Evaluation of the adhesive strength of the geko™ X-T3 neuromuscular stimulator incorporating a new skin adhesive hydrogel formulation designated KM40C

Protocol No.:	FSK-R&D-001
Date:	29SEPT2020
Version:	2.0
IRAS ID:	289498
Short Title:	Efficacy of Adhesive Strength of New Hydrogel Formulation
Investigational Product:	Hydrogel Formulation KM40C
Indication:	Venous Thromboembolism Prevention

Author:

Marie-Thérèse Targett PhD
Clinical Project Manager
Firstkind Ltd.

FUNDER

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

Firstkind Ltd

Firstkind Ltd., is a wholly own subsidiary of Sky Medical Technology Ltd., Daresbury Science and Innovations Campus, Keckwick Lane, Daresbury, Cheshire, WA4 4FS, UK

Sponsor Contacts

Clinical Project Manager

Marie-Thérèse Targett PhD

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

Tel: +44 (0) 7340 903 377

Clinical Trial Administrator

Anne-Marie Piftor

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

Tel: +44 (0) 1494 572 056

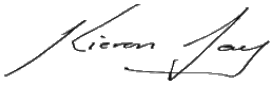
PROTOCOL APPROVAL SIGNATURES

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.

Rachel Fallon
Rachel Fallon (Sep 30, 2020 15:57 GMT+1)

Sep 30,

Mrs Rachel Fallon — Date
Chief Technical Officer
Firstkind Ltd
Hawk House, Peregrine Business Park
Gomm Road, High Wycombe,
Buckinghamshire, HP13 7DL, UK



Oct 27, 2020

Dr Kieron Day, DPhil — Date
Head of Clinical Affairs
Firstkind Ltd
Hawk House, Peregrine Business Park
Gomm Road, High Wycombe,
Buckinghamshire, HP13 7DL, UK

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) 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	
Site Number	

Table of Contents

1.0 Introduction

1.1 Electrically Conductive Adhesive Solid Hydrogels

Electrically conductive adhesive solid hydrogels are used in the medical device field to provide an electrical interface to the skin of a subject to couple electrical signals into and/or out of the subject (e.g., for diagnostic and/or monitoring uses) and/or to couple electrical stimulus into the subject (e.g., for treatment and/or preventative uses).

Current hydrogels have been developed to be sufficiently adhesive to provide good skin adherence and good electrical contact thus ensuring an even spread of current density to prevent burns. At the same time, the hydrogels must be insufficiently cohesive to allow for easy removal from the skin[1].

A number of different hydrogel precursor formulations are commercially available. These generally include a monomer, a first initiator to promote polymerisation of the monomers in the precursor, a solubiliser, and a cross-linking agent. Some prior formulations have in the past exhibited undesirable properties including issues with adhesiveness, electrical conductivity, odour and skin irritation. It has been discovered that some of those problems are the result of poor polymerization of the monomers in the hydrogel precursors thereby leaving residual monomer and/or by-products, which can cause or result in the some of the above undesirable properties.

The present hydrogels have unique and improved properties. More particularly, the present polymerising formulations or hydrogel precursors exhibit enhanced polymerisation, thereby reducing the amount of residual functional monomer and/or other monomeric residues in the hydrogel which are un-polymerised. The present hydrogels also desirably include a buffer system to help prevent discoloration and/or hydrolysis of the hydrogels as well as to improve shelf-life. Other additives can include conductivity enhancers, pharmaceuticals, humectants and skin health agents to provide for reduced skin irritation.

1.2 The geko™ T3 Neuromuscular Stimulation Device

The innovative geko™ T3 device manufactured by Firstkind Ltd (High Wycombe, United Kingdom), is a small, self-adhesive disposable, battery powered, neuromuscular stimulation device designed to enhance blood flow in the lower limbs.

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 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. Please see Figure 1 for an illustration of the device (front view)

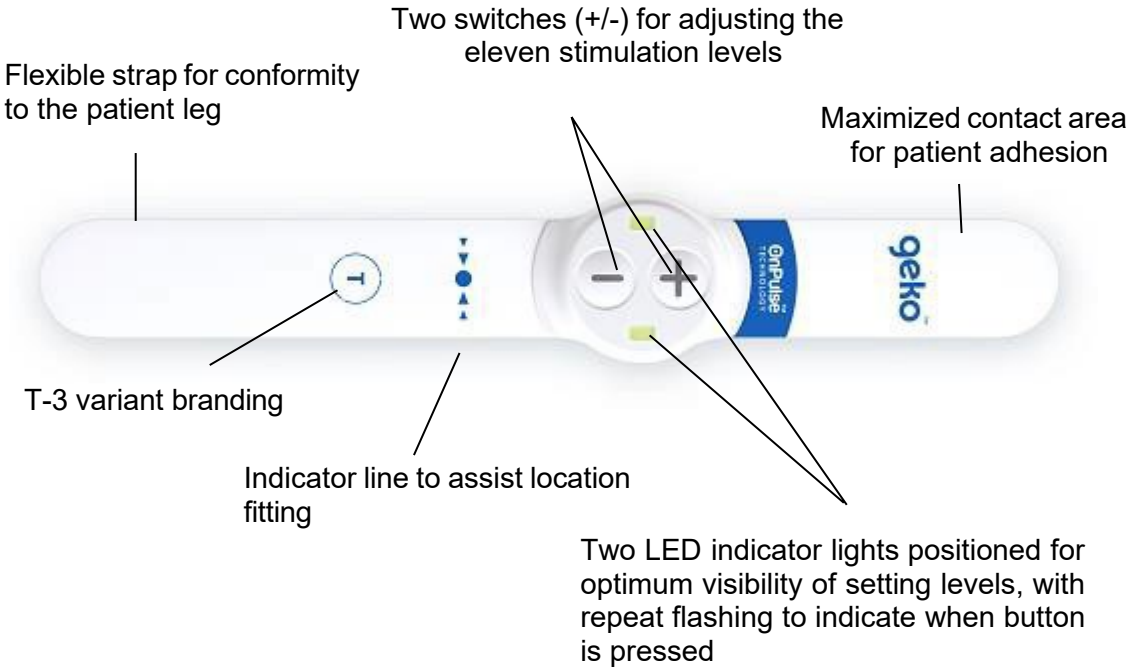


Figure 1: The T-3 geko™ device (front view).

The geko™ T3 device utilises an electronically conductive skin adhesive solid hydrogel (KM10T) that adheres to the skin and when applied externally to the leg on the lateral/posterior aspect of the knee, electrodes within the hydrogel layer stimulate the common peroneal nerve simultaneously activating the calf and foot muscle pumps that assist in returning blood to the heart. This simultaneous activation has the effect of increasing venous velocity and volume flow in the deep veins of the calf which in turn increases arterial and microcirculatory flow with no change to heart rate or blood pressure[2]. Figure 2 shows an illustration of the device (rear view) with hydrogel layers and electrodes.

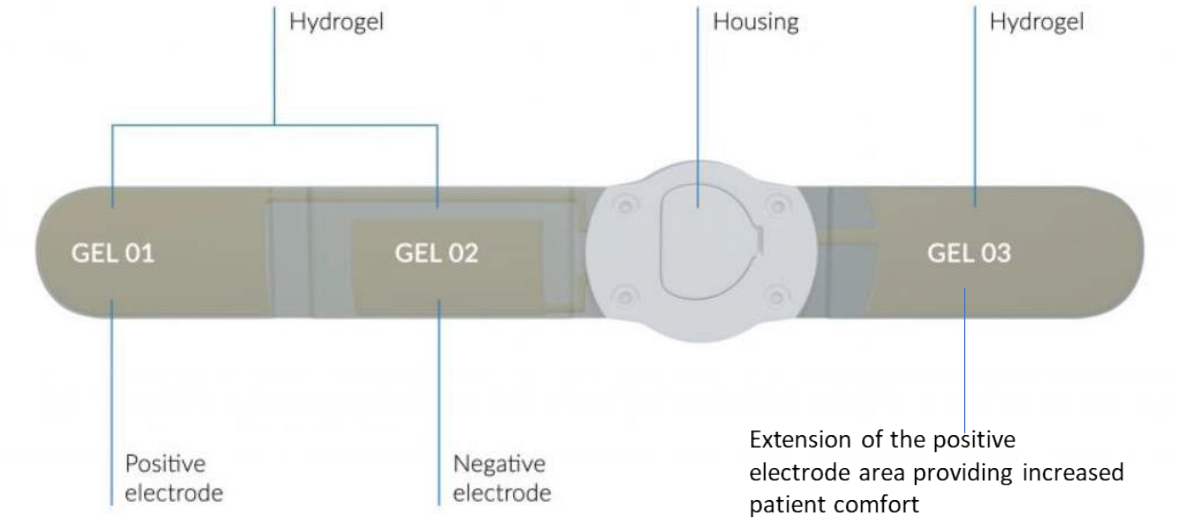


Figure 2: The T-3 geko™ device (rear view) with hydrogel layers and electrodes.

