Protocol Approval Page

Study No: BMR-13-1001

A single-blind, multi-centre, randomised, controlled, non-inferiority, clinical study to assess the safety and performance of the Neurotech Vital Compact device compared to the itouch Sure Pelvic Floor Exerciser for the treatment of stress urinary incontinence in female patients

Version 2.0

The undersigned have read this study protocol and hereby confirm that, to the best of their knowledge, it accurately describes the study to be conducted.

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Managing Director
Expedite Research

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Signature Date

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Signature Date

Study Protocol

A single-blind, multi-centre, randomised, controlled, non-inferiority, clinical study to assess the safety and performance of the Neurotech Vital Compact device compared to the itouch Sure Pelvic Floor Exerciser for the treatment of stress urinary incontinence in female patients

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Version 2.0 27 March 2015

Sponsor

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This study is considered a Nonsignificant Risk Device Study and is being conducted in accordance with the abbreviated Investigational Device Exemption (IDE) requirements set forth in 21 CFR 812.2(b).

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Investigator Approval Page

I, the undersigned, have read and understood the clinical study, and agree on the contents. The Study Protocol and the Investigator's Agreement will serve as a basis for cooperation in the clinical study.

Site No:

Site Address:

Principal Investigator:

Name: _____

Title: _____

_____ _____
Signature Date

Abbreviations

AE	Adverse Event
ALARP	As low as reasonable possible
CE-mark	Certified in Europe
cm	Centimeter
EC	Ethics Committee
ES	Electrical stimulation
FMEA	Full Failure Mode Effects Analysis
FDA	Food & Drug Administration
g	Gram
GCP	Good clinical practice
Hz	Herz
IDE	Investigational Device Exemption
I-QOL	Incontinence Quality of Life
IRB	Institutional Review Board
ITT	Intent-to-treat population
Kg	Kilogram
LOCF	Lost observation carried forward
mA	Milliampere
MAUDE	Manufacturer and User Facility Device Experience
MESA	Medical, Epidemiologic and Social Aspects of Aging Urinary Incontinence Questionnaire
µs	Micro second/milli second
NMES	Neuromuscular electrical stimulation
PF	Pelvic floor
PGI-I	Patient global impression of improvement
PISQ-IR	Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire
PP	Per Protocol population
rms	Root Mean Square
SAE	Serious Adverse Event
SAP	statistical analysis plan
SD	Standard deviation
SUI	Stress urinary incontinence
TENS	Transcutaneous electrical stimulation
UADE	Unanticipated adverse device effect
W	Watt

1 Study Synopsis

Title:	A single-blind, multi-centre, randomised, controlled, non-inferiority clinical study to assess the safety and performance of the Neurotech Vital Compact device compared to the itouch Sure Pelvic Floor Exerciser for the treatment of stress urinary incontinence in female patients.
Regulatory Status:	The itouch Sure Pelvic Floor Exerciser is cleared by FDA through the 510 (k) premarket notification process (K103698) in the USA. The study is classed as a Non-Significant Risk Device Study and the study will be conducted in accordance with the abbreviated Investigational Device Exemption (IDE) requirements set forth in 21 CFR 812.2(b).
Objectives:	To demonstrate that the safety and performance profile of the Neurotech Vital Compact (delivering electrical stimulation through external electrodes) is equivalent to the itouch Sure Pelvic Floor Exerciser (delivering electrical stimulation through an internal vaginal probe).
Primary Endpoint:	The primary endpoint is defined as the proportion of subjects considered to have achieved at least a 50% reduction in pad weight following a provocative pad weight test at 12 weeks compared to baseline.
Key Secondary Endpoints:	The following key secondary endpoints will each be analysed, for superiority, at a 5% two-sided significance level with a view to support labelling. In order to control the type I error rate the endpoints will be analysed in the following hierarchy (Statistical Plan will supply further details). If any endpoint in the sequence fails to show a statistically significant difference then the inference is that there is insufficient evidence both for that endpoint and the subsequent endpoints in the hierarchy. 1. Between group comparison of mean change, with respect to baseline, in urine leakage in a provocative pad weight test at Week 12; 2. Within Neurotech Vital Compact group estimate of mean change, with respect to baseline, in urine leakage in a provocative pad weight test at Week 12; 3. Between group comparison of mean change, with respect to baseline, in urine leakage in the 24-hour pad weight test at Week 12; 4. Within Neurotech Vital Compact group estimate of mean change, with respect to baseline, in urine leakage in the 24-hour pad weight test at Week 12; 5. Between group comparison of mean change, with respect to baseline, in the number of incontinence

