4. **During the past 4 weeks this has applied to me:**

I walk slowly because of pain in my foot/ankle

None of the time	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

5. **During the past 4 weeks this has applied to me:**

I have to stop and rest my foot/ankle because of pain

None of the time	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

6. **During the past 4 weeks this has applied to me:**

I avoid some hard or rough surfaces because of pain in my foot/ankle

None of the time	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

7. **During the past 4 weeks this has applied to me:**

I avoid standing for a long time because of pain in my foot/ankle

None of the time	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

8. **During the past 4 weeks this has applied to me:**

I catch the bus or use the car instead of walking, because of pain in my foot/ankle

None of the time	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

9. **During the past 4 weeks this has applied to me:**

I feel self-conscious about my foot/ankle

None of the time	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

10. **During the past 4 weeks this has applied to me:**

I feel self-conscious about the shoes I have to wear

None of the time	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

11. **During the past 4 weeks this has applied to me:**

The pain in my foot/ankle is more painful in the evening

None of the time	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

12. During the past 4 weeks this has applied to me:

I get shooting pains in my foot/ankle

None of the time	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

13. During the past 4 weeks this has applied to me:

The pain in my foot/ankle prevents me from carrying out my work/everyday activities

None of the time	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

14. During the past 4 weeks this has applied to me:

I am unable to do all my social or recreational activities because of pain in my foot/ankle

None of the time	Rarely	Some of the time	Most of the time	All of the time
☐	☐	☐	☐	☐

15. During the past 4 weeks...

How would you describe the pain you usually have in your foot/ankle?

None	Very mild	Mild	Moderate	Severe
☐	☐	☐	☐	☐

16. During the past 4 weeks…

Have you been troubled by pain from your foot/ankle in bed at night?

No nights	Only 1 or 2 nights	Some nights	Most nights	Every night
☐	☐	☐	☐	☐

Finally, please check that you have answered every question.

Thank you very much.

Appendix 3: Patient Diary

Protocol: FSK-F&A-001_United States

Participant Study ID:_____

Dear Participant,

Please use this Diary to keep a record of your daily geko™ use and return it to your Physician when you return to hospital for your first follow-up visit. If you are unable to use the geko™ device for any reason, please contact your Healthcare team as soon as possible. Please use the geko™ device daily as instructed. If you forget to use the device, please record in the Diary that the geko™ was not used. Do not try to squeeze in extra treatments by using the geko™ device for longer periods the next day.

At the end of the Diary, there is also a section for you to record your feedback on the geko™ device.

Date dd/mm/yyyy	Time you switched on the geko™ device (AM / PM)	Time you switched off the geko™ device (AM / PM)	Device setting (Please circle the setting used)	Any comments
	----------AM ----------PM	----------AM ----------PM Device turned off by itself ☐	1 2 3 4 5 6 7 8 9 10 11	
	----------AM ----------PM	----------AM ----------PM Device turned off by itself ☐	1 2 3 4 5 6 7 8 9 10 11	

Date dd/mm/yyyy	Time you switched on the geko™ device (AM / PM)	Time you switched off the geko™ device (AM / PM)	Device setting (Please circle the setting used)	Any comments
	----------AM ----------PM	----------AM ----------PM Device turned off by itself ☐	1 2 3 4 5 6 7 8 9 10 11	
	----------AM ----------PM	----------AM ----------PM Device turned off by itself ☐	1 2 3 4 5 6 7 8 9 10 11	
	----------AM ----------PM	----------AM ----------PM Device turned off by itself ☐	1 2 3 4 5 6 7 8 9 10 11	
	----------AM ----------PM	----------AM ----------PM Device turned off by itself ☐	1 2 3 4 5 6 7 8 9 10 11	
	----------AM ----------PM	----------AM ----------PM Device turned off by itself ☐	1 2 3 4 5 6 7 8 9 10 11	

Date dd/mm/yyyy	Time you switched on the geko™ device (AM / PM)	Time you switched off the geko™ device (AM / PM)	Device setting (Please circle the setting used)	Any comments
	----------AM ----------PM	----------AM ----------PM Device turned off by itself ☐	1 2 3 4 5 6 7 8 9 10 11	
	----------AM ----------PM	----------AM ----------PM Device turned off by itself ☐	1 2 3 4 5 6 7 8 9 10 11	
	----------AM ----------PM	----------AM ----------PM Device turned off by itself ☐	1 2 3 4 5 6 7 8 9 10 11	
	----------AM ----------PM	----------AM ----------PM Device turned off by itself ☐	1 2 3 4 5 6 7 8 9 10 11	

Date dd/mm/yyyy	Time you switched on the geko™ device (AM / PM)	Time you switched off the geko™ device (AM / PM)	Device setting (Please circle the setting used)	Any comments
	----------AM ----------PM	----------AM ----------PM Device turned off by itself ☐	1 2 3 4 5 6 7 8 9 10 11	
	----------AM ----------PM	----------AM ----------PM Device turned off by itself ☐	1 2 3 4 5 6 7 8 9 10 11	
	----------AM ----------PM	----------AM ----------PM Device turned off by itself ☐	1 2 3 4 5 6 7 8 9 10 11	

Thank you for completing the Diary - Please now record your feedback on the geko™ device by completing the following section

FEEDBACK

Q1. How was it to apply the geko™ device to the leg?

Very Easy ☐	Easy ☐	Difficult ☐	Very Difficult ☐

If there were any difficulties, please provide a comment below:

Q2. Did you need any additional adhesive?

None ☐	geko™ Adhesive Accessory ☐	Micropore Tape ☐

Comment:

Q3. How were the fitting instructions to follow?

Very Easy ☐	Easy ☐	Difficult ☐	Very Difficult ☐

If there were any difficulties, please provide a comment below:

Q4. How was it to start / stop / change the settings on the device?

Very Easy ☐	Easy ☐	Difficult ☐	Very Difficult ☐

If Difficult, Very Difficult or Impossible has been indicated, please provide a comment below:

Q5. Did you sleep with the device on?

Yes☐ No☐

If no, please comment below:

Q6. How did the geko™ device stick to the leg?

Very Well *remained attached* ☐	Well *Detached in small area* ☐	Poorly *Detached over large area* ☐	Very Poorly *Detached completely* ☐

If any level of detachment has been indicated, please provide a comment below:

Q7. Did you have to remove the geko™ device at any time? Yes☐ No☐ *If yes, when and why, please comment below:*
Q8. Were you able to re-apply the device easily? Yes☐ No☐ *If no, please comment below*

To be completed by member of the patient's Healthcare team:
Date diary collected (dd/mm/yyyy): __ __/__ __/_____
Signature of person collecting Diary: _____

Appendix 4: geko™ T-3 Instructions for Use (United States)