The geko™ T3 device has a range of stimulation levels to ensure activation of the muscle pumps irrespective of individual skin impedance balanced with patient comfort. The optimal stimulation level which maximises blood circulation varies between patients and is achieved when a stimulus results in a dorsi-flexion i.e. an involuntary upward outward movement of the foot. Please see Figure 3 for an illustration of the device fitted to the lower leg.

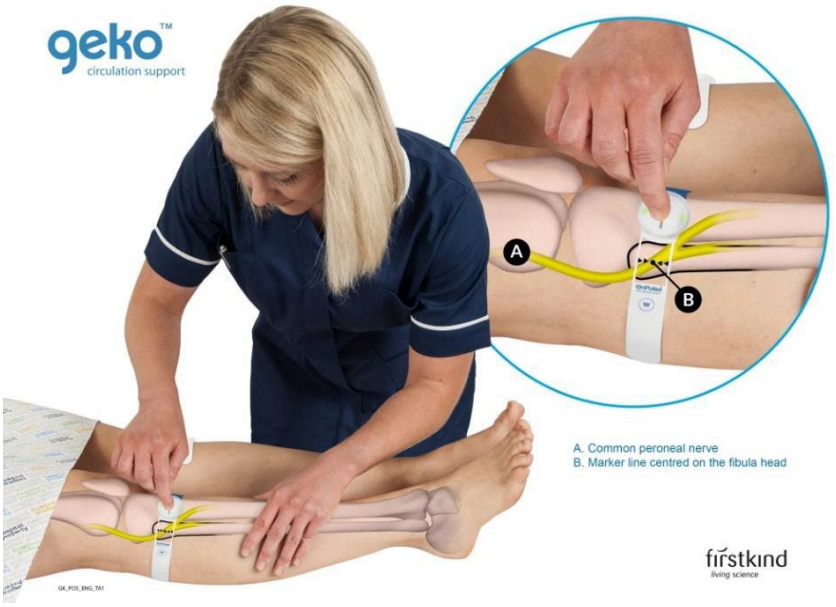


Figure 3: Administering non-invasive neuromuscular electrical stimulation via the geko™ T3 device applied at the peroneal nerve proximal to the posterior / anterior bifurcation.

The geko™ T3 device meets recognised International and European safety standards and is CE marked for its' indicated use in humans for increasing blood circulation and preventing venous thrombosis in patients known to be at high risk of venous thromboembolism (VTE). The device is currently in use within the NHS network as a mechanical VTE prophylaxis strategy for acute stroke patients.

1.3 Rationale

As outlined above, some hydrogel precursor formulations have previously exhibited undesirable properties including issues with adhesiveness, electrical conductivity and skin irritation. Some of these negative properties are the result of poor polymerisation of the monomer in the hydrogel precursors thereby leaving residual monomer and/or by-products, which can cause or result in the some of these undesirable effects. By adjusting the monomer component of the hydrogel precursor, polymerisation can be enhanced thus reducing the amount of residual monomer and/or by-products remaining and negating negative properties.

The KM10T hydrogel used in the geko™ T3 device is derived from an acrylic acid monomer and has good skin adhesion properties with low skin irritation. A new hydrogel designated KM40C has been developed that promises even lower skin irritation due to zero residual acrylic acid, following replacement of the acrylic acid monomer component of the hydrogel precursor with an acrylamide monomer. KM40C also promises good skin adhesion properties, like those of KM10T used in the geko™

T3 device.

As with KM10T, the new KM40C hydrogel formulation has been tested for safety in humans to current international biocompatibility standards (ISO10993) and subsequently, this new formulation has been used in the development of the geko™ device designated geko™ XT-3.

Both the T3 and XT-3 devices are identical in terms of the therapy they deliver to patients, they differ only in the hydrogel used for adhesion to the skin and although the new formulation promises good adhesion properties, this has not yet been tested in a clinical environment on patients receiving geko™ therapy.

As with the T3 device, the XT-3 device meets recognized, International and European safety standards and is also CE marked for its' indicated use in humans for increasing blood circulation and preventing venous thrombosis in patients known to be at high risk of VTE e.g. stroke patients

2.0 Objective

The aim of this study is to test the skin adhesion property of the new hydrogel KM40C during routine clinical use of the geko™ XT-3 device for VTE prophylaxis to ensure that skin adhesion is at least equivalent if not superior to the hydrogel KM10T incorporated into the geko™T3 device which is currently in use in hospitals.

2.1 Study Endpoints

2.1.1 Primary Efficacy Endpoints

- Skin adhesion performance of new hydrogel formulation KM40C during routine clinical use of the geko™ XT-3 device will be compared to that of the current formulation used in the geko™ T3 device. Skin adhesion will be observed and scored numerically for statistical comparison to test for equivalency of the two formulations (new vs current).

2.1.2 Secondary Efficacy Endpoints

- The secondary endpoints are the incidence of adverse events (AEs), incidence of serious AEs (SAEs), incidence of study treatment related AEs, and the incidence of investigational device related AEs

3.0 Study Design

The study will be carried out at one clinical site and will be a non-blinded, non-randomised cohort observation study.

The study objective is to compare how well the geko™ device with a new skin adhesive (geko™XT-3) sticks to the skin compared to that of the adhesive currently used to stick the current device (geko™ T3) to the skin. The performance of the new adhesive is expected to be at least the same if not better than the current one. This is an observational study or cohort study where the performance of the adhesives is observed and rated. There is no intervention to control the performance of the adhesives. As such, a randomized controlled trial is not required as the protocol does not aim to prove a causal relationship between an intervention and adhesive performance.

To enable a direct comparison of performance, patients will be divided naturally into two sequential groups or cohorts. This will also ensure that the XT-3 and T3 devices are not mixed during routine clinical use.

Group 1 patients will be consented and enter Phase 1 of the study. They will continue their treatment pathway with the geko™ T3 device as per hospital clinical protocol for VTE prevention. Group 1 patients will complete the 10-day, study period, before Group 2 patients are consented and enter Phase 2 of the study. Group 2 patients will continue their treatment pathway as per hospital clinical protocol but with the geko™ XT-3 device.

As both the T3 and XT-3 devices are identical in terms of the therapy they deliver to patients, the treatment pathway for both group 1 & 2 patients will be unaffected. The devices differ only in the hydrogel used for adhesion to the skin. Please see Figure. 4 for a schematic of the patient journey.