	episodes/day recorded using a 7-day voiding diary at Week 12; 6. Within Neurotech Vital Compact group estimate of mean change, with respect to baseline, in the number of incontinence episodes/day recorded using a 7-day voiding diary at Week 12; 7. Between group comparison of the mean improvement, with respect to baseline, in Incontinence Quality of Life Questionnaire (I-QOL) score at Week 12; 8. Within Neurotech Vital Compact group estimate of mean improvement, with respect to baseline, in Incontinence Quality of Life Questionnaire (I-QOL) score at Week 12; 9. Between group comparison of mean change, with respect to baseline, in the number of pads used/day recorded using a 7-day voiding diary at Week 12; 10. Within Neurotech Vital Compact group estimate of mean change, with respect to baseline, in the number of pads used/day recorded using a 7-day voiding diary at Week 12; 11. Between group comparison of the proportion of subjects achieving dryness at Week 12 (<1g on the provocative pad weight test).
Other Secondary Endpoints:	Other secondary endpoints that will be evaluated at 4 weeks and 26 weeks are as follows: • Proportion of subjects considered to have achieved significant improvement, defined as a greater than 50% reduction in pad weight, from baseline on the provocative pad weight test. • Urine leakage on the provocative pad weight test (following standardized bladder-filling protocol). • Urine leakage experienced by the subject at home in the 24-hour pad weight test; • Incontinence episodes/day recorded using a 7-day voiding diary; • Proportion of subjects achieving dryness (<1g on the provocative pad weight test) • Improvement in quality of life assessed using the Incontinence Quality of Life Questionnaire (I-QOL); • Number of pads/day recorded using a 7-day voiding diary; • Dryness, defined as a pad weight of less than 1.3g on the 24-hour pad weight test (including an evaluation at 12 weeks); • Proportion of subjects considered to have achieved

	significant improvement, defined as a greater than 50% reduction in pad weight, from baseline on the 24-hour pad weight test (including an evaluation at 12 weeks). Other data that will be evaluated are as follows: • Proportion of subjects achieving dryness at Week 12 in each group (<1g on the provocative pad weight test). • Within Neurotech Vital Compact group estimate of mean change, with respect to baseline, in sexual function as measured by the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-IR) at Week 12; • Between group comparison of mean change, with respect to baseline, in sexual function as measured by the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-IR) at Week 12; • Within Neurotech Vital Compact group estimate of patient response to the Patient Global Impression of Improvement (PGI-I) at Week 12. • Between group comparison of patient response to the Patient Global Impression of Improvement (PGI-I) at Week 12; • Safety in relation to adverse events and device deficiencies reported; • Evaluation of reduction in urine leakage on the provocative pad weight test in relation to the mean intensity of the stimulation delivered during the 12-week treatment programme; • Evaluation of the reduction in urine leakage on the provocative pad weight test at Week 12 in relation to the BMI category (underweight/normal/overweight/obese) of the subjects; • Evaluation of the reduction in urine leakage on the provocative pad weight test at Week 12 in relation to the baseline severity of stress urinary incontinence of the subjects; • Device compliance of the Neurotech Vital Compact device with the treatment protocol during the 12-week treatment programme; • Device compliance of the itouch Sure Pelvic Floor Exerciser with the treatment protocol during the 12-week treatment programme;
Indication:	Stress urinary incontinence defined as ‘complaint of involuntary leakage on effort or exertion, or on sneezing

	and coughing' (International Continence Society).
Inclusion Criteria:	• Subjects who are female and at least 18 years of age, and not more than 65 years of age. • Subjects who have signed an informed consent form prior to any study related activity. • Subjects who have previously tried and failed to improve their condition using Kegel exercises. • Subjects who have been clinically diagnosed with stress urinary incontinence and demonstrate a greater than or equal to 3g urine leakage and a less than or equal to 90g urine leakage (≥3g and ≤ 90g) following a bladder-filling protocol and then a standardised stress test (provocative pad weight test) at the baseline assessment. • Subjects who score 9 or less (≤9) out of 18 for the Urge Incontinence Questions and are confirmed as having predominant stress urinary incontinence on the Medical, Epidemiologic and Social Aspects of Aging Urinary Incontinence (MESA) Questionnaire completed at the screening assessment. • Subjects with a Body Mass Index of ≤ 35 kg/m^2. • Subjects of child-bearing potential who are using a highly effective contraceptive method (established use of oral, injected, implanted hormonal method of contraception or barrier method of contraception with spermicide). • Subjects who are willing not to seek any other treatment for stress incontinence during the study period. • Subjects who are able to give voluntary, written informed consent to participate in this study and from whom consent has been obtained. • Subjects who are able to understand this study and are willing to complete all the study assessments.
Exclusion Criteria:	• Subjects who have an existing medical condition that would compromise their participation in the study, e.g. reduced sensory perception in the contact area of the stimulation electrodes; scars or vaginal tissue wounds, lesions or inflamed/infected areas in the contact area of the stimulation electrodes; vaginal bleeding between menstrual periods; uncontrolled diabetes. • Subjects who have a physical condition that would make them unable to perform the study procedures, e.g. pelvic or hip surgery within the past 6 weeks. • Subjects who have been diagnosed with Chronic Obstructive Pulmonary Disease (COPD). • Subjects with a history of an underlying neurological condition, e.g. Multiple Sclerosis, Parkinson's disease,