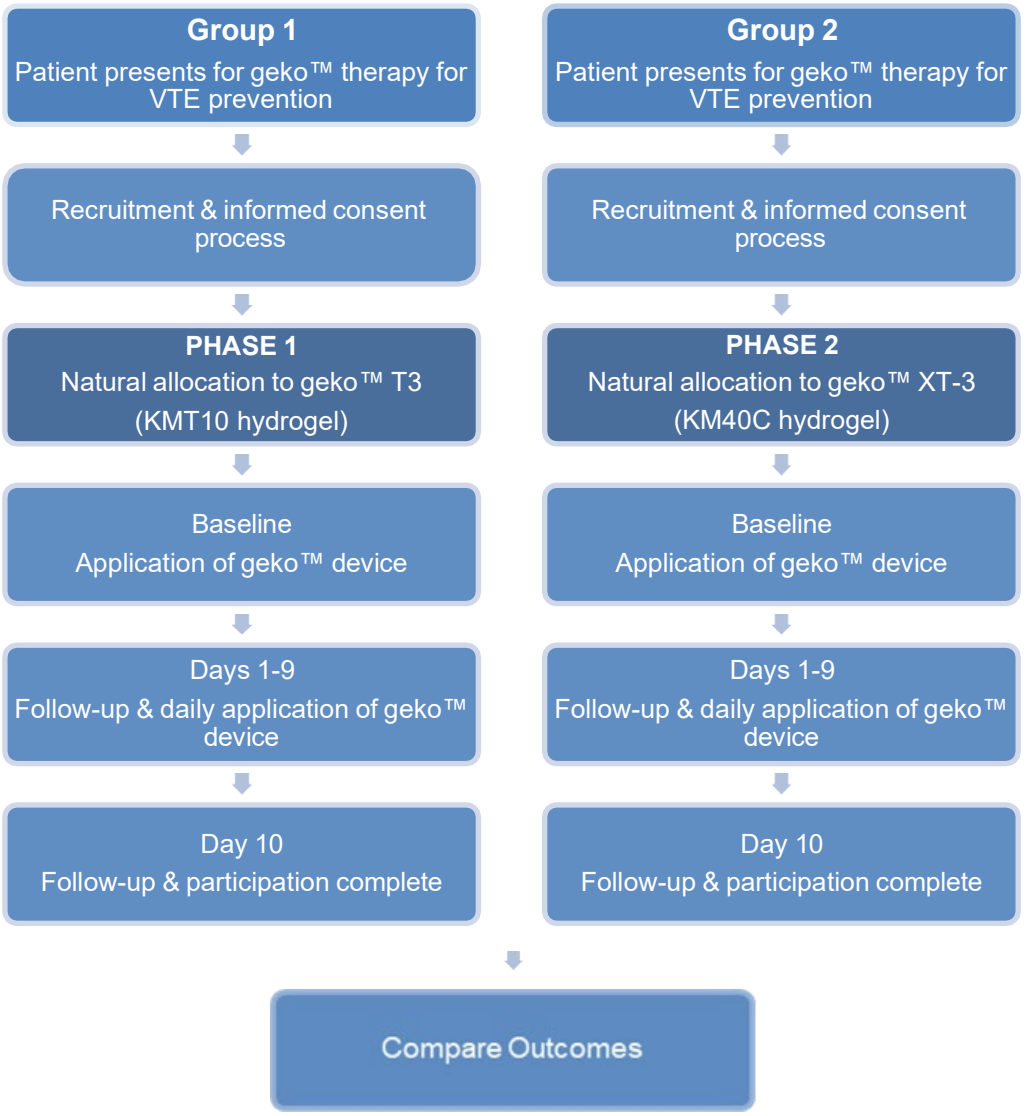


Figure 4: Schematic diagram of the patient journey for Groups 1 & 2.

3.1 Study Population

It is important that the skin adhesion strength of the new hydrogel formulation is evaluated together with that of the current formulation during clinical use of the geko™ devices. The use of healthy volunteers would not allow for this as the devices would not be being used in a population for the purpose for which they are intended. The study population will be patients who are immobile and bedbound following acute stroke, this population cannot be replicated within a healthy population.

Both hydrogel formulations have been tested for biocompatibility in humans and both geko™ devices are CE marked and indicated for use in humans for increasing blood circulation and preventing venous thrombosis in patients known to be at high risk of VTE. Please refer to Appendix 1 for a list of regulatory approvals.

As such, patients who have been admitted to the Acute Stroke Unit who will receive daily treatment with geko™ as an alternative VTE prophylaxis strategy as part of their standard care will be asked to participate.

3.2 Number of Participants

A total of 40 patients will be recruited, 20 into each phase of the study.

3.3 Eligibility Criteria

Eligible patients are those who meet all the following inclusion criteria and who do not have any listed exclusion criteria.

3.3.1 Inclusion Criteria

- Male or female aged ≥ 18 years
- Currently an in-patient hospitalised for acute stroke
- Use of geko™ as a mechanical prophylaxis strategy for venous thromboembolism
- Patient understands and is willing to participate in the study and can comply with study procedures

3.3.2 Exclusion Criteria

- Pregnancy or breast feeding
- Use of any neuro-modulation device other than geko™
- Participation in any other clinical study that may interfere with the outcome of either study

4.0 Schedule of Events

Procedures should take place in the following order:

4.1 Recruitment and Baseline (Day 0)

- Patient presents for geko™ therapy for VTE prevention following acute

stroke

- Confirm patient eligibility
- Obtain written informed consent
- Collect demographic data
- Fit geko™ device bilaterally for VTE prevention as per hospital standard care. The devices fitted will be as per allotted patient group and study phase.
- Record
    - Ease with which device fitted (rate from very easy to impossible)
    - Adhesion to patient's leg (rate from very well to not at all)
    - Use of additional fixation to keep the device in position
    - Ease of re-application if removed
    - Patient comfort (rate from very comfortable to extremely uncomfortable)
    - Device setting (1-11)
- Assess for any AEs

4.2 Follow-up and Daily Application of geko™ therapy (Days 1-9)

During daily review of the patient by a member of the healthcare team, a new geko™ device will be fitted bilaterally as per standard care. In addition, the following information will be collected each day or until the patient is able to mobilize independently:

- Length of time device worn for since fitting (hours)
- Adhesion to patient's leg (rate from very well to not at all)
- Use of additional fixation to keep the device in position
- Ease of re-application if removed
- Patient comfort (rate from very comfortable to extremely uncomfortable)
- Patient sleep post-fitting
- Patient's current mobility

Fit new geko™ device bilaterally for VTE prevention as per hospital standard care. Devices fitted will be as per allotted patient group and study phase and the following post-application information recorded:

- Ease with which device fitted (rate from very easy to impossible)

- Adhesion to patient's leg (rate from very well to not at all)
- Use of any additional fixation to keep the device in position.
- Patient comfort (rate from very comfortable to extremely uncomfortable)
- Device setting (1-11)

- Assess for any AEs

4.3 Final Follow-up and End of Participation (Day 10)

At the final follow-up, the following information will be collected

- Length of time device worn for since fitting (hours)
- Adhesion to patient's leg (rate from very well to not at all)
- Use of additional fixation to keep the device in position
- Ease of re-application if removed
- Patient comfort (rate from very comfortable to extremely uncomfortable)
- Patient sleep post-fitting
- Patient's current mobility

Once the final follow-up has been completed the patient's participation will end and the patient will be exited from the study.

See Table 1 for full schedule of events.

Procedure / Assessment	Baseline (Day 0)	Follow-up (Days 1-10)
Confirmation of eligibility	X	
Informed Consent	X	
Demographics (age in years, date of birth, gender, date of stroke diagnosis, mobility, adjunctive treatments to the geko™ device e.g. drugs, stockings	X	
Bilateral fitting of geko™ devices as per standard care	X	X
Ease of fitting	X	X
Adhesion to patient's leg	X	X
Additional fixation	X	X
Ease of re-application if device removed	X	X
Patient comfort post fitting	X	X
Device setting	X	X
Patient sleep post-fitting	X	X
Hours of wear since fitting	X	X
Patient mobility	X	X
Assess for AEs	X	X

Table 1: Schedule of Events.

5.0 Participant Completion and Withdrawal / Discontinuation

5.1 Participant Completion

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

5.2 Premature Withdrawal / Discontinuation

All patients have the right to withdraw at any point without prejudice to their treatment. If necessary, the Investigator may discontinue a patient at any time if it is considered medically necessary e.g. loss of mental capacity. The Investigator may also withdraw a patient if it is considered that the scientific, and therefore, ethical standards of the study are compromised. In addition, patients will be withdrawn from the study, at the Investigator's discretion, if they fail to wear the geko™ device as part of their standard care as directed by the treating physician. The reasons for withdrawal will be fully recorded in the patient's source documents and on the appropriate case report form.

If a participant is prematurely discontinued from the study at any time due to an adverse event (AE) or serious adverse event (SAE), the procedures stated in Section 9.0 must be followed.

6.0 Study Treatments

6.1 Method for Assigning Eligible Patients

The study aims to compare the skin adhesive strength of two hydrogel formulations (new vs current) to ensure that adhesion strength is at least equivalent if not superior

with the new formulation. As such, there is no objective to prove a causal relationship between a treatment and an outcome, therefore patients will be divided naturally into two sequential groups for comparison purposes only. This will also ensure that the T3 and XT-3 devices are not mixed during routine clinical use.

Group 1 patients will enter Phase 1 of the study. They will continue their treatment pathway with the geko™ T3 device as per hospital clinical protocol for VTE prevention. Group 1 patients will complete the 10-day study period, before Group 2 patients are consented and enter Phase 2 of the study. Group 2 patients will continue their treatment pathway as per hospital clinical protocol but with the geko™ XT-3 device.

As both the T3 and XT-3 devices are identical in terms of the treatment they deliver to patients, the treatment pathway for both group1 & 2 patients will be unaffected. The devices differ only in the hydrogel used for adhesion to the skin.

6.2 Description of Device for Evaluation

The geko XT-3™ device is CE marked for use in humans (GB12/87339; SGS, United Kingdom Ltd). It is made from mylar (polyethylene terephthalate (PET)) and is enclosed in a polypropylene casing and has a hydrogel layer which will stick it to the skin. This hydrogel layer is composed of a new formulation hydrogel designated KM40C and has already been tested to current international biocompatibility standards in humans (ISO 10993). Please refer to Appendix 4 for fitting instructions.

6.3 Device Use

The geko™ T3 and XT-3 devices will be used.

6.4 Device Labelling

Devices will be labelled in accordance with all applicable regulatory requirements.

6.5 Device Storage, Handling, Application and Disposal

Patients will receive treatment with the device as part of their standard care for VTE prevention following acute stroke. Moreover, there is no requirement or need to provide specific labelling, storage, handling, application, and disposal instructions.

6.6 Device Accountability

Patients will be receiving treatment with the device as part of their standard care for VTE prevention following acute stroke, therefore there is no requirement to provide product accountability instructions.

7.0 Description of Protocol Procedures and Assessments

7.1 Assessment of Eligibility

The Investigator must assess a patient's suitability and eligibility for the study, especially with regards to the Inclusion and Exclusion criteria of this Protocol described in Sections 3.3.1 and 3.3.2.

Although potential participants will be in-patients hospitalised following acute stroke, in order to be eligible to participate all patients must be capable of giving consent for themselves. They must understand and be willing to participate in the study and be able to comply with all procedures and provide written informed consent. Patients who do not fulfil these requirements will not be recruited.

7.2 Informed Consent

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

The investigator will explain to each participant 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 participant will be informed that the 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 participant must be informed that his/her medical records may be examined by authorised individuals other than their treating physician. All participants for the study will be provided a participant information sheet and a consent form describing the study and providing enough information for participant to make an informed decision about their participation in the study. The participant must be given ample time to decide whether to participate in the study or not. The formal consent of a participant, using the approved consent form, must be obtained before the participant is submitted to any study procedure. The participant 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 his 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.

7.3 Patient Profile / Demographics

For the purposes of this observational study, demographic information will be collected at baseline (Day 0) and include:

- Patient age in years
- Patient gender
- Date of stroke diagnosis
- Current mobility – is patient able to walk independently
- Adjunctive treatments to the geko™ device e.g. drugs, stockings

7.4 Application of geko™ Device and Collection of Device Performance Data

Patients will receive treatment with either the geko™ T3 or XT-3 device as part of their standard care for VTE prevention as per hospital clinical protocol. During daily review of the patient by a member of the healthcare team, the following information will be collected for a maximum of 10 days or until the patient is able to mobilize independently:

- Length of time device worn for since fitting (hours)
- Adhesion to patient's leg (score from very well to not at all)
- Use of additional fixation to keep the device in position.
- Patient comfort
- Patient sleep post-fitting
- Patient's current mobility
- Ease with which device fitted (score from very easy to impossible)
- Device setting
- Assess for any AEs

8.0 Statistical Analysis and Sample Size Determination

8.1 Statistical Analysis

The ability of the geko™ XT-3 device to adhere to skin will be numerically scored and compared to the geko™ T3 using a non-paired t-test for equivalence.

8.2 Sample Size Determination

The sample size of 20 patients per phase has been determined using MIL-STD-105, a standard commonly used in the medical device industry to specify sample size and provide the basis for acceptance and rejection. We set an acceptable quality level (AQL) of 0.15 for the function of the new formulation hydrogel and using the C=0 sampling plan (Table 2), 100% testing of 80 devices with no failures would confirm that we meet our specified AQL.

If completed on 20 patients and assuming 4 days of use (on both legs), this equates to a minimum of 80 XT-3 devices to test the new formulation the same numbers would be required for the T3 device with current hydrogel formulation for statistical comparison.

Table 2: MIL-STD-105 Statistical Sampling Plan (C=0 Sampling Plan)

MIL-STD-1916																
Verification Level	VII		VI			V		IV		III		II		I		
INDEX VALUE																
AQL	.010	.015	.025	.040	.065	.10	**.15**	.25	.40	.65	1.0	1.5	2.5	4.0	6.5	10
LOT SIZE	SAMPLE SIZE															
2 TO 5	*	*	*	*	*	*	*	*	*	*	*	*	5	3	2	2
9 TO 15	*	*	*	*	*	*	*	*	*	*	13	8	5	3	2	2
16 TO 25	*	*	*	*	*	*	*	*	*	20	13	8	5	3	3	2
26 TO 50	*	*	*	*	*	*	*	*	32	20	13	8	5	5	5	3
51 TO 90	*	*	*	*	*	*	**80**	50	32	20	13	8	7	6	5	4
91 TO 150	*	*	*	*	*	125	80	50	32	20	13	12	11	7	6	5
151 TO 280	*	*	*	*	200	125	80	50	32	20	20	15	13	10	7	6
281 TO 500	*	*	*	315	200	125	80	50	48	47	29	21	16	11	9	7
501 TO 1,200	*	800	500	315	200	125	80	75	73	47	34	27	19	15	11	8
1,201 TO 3,200	1250	800	500	315	200	125	120	116	73	53	42	35	23	18	13	9
3,201 TO 10,000	1250	800	500	315	200	192	189	116	86	68	50	38	29	22	15	9
10,001 TO 35,000	1250	800	500	315	300	294	189	135	108	77	60	46	35	29	15	9
35,001 TO 150,000	1250	800	500	400	4776	294	218	170	123	96	74	56	40	29	15	9
150,001 TO 500,000	1250	800	750	715	476	345	270	200	156	119	90	64	40	29	15	9
500,001 AND OVER	1250	1200	1112	715	536	435	303	244	189	143	102	64	40	29	15	9

* Indicates entire Lot must be inspected 100%. **Note:** Acceptance number in all cases is zero.

8.3 Treatment Groups

The following treatment groups will be assessed

Group	Description
Group 1 (Phase 1, n=20)	Standard care with hydrogel KM40C (geko™ XT-3)
Group 2 (Phase 2, n=20)	Standard care with hydrogel KMT10 (geko™ T3)

8.4 Analysis of Study Endpoints

8.4.1 Primary Efficacy Endpoints

The primary efficacy endpoint for the study is:

- the skin adhesion performance of new hydrogel formulation

KM40C used in the geko™ XT-3 device compared to that of the current formulation KMT10 used in the geko™ T3 device. As this is a cohort observation study, this will be a direct comparison between two different patient groups / cohorts (Groups1 and 2) to evaluate efficacy.

Primary endpoint data from this observational study will be summarised descriptively. Continuous parameters may include mean, standard deviation, median, minimum, and maximum.

8.4.2 Secondary Efficacy Endpoints

The secondary endpoints are:

- The incidence of adverse events (AEs), incidence of serious AEs (SAEs), incidence of study treatment related AEs, and the incidence of investigational device related AEs

Secondary endpoint data from this observational study will be summarised descriptively. Continuous parameters may include mean, standard deviation, median, minimum, and maximum.

9.0 Reporting of Adverse Events and Device Deficiencies

9.1 Serious Adverse Events

Once the treating physician becomes aware of a device related adverse event, he/she must report this to the Sponsor, within 24 hours.

Sponsor SAE Contact:

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

The report must include a full description of the event. Additional supporting documentation may be requested and should be provided to Sponsor as and when it becomes available. Such documentation includes but is not limited to lab reports, discharge summary, hospital notes, etc.

The treating physician is responsible for reporting all SAEs in accordance with local laws and regulations.

9.2 Device Deficiencies

Any device deficiencies should be reported via Firstkind's proprietary complaints system.