	epilepsy. • Subjects with any bladder abnormality that would affect the urinary flow through the lower urinary tract including symptoms of a urinary tract infection, abnormal bladder capacity (e.g., >300 cc), post void residual volume >200 cc, spastic bladder, vesico-ureteral reflux or bladder stones. • Subjects with a blood clotting disorder or who are taking anti-coagulant medications. • Subjects who have previously had any uro-gynaecological related surgery that would affect the pelvic floor muscles or urinary flow through the urethra (excluding hysterectomy). • Subjects who have previously had pelvic floor radiation. • Subjects who have previously been treated for stress incontinence with injectable bulking agents and/or vaginal probes within the past 6 months. • Subjects with a clinical diagnosis of prolapse greater than Stage 2. • Subjects who are pregnant or could be pregnant. • Subjects who are less than 6 months post-partum or who are lactating. • Subjects who have any conductive intra-uterine devices or metal implants in the pelvic area, including hip and lumbar spine. • Subjects with pelvic pain or fibromyalgia or paravaginal defect. • Subjects with an active implanted medical device (e.g. pacemaker, insulin pump) or conditions that may be adversely affected by electrical stimulation (e.g. cardiac arrhythmias). • Subjects with a current or active history of pelvic cancer and/or subjects with a life expectancy of less than 12 months. • Subjects who are currently involved in any injury litigation claims. • Subjects who have participated in a clinical study in the last 3 months or any previous clinical study with Bio-Medical Research Ltd. • Subjects who have been committed to an institution by virtue of an order issued either by the courts or by an authority.
Study Sites:	Approximately 12 USA sites
Number of subjects planned:	Approximately 180 subjects (90 subjects per group).
Target population:	The patient population will be females with stress incontinence.

Study duration:	Subjects included in the clinical study will be evaluated at screening, on enrolment into the study (baseline) and during the 12-week treatment programme at 4 and 12 weeks. Telephone calls will be made at 1 week to check on the patient's progress during their initial use of the device. Subjects will also be evaluated at 26 weeks following the commencement of the treatment. The recruitment period is estimated as 12 months with an anticipated study duration of 28 months.
Study device/procedure:	Neurotech Vital Compact device is CE approved as a Class IIa Device in Europe, in line with Medical Device Directive 93/42/EC as amended by 2007/47/EC. FDA has determined that Neurotech Vital Compact is a Non-Significant Risk device. The study is therefore classed as a Non-Significant Risk Device Study and accordingly it will be conducted in accordance with the abbreviated Investigational Device Exemption (IDE) requirements set forth in 21 CFR 812.2(b) in the USA.
Comparator device/procedure:	The itouch Sure Pelvic Floor Exerciser (manufactured by TensCare Ltd., UK) is cleared by the FDA through the 510 (k) premarket notification process (K103698) in the USA.
Device treatment program:	Subjects who are considered eligible to participate in the clinical study and give consent will be randomised to complete either a 12-week treatment programme with the Neurotech Vital Compact or a 12-week treatment programme with the itouch Sure Pelvic Floor Exerciser. The 12-week treatment programme will be completed by the subjects at home with the device in accordance with the device Instructions for Use. The Neurotech Vital Compact is used for five days each week (each daily session of 30 minutes) with two rest days taken within a 7 day week period, for the 12-week period. The itouch Sure Pelvic Floor Exerciser is used once per day (each daily session of 20 minutes) during the 12-week period.
Performance assessments:	Performance will be assessed by: provocative pad weight test following a standardized bladder-filling protocol verified by ultrasound bladder scanning; 24-hour pad weight test; Incontinence Quality of Life Questionnaire (I-QOL); incontinence episodes/day and number of pads used/day from 7-day voiding diary; and assessment of 'dryness' and 'significantly improved'.
Safety assessments:	Safety will be assessed in terms of severity, frequency and seriousness of any adverse events or adverse device effects.
Concomitant Medication and/or	• Subjects may use any medication that has an effect upon urinary output function if a) the medication has

Treatments:	been used for at least 4 weeks prior to study enrolment and b) the medication regimen is not changed during the 12-week device treatment program • No device re-treatment will be allowed during the subject's participation in the study.
Single-Blind Status:	The study is considered single-blind as the subjects will be randomised to the Neurotech Vital Compact device or the itouch Sure Pelvic Floor Exerciser (ratio 1:1). Since the two devices will be described in detail in the patient information sheet, the patients will know which device they have been randomised to i.e. the Neurotech Vital Compact device delivers electrical stimulation through external electrodes and the itouch Sure Pelvic Floor Exerciser delivers electrical stimulation through an internal vaginal probe. It is not believed this will introduce any bias since patients would not have an expectation that either device is better than the other. The site personnel who allocate the devices, perform the device training at baseline and monitor the device compliance at the follow-up visits will not be blinded, but the personnel who perform the follow-up assessments will be blinded. The statistical analysis will be blinded until data base lock Verification to ensure that this blinding is maintained will be assessed at the monitoring visits.
<u>STUDY ASSESSMENTS</u> **Visit 1: Screening**	• Demographic data including height and weight. • Medical history including details of stress urinary incontinence, previous bladder/kidney infections and any current/previous urological treatments. • Physical examination including a detailed urological examination to assess urinary symptoms and symptoms of bowel function, sexual function and pelvic organ prolapse. • Details of all medication (over-the-counter and prescription) and dietary/herbal supplements in the previous 6 months. • Urine pregnancy test to confirm subject is not pregnant (women of child-bearing potential only). • Complete the Medical, Epidemiologic and Social Aspects of Aging Urinary Incontinence (MESA) Questionnaire (patient quality of life questionnaire). • Complete a standardized stress test to evaluate amount of urine lost following a standardized bladder-filling protocol verified by ultrasound (provocative pad weight test). The data from this test will not be used for

	analysis purposes, it is only to allow patients to practise the stress test. Further details are provided in Appendix I. • Record any cough or cold symptoms. • Record any adverse events. Prior to leaving the clinic, subjects will also be provided with the following: • A 7-day voiding diary to complete prior to Visit 2 (baseline) appointment. • Pre-weighed incontinence pads in a sealed bag to complete the 24-hour pad collection for three days prior to the Visit 2 (baseline) appointment. Any subjects menstruating during this time will also be asked to record this on the voiding diary. Any subjects who have sexual intercourse during this time will be asked to expel any fluid post-intercourse and will be asked also to record this on the voiding diary.
Assessments Visit 2: Baseline	• Complete the Incontinence Quality of Life Questionnaire (I-QOL) (patient quality of life questionnaire). • Complete the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-IR) • Complete a standardized stress test to evaluate amount of urine lost following a standardized bladder-filling protocol verified by ultrasound bladder scanning (provocative pad weight test). This is used to determine eligibility to participate. Further details are provided in Appendix I. • Number of incontinence episodes/day from 7-day voiding diary. • Number of pads used/day from 7-day voiding diary. • Mean weight of urine lost during three consecutive 24-hour periods at home (difference in post- and pre-weight incontinence pads) (24-hour pad weight test). • Record any medication use since the last visit. • Record any cough or cold symptoms since the last visit. • Record any adverse events since the last visit. • Subject training on use of device and complete one session in clinic Prior to leaving the clinic, subjects will also be provided with the following: • A 7-day voiding diary to complete prior to Visit 3 appointment. • Pre-weighed incontinence pads in a sealed bag to complete the 24-hour pad collection for three days prior to the Visit 3 appointment. Any subjects menstruating during this time will also be asked to record this on the

	voiding diary. Any subjects who have sexual intercourse during this time will be asked to expel any fluid post-intercourse and will be asked also to record this on the voiding diary.
Telephone call: 1 week	• Telephone call to check the patient is happy with the treatment set up and using the device as per the instructions and to assess if there any adverse events and/or changes to medication.
Assessments Visit 3: 4 weeks **Assessments Visit 4: 12 week** **Assessments Visit 5: 26 week**	• Urine pregnancy test to confirm subject is not pregnant (pre-menopausal subjects only) (Week 4 assessment only). • Complete the Incontinence Quality of Life Questionnaire (I-QOL) (patient quality of life questionnaire). • Complete Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-IR) (Week 12 assessment only). • Complete Patient Global Impression of Improvement (PGI-I) (Week 12 assessment only). • Complete a standardized provocative stress test to evaluate amount of urine lost following a standardized bladder-filling protocol (provocative pad weight test) • Number of incontinence episodes/day from 7-day voiding diary. • Number of pads used/day from 7-day voiding diary. • Mean weight of urine lost during a three day 24-hour period at home (difference in post- and pre-weight incontinence pads) (24-hour pad weight test). • Record any medication use since the last visit. • Record any cough or cold symptoms since the last visit. • Record any adverse events since the last visit. • Data from the device will be downloaded to determine stimulation intensity and duration of treatment were completed according to the planned treatment programme (Week 4 and 12 assessment only and completed by unblinded study personnel). At Visit 4, subjects will also be provided with training and an instruction flyer for pelvic floor exercises (Kegel exercises). Participants will be advised to perform Kegel exercises from 12 weeks to the 26 weeks follow-up. Prior to leaving the clinic at Visit 3 and 4, subjects will also be provided with the following: • A 7-day voiding diary to complete prior to next appointment. • Pre-weighed incontinence pads in a sealed bag to complete the 24-hour pad collection for three days prior to the next appointment. Any subjects menstruating

	during this time will also be asked to record this on the voiding diary. Any subjects who have sexual intercourse during this time will be asked to expel any fluid post-intercourse and will be asked also to record this on the voiding diary.