10.0 Direct Access to Source Data / Documentation

Data will be collected on paper case report forms (CRFs) by appropriately trained delegated members of the patient's healthcare team at the clinical site. Only designated members of the team will be allowed to record and / or correct data in the CRFs. CRFs

will be provided by the Sponsor to the site for completion together with CRF completion guidelines. All CRFs for the study, can be found in Appendix 3 of this protocol. Patients will be assigned a unique study identification number (participant number and initials) and will be identified only by this unique identifier on CRFs 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 authorised by the Sponsor, the local IRB, 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.

11.0 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 visit the centres 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 CRO to inspect all pCRFs 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, quality of life questionnaire, 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 and Storage of Case Report Forms

A CRF must be completed for each participant who has signed an informed consent form. All source documents and CRFs will be completed during or as soon as possible after the patient’s assessments have been completed. The Investigator will review the

CRFs to indicate that, to his / her knowledge, they are complete and accurate. CRFs will be reviewed by the Sponsor's CRA / Monitor, at the time of a monitoring visit, for adherence to completion guidelines and verified against source documents.

Verified / corrected CRFs will then be photocopied and submitted to the Sponsor, leaving the original copies of the CRFs
at the site e.g. CRA / Monitor may hand carry completed CRFs to the Sponsor. If data is not retrieved at the time of the monitoring visit, the Sponsor may want copies of the CRFs submitted via Email or mail. As patients will be identified only by a unique study identification number (participant number and initials), the CRFs are already fully anonymized prior to being sent to the Sponsor. It is the responsibility of both the Investigator and the Sponsor to ensure that all CRFs are stored in a secure location during the course of the study and archived when the study has finished.

11.3 Protocol Amendments

A modification or alteration to this protocol may not be undertaken without first obtaining the concurrence of Sponsor. Both the Lead Investigator and the Sponsor representative must sign and date the amendment prior to implementation. In addition, the Lead 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 Centre, with two exceptions:
1. When necessary to eliminate apparent immediate hazard to the participant; or
2. When the modification involves only logistics or administration.

If a protocol change is proposed for all participants, the following procedure for ra 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.

12.0 Ethics and Regulatory Requirements

The study will be carried out in accordance to the protocol and with principles specified in the current version of the Declaration of Helsinki, the guidelines of Good Clinical Practice, the European Directive on medical devices 93/42/EEC and the ISO Norm 14155 and ISO 14971.

12.1 Institutional Review Board / Independent Ethics Committee

The Principal Investigator will provide the IRB / IEC with all appropriate materials as required by their IRB / IEC, 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 IRB or IEC 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 IRB / IEC 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 IRB / IEC 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
IRB / IEC' 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, Good Clinical Practice and currently applicable regulations. Information regarding any study centres 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 be in compliance with Good Clinical Practice guidelines. The Sponsor and / or designated Contract Research Organisation (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.

13.0 Data Handling and Record Keeping

13.1 Recording, Collection and Transfer 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 patient's assessments have been completed.

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 computerised 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 CRO's 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 Vitaes (CVs)
- Signed ICFs
- Patient screening and randomisation log
- 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.

14.0 References

1. McAdams E., "Surface Biomedical Electrode Technology," Int'1 Med. Device & Diagnostic Indus. pp. 44-48 (Sept./Oct. 1990)

2. Tucker, A., Maass, A., Bain, D., Chen, L-H., Azzam, M., Dawson, H., Johnston, A Augmentation of venous, arterial and microvascular blood supply in the leg by isometric neuromuscular stimulation via the peroneal nerve. 2010 Int J Angiol: Vol 19 No 1 Spring.

Appendices

Appendix 1: Details of Protocol Amendments.

Change	Protocol Version No. and date	Details of changes made
1	Version 1.0 14FEB2020	New document
2	Version 2.0 25AUG2020	Section 1.2 added to expand background information on device mechanism and function Figs 1 & 2 added illustrating device and hydrogel layers Section 1.3 Rationale for testing the new formulation hydrogel expanded. More detail regarding hydrogel formulations and testing in humans added. Clarified that devices are the same they differ only by their hydrogel layer. Section 2.0 Endpoints amended for clarity Section 3.0 Expanded for clarification of study design, more detail added regarding patient groups and new schematic of patient journey added. Rationale for not randomising patients clarified Section 3.1 More detail added to clarify why stroke acute stroke patients are to be recruited instead of using healthy volunteers Section 4.0 Schedule of Events added Section 5.0 Participant Completion and Withdrawal / Discontinuation added Section 6.0 Study Treatments added, method for device allocation also expanded to include rationale for a non-randomised cohort observation study and not a randomised controlled study Section 7.0 Description of Protocol Procedures and Assessments added. Process for obtaining informed consent expanded and assessment of eligibility added to ensure that stroke patients will only be recruited if they can give consent for themselves. Patients with impaired mental capacity will not be recruited on to the study Section 8.0 Statistical Analysis and Sample Size Determination added Section 9.0 Reporting of Adverse Events & Device Deficiencies added Section 10.0 Source Data and Documentation added Section 11.0 Quality Control and Quality Assurance added to clarify management of data Section 12.0 Ethics and Regulatory Requirements added Section 13.0 Data Handling and Record keeping added Appendix 2 Regulatory Approval for the devices added Appendix 3 Sample Case Report Forms added

Appendix 2: Regulatory Approvals.

EMEA Regulatory Clearances by Country	Clinical Indications	Reference	Date
EU/EFTA	– To increase blood circulation, – For the prevention of venous thrombosis – For the prevention and treatment of oedema – For promoting wound healing – For promoting healing of tendon and ligament injuries – For the treatment of venous insufficiency and ischemia	CE Marking GB12/87339 (T3, XT-3)	Oct 2010
Saudi Arabia	– DVT prevention – Increasing blood circulation	MDMA 18020263	Feb 2018
AMERICAS Regulatory Clearances by Country	**Clinical Indications**	**Reference**	**Date**
USA	– stimulation of healthy muscles in order to improve or facilitate muscle performance.	K134001	May 2014
	– Increasing local blood circulation, and – Immediate post-surgical stimulation of the calf muscles to prevent venous thrombosis. – Oedema reduction – Stimulation of the calf muscles to prevent venous thrombosis in non-surgical patients at risk for venous thromboembolism	K133638 K152667 K160299 K163125 (T-2, R-2) K180082 (T-2, R-2) K181059 (T-3) K191113 (T-2, T-3)	Aug 2014) Oct 2015 Apr 2016 Apr 2017 Feb 2018 May 2018 Sep2019
	– Increasing local blood circulation, and – oedema reduction	K193045 (W-2)	Jan 2020

Canada	– To increase blood circulation, – For the prevention of venous thrombosis – For the prevention and treatment of oedema – For promoting wound healing – For promoting healing of tendon and ligament injuries – For the treatment of venous insufficiency and ischemia	License 86311	Jun 2011
Costa Rica	– For use in patients with high risk of venous thrombus-embolism and in patients in which other pharmacological and mechanical prophylaxis methods are impractical or contraindicated	184102	Sep 2016
Ecuador	– To increase blood circulation, – For the prevention of venous thrombosis – For the prevention and treatment of oedema	67680993	Jun 2017
Panama	– To increase blood circulation, – For the prevention of venous thrombosis – For the prevention and treatment of oedema	8-211-2528	Aug 2016
Mexico	– To increase blood circulation, – For the prevention of venous thrombosis – For the prevention and treatment of oedema – For the treatment of venous insufficiency and ischemia	2301C2017	Sep 2017

Brazil	– To increase blood circulation, – For the prevention of venous thrombosis – For the prevention and treatment of oedema – For the treatment of venous insufficiency and ischemia –	80686360256	Dec 2019

Appendix 3: Sample Case Report Forms

Baseline (Day 0)

CASE REPORT FORM	BASELINE (DAY 0)	DATE (DD/MM/YYYY) __ __ / __ __ / __ __ __ __
STUDY SITE:	THE ROYAL STOKE UNIVERSITY HOSPITAL	
PRINCIPAL INVESTIGATOR:	INDIRA NATARAJAN	

SITE NUMBER	0	2	5	PATIENT NUMBER	0			PATIENT INITIALS		

Inclusion Criteria (All answers must be **YES** to include patient in study)

Male or female aged ≥ 18 years	Yes ☐	No ☐
Currently an in-patient with diagnosis of acute stroke	Yes ☐	No ☐
Use of geko™ as a mechanical prophylaxis strategy for venous thromboembolism	Yes ☐	No ☐
Patient understands and is willing to participate in the study and is able to comply with study procedures	Yes ☐	No ☐