Personnel Involved in the Study

Role	Name
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Technical Director:	Dr Conor Minogue Technical Director Bio-Medical Research Ltd
Regulatory Affairs:	Brendan McCormack Quality Manager Bio-Medical Research Ltd
Sponsor Medical Advisor:	Dr Patricia Smith Chief Executive Officer (CEO) Bio-Medical Research Ltd
Statistician:	Diane Tipping, MS Senior Director, Biostatistics Prosoft Clinical
Data Management:	Jeff Harbaugh Senior Manager, Data Management Prosoft Clinical

2 Introduction

2.1 Background

The International Continence Society (ICS) defines urinary incontinence as the involuntary loss of urine that is a social or hygienic problem and one that is objectively demonstrable. Stress urinary incontinence (SUI) is urinary incontinence during physical activities that increase intra-abdominal pressure such as coughing, sneezing or lifting. Stress urinary incontinence often leads to patients limiting their participation in social activities, which in turn has a subsequent impact on a person's quality of life. While some seek surgical intervention, physical therapy is seen as the first treatment option in this often under-reported condition. There are a number of treatments available to the therapist. Most women treated for stress urinary incontinence will have been introduced to pelvic floor muscle training exercises however adjunctive approaches such as biofeedback, vaginal weights and electrical stimulation are also treatment options.

Bo (2004) described the goal of physical therapy in the treatment of stress urinary incontinence as an attempt to improve pelvic floor muscle function by increasing strength, coordination, speed and endurance. The effect of these training adaptations is the maintenance of an elevated position of the bladder neck during raised intra-abdominal pressures and a subsequent adequate urethral closing force as described by Ashton-Miller et al. (2001).

Castro (2008) reported a significant decrease in urine lost during pad tests and in the number of stress urinary episodes, as well as a significant improvement in the quality of life, in subjects who underwent a programme of pelvic floor exercises, electrical stimulation or use of vaginal weights compared to a control group. In this study there was no observed difference between treatment groups suggesting each intervention to be equally effective. While it is reported that these interventions can be effective in the treatment of stress urinary incontinence the issues of technique, comfort of treatment and compliance with treatment are often limiting factors that impact patient outcomes. This has motivated the search to identify an electrical stimulation treatment modality that ensures satisfactory recruitment of the pelvic floor muscles and that is easy to administer and more comfortable for the patient. This resulted in the development of a novel electrical stimulation (ES) device that includes a wired garment which locates a set of skin contact electrodes around the pelvic area.

A pilot study (n=9) with this novel ES system (first generation device called UCD RS device) conducted at University College Dublin has shown improved outcomes (Maher and Crowe, 2008) following an 8 week treatment programme. In particular, subjects using the ES system achieved a significant decrease in symptoms when compared to the control group. At Week 1 all subjects could perform appropriate volitional contractions of their pelvic floor muscle in standing but more importantly there was a reported 87.43% decrease in leakage. At Week 8, subjects reported a 97.71% decrease in leakage ($P<0.01$) and the IIQ-7 and Modified Oxford scores also changed significantly ($P<0.01$).

A pilot study (n=19) has recently been completed in Germany at St. Hedwig Krankenhaus (Soeder and Tunn, 2013) which looked at a 12 week treatment programme with the second generation device (called Inko RS device). Sixteen subjects completed baseline measurements while 14 and 13 subjects completed the 12-week and 26-week assessments, respectively. Mean (SD) urine leakage on the 1-hour and 24-hour pad weight tests improved ($p<0.05$) from 41.6g (43.92) to 5.8g (13.19) and 21.8g (19.41) to 5.6g (5.16) respectively after completion of the 12 week programme. These improvements were substantially retained at the 26 week point. In

addition, 57% of subjects were classified as dry at the 12 week point, based on a 1-hr stress test result of less than 2g. This coincided with enhanced quality of life scores during and following the intervention period. Secondary measures also identified a reduction ($p<0.05$) in the number of leakages experienced per day, from 2.5 (2.81) at baseline to 1.2 (2.28) at 26 weeks with an improvement in the modified Oxford scale. One patient suffered an allergic skin reaction to the hydrogel electrodes.

A randomised study (n=51) is currently ongoing in Germany at three sites with the third generation device (Neurotech Vital device). The purpose of this study is to test whether a 12-week programme with the Neurotech Vital device significantly improves the symptoms of stress incontinence in female subjects compared to a modified Neurotech Vital device (sham device). In addition, the long term effects of a 12-week treatment with the Neurotech Vital device will be evaluated.

The purpose of this proposed study is to conduct a pivotal study comparing the Neurotech Vital Compact device (fourth generation device) to an FDA 510(k) approved predicate device (itouch Sure Pelvic Floor Exerciser) to generate clinical date to submit to the FDA to obtain regulatory clearance.

2.2 Rationale of Study Population

The clinical study is designed to be prospective to ensure that the population is representative of the type of population for which the Neurotech Vital Compact device is intended to treat. Subjects will be drawn from clinics focusing on this type of treatment. These clinics may advertise using an approved advertisement to recruit additional subjects.

The patient population will be female patients identified by the clinic as seeking treatment for urinary stress incontinence. These patients will have previously tried volitional pelvic floor muscle exercises and have been unsuccessful in their attempts to alleviate their symptoms.

2.3 Rationale of Neurotech Vital Compact Device

The research evidence supporting the use of electrical stimulation (ES) in pelvic floor neuromuscular rehabilitation for stress urinary incontinence (SUI) is somewhat equivocal. While some studies (Castro, 2008; Sand, 1995) have shown a beneficial effect of ES that is comparable to other conservative interventions, there are other studies which have failed to show a clear benefit (Bo, 1999). There has been a lack of homogeneity in the study designs and most especially in the equipment used. Most studies have used one or other of the commercially available trans-vaginal ES systems and little information has been provided as to the effectiveness of the particular system used in activating the target muscle group. A further difficulty with transvaginal ES is that some patients object to using the intra-vaginal probe electrodes. A novel form of ES for pelvic floor stimulation has been developed which utilises an array of external electrodes and this is believed, based on observation using pelvic floor (PF) ultrasonography, to deliver much greater levels of PF muscle activation than the transvaginal approach.

Thus in this study we will be using the Neurotech Vital Compact device to deliver neuromuscular electrical stimulation (NMES) to the pelvic floor muscles via an arrangement of external electrodes optimally positioned to successfully stimulate these muscles and held in place by a garment to facilitate good skin contact and repeatability of positioning. The

Neurotech Vital Compact device is the fourth generation of the device which has been developed using the same technology as the UCD RS device (first generation device) and Inko RS device (second generation device).

Previous experience indicates that NMES muscle training effects are cumulative over a period of time and early indication using the device for five days with two rest days in a 7 day period for a stipulated period of weeks provides an optimum effect. A treatment regimen has therefore been selected where patients self-administer 30 minutes of treatment for 5 days each week for a 12 week period. It is anticipated that most patients would respond in a quicker time with short term beneficial results within 8 weeks, however, a 12-week treatment period is more likely to result in cumulative muscle training effects. Patients will control the intensity of stimulation within predefined levels from the control unit which will also maintain an electronic record of usage times and intensity to check for compliance.

2.4 Rationale for Using the itouch Sure Pelvic Floor Exerciser

After consideration of the recommendations made by the Food and Drug Administration (FDA) at a meeting in October 2013, the itouch Sure Pelvic Floor Exerciser has been selected since it is a 510 (k) approved device in the USA. The comparator device is cleared by the FDA through the 510 (k) premarket notification process (K103698) and also CE Mark approved in Europe.

The iTouch Sure Pelvic Floor Exerciser was specifically selected since its intended use is very similar to the Neurotech Vital Compact device. The iTouch device is intended to provide electrical stimulation and neuromuscular re-education for the purpose of rehabilitation of weak pelvic floor muscles for the treatment of stress, urge and mixed urinary incontinence in women. In addition, the device is intended for home use by the patient with a pre-set programme for stress incontinence with a compliance monitor. In this study the itouch device will be used daily, as recommended by the manufacturer.

There are no significant additional risks related to the treatment of the patients with the itouch Sure Pelvic Floor Exerciser. Previous studies with vaginal electrodes have reported isolated incidents of vaginal irritation and infection. (Sand *et al* 1995)

2.5 Rationale of a Single-Blind Study Design

The study is considered single-blind as the subjects will be randomised to either the Neurotech Vital Compact device or the itouch Sure Pelvic Floor Exerciser. Since the two devices will be described in detail in the patient information sheet, the patients will know to which device they have been randomised, i.e. the Neurotech Vital Compact device delivers electrical stimulation through external electrodes and the itouch Sure Pelvic Floor Exerciser delivers electrical stimulation through an internal vaginal probe. This should not introduce any bias since patients would not have an expectation that the new device (Neurotech Vital Compact device) is better than the existing active control device (itouch Sure Pelvic Floor Exerciser).

The site personnel who allocate the devices, perform the device training at baseline and monitor the device compliance at the follow-up visits will not be blinded, but the personnel who perform the follow-up assessments will be blinded.

Verification to ensure that this blinding is maintained will be assessed at the monitoring visits.

2.6 Risk/Benefit of the Neurotech Vital Compact Device

2.6.1 Residual Risks Identified in Risk Analysis Report

As part of the risk analysis process conducted during development, all identified risks were subjected to review and were either eliminated or reduced to 'as low as reasonably possible' (ALARP) by changes in process, documentation and planned user training.

Potential risks under these ALARP categories include manufacturing, labelling, storage and user error problems.

2.6.2 Risks Associated with Participation in the Clinical Study

There are no anticipated additional risks to involvement in this clinical study than would be expected for normal treatment of this condition with alternative NMES devices with the possible but unlikely exception of patient sensitivity to the constituent materials of the garment/device materials. However, there is no reason to suspect that any reaction would occur or that there would be any subsequent long term health problems. All of these materials have been extensively used and documented for their biocompatibility with human skin. The garment and devices will be used in accordance with the Instructions for Use.

2.6.3 Possible Interactions with Concomitant Medical Treatments

There is no reason to suspect that NMES treatment would cause any interaction with concomitant medications. A full list of conditions contraindicated for use with NMES is documented in the Instructions for Use and subjects with these conditions are excluded via the inclusion/exclusion criteria for the study.