Exclusion Criteria (All answers must be **NO** to include patient in study)

Pregnancy or breast feeding	Yes ☐	No ☐
Use of neuro-modulation device other than the geko™ device	Yes ☐	No ☐
Participation in any other clinical study that may interfere with the outcome of either study	Yes ☐	No ☐

Informed Consent

Has the patient freely given written informed consent?	Yes ☐	No ☐
Copy given to participant?	Yes ☐	No ☐
Date consent signed (DD/MM/YYYY)	__ __ / __ __ / __ __ __ __	

Patient Profile

Patient Age	18-30☐	31-40☐	41-50☐	51-60☐	61-70☐	71-80☐	Over 81☐
Gender	Male ☐ Female ☐						
Date of stroke diagnosis (DD/MM/YYYY)	__ __ / __ __ / __ __ __ __						
Current mobility - Is patient able to walk independently?	Yes ☐						
	No ☐						
Adjunctive treatments (if any)	Drugs ☐		Stockings ☐		IPC ☐		None ☐

DAY 0: Application of the geko ™ device

Study Phase		geko™ Device Fitted		Lot Number	Expiry Date
Phase 1		geko™ T3			
Phase 2		geko™ X-T3			

CASE REPORT FORM	BASELINE (DAY 0)	DATE (DD/MM/YYYY) __ __ / __ __ / __ __ __ __
STUDY SITE:	THE ROYAL STOKE UNIVERSITY HOSPITAL	
PRINCIPAL INVESTIGATOR:	INDIRA NATARAJAN	

SITE NUMBER | 0 | 2 | 5 | PATIENT NUMBER | 0 | | | PATIENT INITIALS | | |

How easy was it to apply the geko™ device to the patients leg?

Very Easy	Easy	Difficult	Very Difficult	Impossible
☐	☐	☐	☐	☐

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

_____

How well did the geko™ device stick to the patients leg?				
Very Well Remained attached	**Well** Detached in small area	**Poorly** Detached over large area	**Very Poorly** Detached completely	**Not at all** Would not stick at all
☐	☐	☐	☐	☐

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

_____

Did the patient need any additional fixation to keep the geko™ device in position?			
None	Micropore Tape	Adhesive Accessory	OnPulse™ Knee Strap
☐	☐	☐	☐

If removed was the geko ™ device easily re-applied?		
Yes ☐	No ☐	N/A ☐

Once applied, how comfortable for the patient was the geko™ device?

Very Comfortable	Comfortable	Uncomfortable	Very Uncomfortable	Extremely Uncomfortable
☐	☐	☐	☐	☐

If any discomfort has been indicated, please provide a comment below:

_____

Which setting was the geko™ device set to?

1	2	3	4	5	6	7	8	9	10	11
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

CASE REPORT FORM	BASELINE (DAY 0)	**DATE** (DD/MM/YYYY) __ __ / __ __ / __ __ __ __
STUDY SITE:	THE ROYAL STOKE UNIVERSITY HOSPITAL	
PRINCIPAL INVESTIGATOR:	INDIRA NATARAJAN	

SITE NUMBER	0	2	5	**PATIENT NUMBER**	0			**PATIENT INITIALS**		

Has the patient experienced any Adverse Events since signing the Informed Consent?

Yes ☐ No ☐

If yes, please comment below:

_____

CRF completed by:

Print Name: _____ **Signature:** _____ **Date:** __ __ / __ __ / __ __ __ __

To be completed by Principal Investigator:

I am confident that the information supplied in this case record form is complete and accurate data.

Signature: _____ **Date:** __ __ / __ __ / __ __ __ __

Follow-up Day 1 (please note days1-9 CRFs will be the same)

CASE REPORT FORM	FOLLOW-UP 1 (DAY 1)	
STUDY SITE:	THE ROYAL STOKE UNIVERSITY HOSPITAL	DATE (DD/MM/YYYY) / /
PRINCIPAL INVESTIGATOR:	INDIRA NATARAJAN	

SITE NUMBER	0	2	5	PATIENT NUMBER	0			PATIENT INITIALS		

How many hours did the patient wear the geko™ device for?	____ ____ hours

How well did the geko™ device stick to the patients leg?				
Very Well	**Well**	**Poorly**	**Very Poorly**	**Not at all**
Remained attached ☐	Detached in small area ☐	Detached over large area ☐	Detached completely ☐	Would not stick at all ☐

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

_____

Did the patient need any additional fixation to keep the geko™ device in position?			
None ☐	Micropore Tape ☐	Adhesive Accessory ☐	OnPulse™ Knee Strap ☐

If removed was the geko ™ device easily re-applied?		
Yes ☐	No ☐	N/A ☐

If no, please comment below:

_____

Overall, how comfortable was the geko™ device for the patient to wear?				
Very Comfortable	Comfortable	Uncomfortable	Very Uncomfortable	Extremely Uncomfortable
☐	☐	☐	☐	☐

If any discomfort has been indicated, please provide a comment below:

_____

Did the patient sleep with the device on?	Yes ☐	No ☐

DAY 1: Application of geko ™ device

Current mobility - Is patient able to walk independently? (If YES is selected patient CANNOT continue in the study – please complete EXIT form)	Yes ☐	No ☐

Study Phase		geko™ Device Fitted		Lot Number	Expiry Date
Phase 1		geko™ T3			
Phase 2		geko™ X-T3			

CASE REPORT FORM	FOLLOW-UP 1 (DAY 1)	
STUDY SITE:	THE ROYAL STOKE UNIVERSITY HOSPITAL	DATE (DD/MM/YYYY) / /
PRINCIPAL INVESTIGATOR:	INDIRA NATARAJAN	

SITE NUMBER	0	2	5	PATIENT NUMBER	0			PATIENT INITIALS		

How easy was it to apply the geko™ device to the patients leg?

Very Easy	Easy	Difficult	Very Difficult	Impossible
☐	☐	☐	☐	☐

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

_____

Once applied, how comfortable for the patient was the geko™ device?

Very Comfortable	Comfortable	Uncomfortable	Very Uncomfortable	Extremely Uncomfortable
☐	☐	☐	☐	☐

If any discomfort has been indicated, please provide a comment below:

_____

Which setting was the geko™ device set to?

1	2	3	4	5	6	7	8	9	10	11
☐	☐	☐	☐	☐	☐	☐	☐	☐	☐	☐

Has the patient experienced any Adverse Events since signing the Informed Consent?

Yes ☐ No ☐

If yes, please comment below:

_____

CRF completed by:

Print Name: _____ **Signature:** _____ **Date:** __ __/__ __/__ __ __ __

To be completed by Principal Investigator:

I am confident that the information supplied in this case record form is complete and accurate data.

Signature: _____ **Date:** __ __/__ __/__ __ __ __

Final Follow-up Day 10

CASE REPORT FORM	FINAL FOLLOW-UP 10 (DAY 10)	
STUDY SITE:	THE ROYAL STOKE UNIVERSITY HOSPITAL	DATE (DD/MM/YYYY) __ __ / __ __ / __ __ __ __
PRINCIPAL INVESTIGATOR:	INDIRA NATARAJAN	

SITE NUMBER	0	2	5	PATIENT NUMBER	0			PATIENT INITIALS		

How many hours did the patient wear the geko™ device for?	____ ____ hours

How well did the geko™ device stick to the patient's leg?

Very Well	Well	Poorly	Very Poorly	Not at all
Remained attached ☐	Detached in small area ☐	Detached over large area ☐	Detached completely ☐	Would not stick at all ☐

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

_____

Did the patient need any additional fixation to keep the geko™ device in position?			
None ☐	Micropore Tape ☐	Adhesive Accessory ☐	OnPulse™ Knee Strap ☐

If removed was the geko ™ device easily re-applied?		
Yes ☐	No ☐	N/A ☐

If no, please comment below:

_____

Overall, how comfortable was the geko™ device for the patient to wear?				
Very Comfortable	Comfortable	Uncomfortable	Very Uncomfortable	Extremely Uncomfortable
☐	☐	☐	☐	☐

If any discomfort has been indicated, please provide a comment below:

_____

Did the patient sleep with the device on?	Yes ☐	No ☐

Any other comments – please add below

_____

Day 10 final assessment and patient participation completed. Please complete Exit CRF

CASE REPORT FORM	FINAL FOLLOW-UP 10 (DAY 10)	
STUDY SITE:	THE ROYAL STOKE UNIVERSITY HOSPITAL	DATE (DD/MM/YYYY) __ __ / __ __ / __ __ __ __
PRINCIPAL INVESTIGATOR:	INDIRA NATARAJAN	

SITE NUMBER	0	2	5	PATIENT NUMBER	0			PATIENT INITIALS		

CRF completed by:

Print Name: _____ **Signature:** _____ **Date:** __ __ / __ __ / __ __ __ __

To be completed by Principal Investigator:

I am confident that the information supplied in this case record form is complete and accurate data.