2.6.4 Steps to be Taken to Control or Mitigate Risks

Full Failure Modes Effects Analysis (FMEA) has been conducted, in line with ISO14971, for all stages of design, manufacturing, storage, shipping and clinical use of this device. These have been continually updated at various stages during the introduction of this device aiming to identify and then address each potential risk in terms of severity of risk, potential frequency of occurrence (i.e. what could go wrong, what is the probability it could go wrong, what are the implications/severity if it does go wrong). Each identified risk was then subject to discussions over whether any action could be taken internally or through 'Instructions for Use' to reduce these risk scores to the ALARP (as low as reasonably possible) level felt to be acceptable.

2.7 Risk/Benefit Rationale

NMES is a safe treatment option for stress urinary incontinence. Once patients have been trained in the use of the device and application of the electrodes and associated garments, self-treatment is continued at home for up to 12 weeks without the need for prolonged interim hospital visits as part of routine care. The Neurotech Vital Compact device can be used with external electrode placement which is more acceptable for patients than the use of internal (vaginal or anal) electrodes or other internal devices.

Alternative non NMES treatment options such as Kegel pelvic floor exercises are not successful for many patients for a variety of reasons and may require regular motivational visits during the

training period. Pharmaceutical options for stress urinary incontinence are very limited and are not suitable for all patients.

Ultimately, surgical intervention provides relief for many patients but is obviously fraught with inherent surgical and anaesthetic risks not seen in less invasive therapies, in addition to hospital costs.

Therefore, there is a safety and cost benefit for the use of an external NMES device over alternative treatment options including surgery.

2.8 Risk/Benefit of the itouch Sure Pelvic Floor Exerciser

The itouch Sure Pelvic Floor Exerciser is manufactured by TensCare Ltd., 9 Blenheim Road, Longmead Business Park, Epsom, Surrey, KT19 9BE, UK.

In accordance with its regulatory obligation for FDA clearance and European CE approval, Tenscare Ltd. are required to have completed a risk/benefit analysis and Full Failure Modes Effects Analysis (FMEA), in line with ISO14971, for all stages of design, manufacturing, storage, shipping and clinical use of this device As evidenced by their continued certification to ISO13485, TensCare Ltd also maintain updated records in line with Medical Device Directive 93/42/EC, as amended by 2007/47/EC, to ensure the continued device safety and performance profiles.

The risk/benefit for the itouch Sure Pelvic Floor Exerciser is well established since the device is cleared by the FDA through the 510 (k) premarket notification process (K103698) in the USA and also CE Mark approved in Europe.

The Manufacturer and User Facility Device Experience (MAUDE) database details medical device reports submitted to the FDA in the USA by mandatory reporters (manufacturers, importers and device user facilities) and voluntary reporters such as health care professionals, patients and consumers. To date, there are no recorded issues filed for the use of the itouch Sure Pelvic Floor Exerciser on the MAUDE database.

The use of the device in this study poses no additional risks to the subjects since it is being used in accordance with the Instructions for Use (IFU for this device as used in this study are believed to be compliant with the US FDA 501(k) label).

3 Objectives

3.1 Primary Objective

The primary objective of this clinical study is to evaluate and compare the safety and performance profile of the Neurotech Vital Compact device (delivering electrical stimulation through external electrodes) and the itouch Sure Pelvic Floor Exerciser (delivering electrical stimulation through an internal vaginal probe) for the treatment of stress urinary incontinence following a 12-week treatment program.

3.2 Secondary Objectives

The secondary objectives of this clinical study are to further evaluate the safety and performance of the Neurotech Vital Compact device compared to the itouch Sure Pelvic Floor Exerciser.

4 Study Design

This is a prospective, randomised, controlled, single-blind, multi-site clinical study to be conducted in the United States of America (USA) employing Neuromuscular Electrical Stimulation (NMES) to stimulate the pelvic floor muscles of women suffering from stress urinary incontinence.

Approximately one-hundred and eighty (180) female patients diagnosed with stress urinary incontinence will be enrolled in this study. All patients who are considered eligible to participate in the clinical study and give consent will be randomised to complete either a 12-week treatment programme with the Neurotech Vital Compact device or a 12-week treatment programme with the itouch Sure Pelvic Floor Exerciser. The 12-week treatment programme will be completed by the subjects at home with treatment with the device in accordance with the device Instructions for Use.

Subjects included in the clinical study will be evaluated at screening, on enrolment into the study (baseline) and during the 12-week treatment programme at 4 and 12 weeks. A telephone call will be made at 1 week to check on the patient's progress. In addition, subjects will be evaluated at 26 week following their commencement of the treatment.

Telephone support will be available throughout the duration of the study. A clinical study Schedule of Events is presented in Appendix I.

All information provided to the subjects will be provided in a language in which they are conversant for both reading and speaking which will include: Incontinence Quality of Life Questionnaire (I-QOL) (Appendix V); Instructions for Use for the allocated device (Appendices XI and XII); Medical, Epidemiologic and Social Aspects of Aging Urinary Incontinence Questionnaire (MESA) (Appendix VII) ; Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-IR) (Appendix VI); Patient Global Impression of Improvement (PGI-I) (Appendix IX); the voiding diary (Appendix VIII); patient information sheet and consent documents (Appendix X).