Signature: _____ **Date:** __ __ / __ __ / __ __ __ __

Exit Day 10

CASE REPORT FORM	EXIT	
STUDY SITE:	THE ROYAL STOKE UNIVERSITY HOSPITAL	DATE (DD/MM/YYYY) __ __ / __ __ / __ __ __ __
PRINCIPAL INVESTIGATOR:	INDIRA NATARAJAN	

SITE NUMBER	0	2	5	PATIENT NUMBER	0			PATIENT INITIALS		

Study Exit Date (DD/MM/YYYY)	__ __ / __ __ / __ __ __ __
Date of Last Assessment (DD/MM/YYYY)	__ __ / __ __ / __ __ __ __
Last Assessment Completed	Baseline ☐ Follow-up 1 ☐ Follow-up 2 ☐ Follow-up 3 ☐ Follow-up 4 ☐ Follow-up 5 ☐ Follow-up 6 ☐ Follow-up 7 ☐ Follow-up 8 ☐ Follow-up 9 ☐ Follow-up 10 ☐
Reason for Exit from Study	Study completed ☐ Lost to follow-up ☐ Non-compliance ☐ Medical contraindication ☐ Consent withdrawn ☐ Other** ☐
**Additional explanation required:	

CRF completed by:

Print Name: _____ Signature: _____ Date: __ __ / __ __ / __ __ __ __

To be completed by Principal Investigator:

I am confident that the information supplied in this case record form is complete and accurate data.

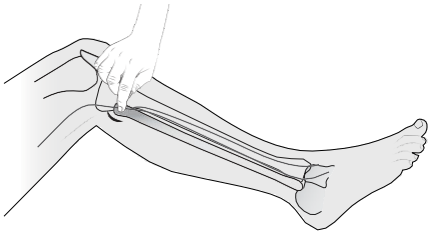
Signature: _____ Date: __ __ / __ __ / __ __ __ __

Appendix 4: Instructions for Use and Fitting Instructions geko™ X-T3

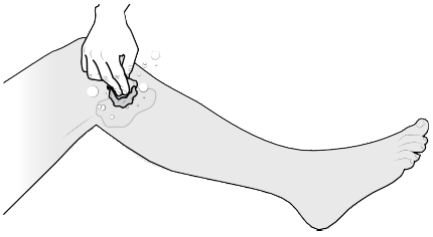
geko™ XT

gekodevices.com

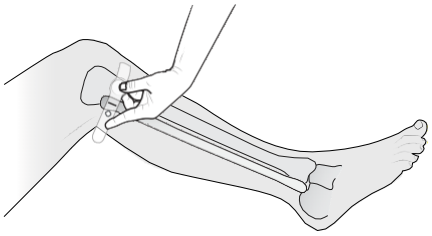
1 Location



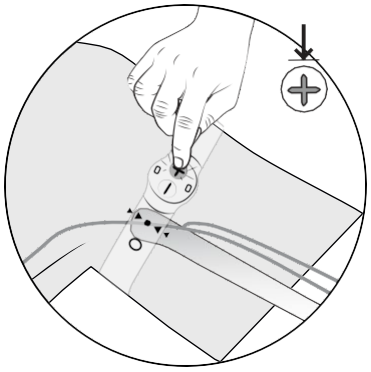
2 Cleaning



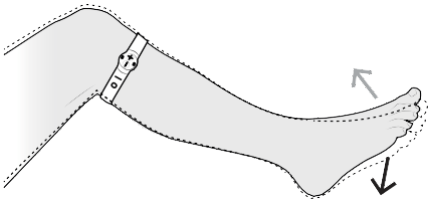
3 Fitting



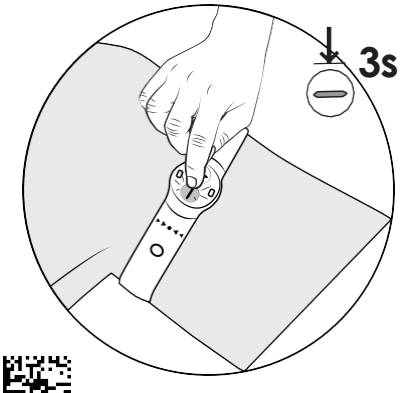
4 Turning On



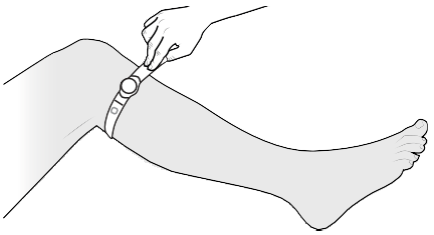
5 Settings



Switching Off



7 Removing



The geko™ device is a neuromuscular electro-stimulation medical device and its intended use is:

- to increase blood circulation
- for the prevention of venousthrombosis
- for the prevention and treatment of oedema
- for the treatment of venous insufficiency and ischemia

The device works by increasing blood circulation by stimulating the common peroneal nerve.

It is to be used on a single patient, in hospital, clinic and home environments. Apply to the affected leg or legs as advised by your Healthcare Professional (e.g. Nurse or Doctor). Patients should be trained in the positioning and operation of the device.

The geko device is intended for up to 24 hours continuous use, until it is no longer needed.
It may be removed for short periods of time when washing or having various tests (see warnings and precautions). Each device is single use and should be replaced every 24 hours, the device has an additional 6 hours run time.

Read this document fully before use and use only as instructed. Improper use of this device can be dangerous. Do not switch on unless correctly attached to the patient.

If assistance is required or to report difficulties, unexpected operation or events, contact the manufacturer. Visit the website for further advice and usage tips.

► Fitting Instructions

1. The marker line ▸▸●◂◂ on the geko device should line up with the fibula head, a round lump below the knee on the lower leg. Ask your healthcare provider if you need help (e.g. nurse or doctor).
2. It should be applied to clean, dry skin. If there is too much hair in the area it should be removed using trimmers or clippers. Do not shave as this may cause irritation. Wash the skin in the area where the device will be fitted with mild soapy water, rinse, and dry thoroughly; do not apply any moisturizer.
3. Remove the film from the geko device and place the marker line ▸▸●◂◂ over the fibula head (round lump). Attach the short end round the front of the leg and the longer end towards the back of the leg. The geko device should not be loose, peel off one end and tighten if needed. When correctly fitted, the ⊕ button will always be at the front of the leg.
4. To turn on, use a short press of the ⊕ button.
5. There are 11 settings, shown by the number of times the light flashes before a pause. Use the ⊕ button to increase the setting and ⊖ button to decrease.

When working properly geko will cause a visible movement of the muscles in the lower leg, moving the foot out and up, which should continue throughout the whole treatment.

6. To turn it off, hold ⊖ button down for 3 seconds. When the button is held the light will flash quickly and when turned off the flashing will stop.
7. Remove carefully in one piece, to avoid damaging the skin.

If stimulation is not achieved geko can also be fitted in alternative positions, see the website for further details.

► Side Effects

Skin Inflammation or Irritation

In some cases, skin inflammation or irritation can develop in the contact area: either remove the device or re-attach in the alternative fitting positions. If the condition persists or recurs, obtain specialist medical advice before resuming use.

► Warnings

Seek specialist medical opinion if the patient is/has:

- Implanted electronic devices (e.g. a cardiac pacemaker).
- Recently diagnosed or suspected DVT.
- Pregnant or breastfeeding.
- Diagnosed heartcondition.
- Epilepsy.
- Had recent surgery where muscle contractions may disrupt thehealing process.
- Used the device for 28 consecutive days.

Do not use:

- During any activity in which involuntary muscle contractions may put the user or others at risk of injury (e.g. Driving or operating machinery).
- When bathing or showering – switch off the device and remove temporarily.
- If the device has been worn by another individual – this will carry risk of infection.
- If packaging is open or damaged.
- If device is damaged.

Device should not be used on the following areas of the body:

- Head.
- Eyes.
- Mouth.
- Neck (especially the carotidsinus).
- On the chest, upper back or crossing over the heart. This may increase the risk of cardiac fibrillation.

Do not apply over or near the following:

- Sore, infected or inflamed areas, broken skin or skin eruptions, e.g. phlebitis, thrombophlebitis, varicose veinsetc.
- Cancerouslesions.

INSTSKY10X/R1 - December 2019

Do not use in proximity of the following equipment/environments (which could result in the possible degradation of the performance of geko):

- Short wave/ microwave equipment (i.e. within 1m).
- Portable RF communications equipment (including peripherals such as antenna cables and external antennas) (i.e. within 30cm).
- Heat sources, such as fires or radiant heaters.

Do not use in oxygen rich environments.

Use on children - the safety of the device has not been tested in children; we do not recommend using the device on children.

► Precaut ions

- Keep out of the reach of children and pets.
- Do not place the geko device in the mouth; it is a choke and potential allergic hazard.
  If geko or any component is swallowed seek IMMEDIATE medical assistance. Serious harm could be caused if the battery is swallowed.
- No modification of this equipment is allowed.
- Excessive force may damage the device.
- MRI -The device should be removed before the patient undergoes MRI as it contains ferromagnetic components.
- ECG -The device should be switched off during ECG monitoring using leg electrodes as it may interfere with ECG leg electrode signals.

► Storage and Operat ion

When storing geko keep it in the protective foil pouch. It can be stored in a temperature range of -25°C to 40°C, but we recommend storing the device up to 30°C.

► Classification

The device is internally powered by a non-replaceable CR2032 lithium ion coin cell battery. The battery is intended for continuous operation.

Type BF applied part – for direct electrical contact to patient but not direct cardiac application. The whole device is the applied part.

► Output Speci ficat ions

The device provides square wave, asymmetric, charge balanced stimulation pulses at a rate of 1Hz. The pulses are of a constant current between 27mA and 54mA, and with pulse widths between 35µs and 560µs, according to the stimulation level set. The stimulation intensity increases progressively by increasing the electrical charge in each pulse. There are 11 settings in total. For further information including operating specifications visit the website.
The software revision level is identifiable through the Lot number.

► EMC Declarat ion

Use of the geko device adjacent to other electrical equipment should be avoided because it could result in improper operation. If such use is necessary, geko and the other electrical equipment should be observed to verify that they are operating normally. The geko device is certified to EN 60601-1-2:2015 regarding Electromagnetic Compatibility.

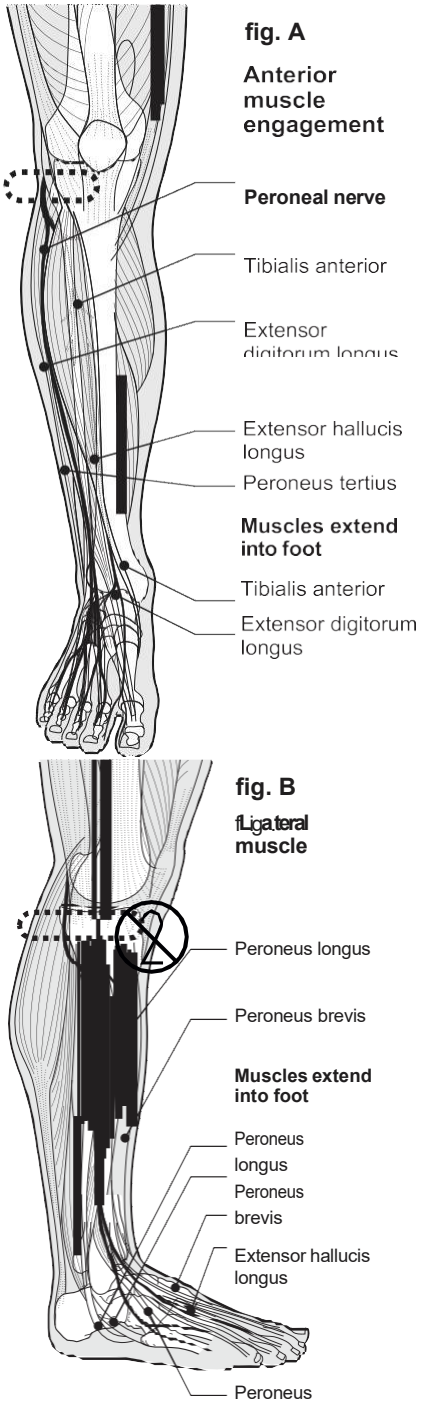
Medical Electrical Equipment needs special precautions regarding EMC and needs to be put into service according to the EMC information provided on the website. The geko device may switch ff if exposed to high levels of electromagnetic disturbance.

► Disposal

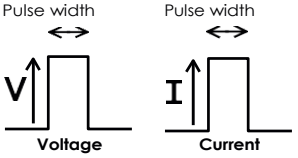
The geko device does not contain any toxic or environmentally hazardous materials. After use it may be potentially contaminated or infected because it has been in contact with skin for several hours, and so needs to be disposed of with care. Batteries must be disposed of in accordance with any local legislation. Some hospital and clinics will have specific requirements for disposal of used medical devices. If used at homegeko may be disposed of in your general waste if regulations permit. For ease of disposal the electrodes may be removed with scissors if necessary. The battery can be removed by breaking open the housing and forcing out. See the website for guidance. Do not incinerate the device.

Symbols

	Type BF applied part
LATEX	Product not manufactured with Latex
	Single use only – use only on one patient for a single course of treatment
LOT	Lot number
REF	Catalogue number
DI	Device identifier
	Expiry date – do not use after this date
IP22	Ingress protection rating 22
	Manufactured by
	Do not use if package is damaged
	See Instructions for Use
CE 1639	CE Mark of Conformity
-25°C +40°	Storage and transportation temperature range whilst within packaging
70kPa 106kPa	Storage and transportation atmospheric pressure range whilst within packaging
0% 93%	Storage and transportation humidity range whilstwithin packaging



Output waveform



Repetition rate: 1Hz

firstkind *living science* OnPulse™ TECHNOLOGY **XT-3**

Firstkind Limited
Hawk House
Peregrine Business Park
Gomm Road
High Wycombe
HP13 7DL, United Kingdom
T: +44 (0)1494 572040
*Firstkind Ltd is a wholly owned subsidiary of Sky Medical Technology Limited.

Protocol v2.0 20200929

Final Audit Report 2020-10-27

Created:	2020-09-30
By:	Marie-Therese Targett (Marie-Therese.Targett@firstkindmedical.com)
Status:	Signed
Transaction ID:	CBJCHBCAABAAe2wVQCAqznl7Egc75Ou_DD5Di6j0eLIM

"Protocol v2.0 20200929" History

Document created by Marie-Therese Targett (Marie-Therese.Targett@firstkindmedical.com)
2020-09-30 - 1:09:31 PM GMT- IP address: 81.153.227.198

Document emailed to Rachel Fallon (rachel.fallon@firstkindmedical.com) for signature
2020-09-30 - 1:11:17 PM GMT

Email viewed by Rachel Fallon (rachel.fallon@firstkindmedical.com)
2020-09-30 - 2:56:45 PM GMT- IP address: 82.69.55.58

Document e-signed by Rachel Fallon (rachel.fallon@firstkindmedical.com)
Signature Date: 2020-09-30 - 2:57:21 PM GMT - Time Source: server- IP address: 82.69.55.58

Document emailed to Kieron Day (kieron.day@firstkindmedical.com) for signature
2020-09-30 - 2:57:32 PM GMT

Email viewed by Kieron Day (kieron.day@firstkindmedical.com)
2020-09-30 - 4:26:58 PM GMT- IP address: 82.1.254.248

Document e-signed by Kieron Day (kieron.day@firstkindmedical.com)
Signature Date: 2020-10-27 - 5:22:28 PM GMT - Time Source: server- IP address: 82.1.254.248

Agreement completed.
2020-10-27 - 5:22:28 PM GMT