5 Trial Endpoints

5.1 Primary Endpoint

The primary endpoint is defined as the proportion of subjects considered to have achieved 'significant improvement' following a provocative pad weight test at 12 weeks compared to baseline.

'Significant improvement' is defined as a greater than 50% reduction in pad weight from baseline.

5.2 Key Secondary Endpoints to Support Indication for Use

The following key secondary endpoints will each be analysed, for superiority, at a 5% two-sided significance level with a view to support labelling. In order to control the type I error rate the endpoints will be analysed in the following hierarchy (see Section 14.0 Statistical Plan for further details). If any endpoint in the sequence fails to show a statistically significant difference then the inference is that there is insufficient evidence both for that endpoint and the subsequent endpoints in the hierarchy.

- Between group comparison of mean change, with respect to baseline, in urine leakage in a provocative pad weight test at Week 12;
- Within Neurotech Vital Compact group estimate of mean change, with respect to baseline, in urine leakage in a provocative pad weight test at Week 12;
- Between group comparison of mean change, with respect to baseline, in urine leakage in the 24-hour pad weight test at Week 12;
- Within Neurotech Vital Compact group estimate of mean change, with respect to baseline, in urine leakage in the 24-hour pad weight test at Week 12;
- Between group comparison of mean change, with respect to baseline, in the number of incontinence episodes/day recorded using a 7-day voiding diary at Week 12;
- Within Neurotech Vital Compact group estimate of mean change, with respect to baseline, in the number of incontinence episodes/day recorded using a 7-day voiding diary at Week 12;
- Between group comparison of the mean improvement, with respect to baseline, in Incontinence Quality of Life Questionnaire (I-QOL) score at Week 12;
- Within Neurotech Vital Compact group estimate of mean improvement, with respect to baseline, in Incontinence Quality of Life Questionnaire (I-QOL) score at Week 12;
- Between group comparison of mean change, with respect to baseline, in the number of pads used/day recorded using a 7-day voiding diary at Week 12;
- Within Neurotech Vital Compact group estimate of mean change, with respect to baseline, in the number of pads used/day recorded using a 7-day voiding diary at Week 12;
- Between group comparison of the proportion of subjects achieving dryness at Week 12 (<1g on the provocative pad weight test).

5.3 Secondary Endpoints - Other

Other secondary endpoints that will be evaluated at 4 weeks and 26 weeks are as follows:

- Proportion of subjects considered to have achieved significant improvement, defined as a greater than 50% reduction in pad weight, from baseline on the provocative pad weight test.
- Urine leakage on the provocative pad weight test (following standardized bladder-filling protocol).
- Urine leakage experienced by the subject at home in the 24-hour pad weight test;
- Incontinence episodes/day recorded using a 7-day voiding diary;
- Proportion of subjects achieving dryness (<1g on the provocative pad weight test)
- Improvement in quality of life assessed using the Incontinence Quality of Life Questionnaire (I-QOL);
- Number of pads/day recorded using a 7-day voiding diary;
- Dryness, defined as a pad weight of less than 1.3g on the 24-hour pad weight test (including an evaluation at 12 weeks);
- Proportion of subjects considered to have achieved significant improvement, defined as a greater than 50% reduction in pad weight, from baseline on the 24-hour pad weight test (including an evaluation at 12 weeks).

Other data that will be evaluated are as follows:

- Proportion of subjects achieving dryness at Week 12 in each group (<1g on the provocative pad weight test).
- Within Neurotech Vital Compact group estimate of mean change, with respect to baseline, in sexual function as measured by the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-IR) (Appendix VI) at Week 12;
- Between group comparison of mean change, with respect to baseline, in sexual function as measured by the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-IR) at Week 12;
- Within Neurotech Vital Compact group estimate of patient response to the Patient Global Impression of Improvement (PGI-I) at Week 12.
- Between group comparison of patient response to the Patient Global Impression of Improvement (PGI-I) at Week 12;
- Safety in relation to adverse events and device deficiencies reported;
- Evaluation of reduction in urine leakage on the provocative pad weight test in relation to the mean intensity of the stimulation delivered during the 12-week treatment programme;
- Evaluation of the reduction in urine leakage on the provocative pad weight test at Week 12 in relation to the BMI category (underweight/normal/overweight/obese) of the subjects;
- Evaluation of the reduction in urine leakage on the provocative pad weight test at Week 12 in relation to the baseline severity of stress urinary incontinence of the subjects;
- Device compliance of the Neurotech Vital Compact device with the treatment protocol during the 12-week treatment programme;
- Device compliance of the itouch Sure Pelvic Floor Exerciser with the treatment protocol during the 12-week treatment programme.

6 Trial Population

6.1 Number of Subjects

Subjects who meet all of the inclusion and none of the exclusion criteria will be randomized into the study until approximately 180 healthy female subjects have completed the study.

6.2 Inclusion Criteria

1. Subjects who are female and at least 18 years of age, and not more than 65 years of age.
2. Subjects who have signed the informed consent form prior to any study related activity.
3. Subjects who have previously tried and failed to improve their condition using Kegel exercises.
4. Subjects who have been clinically diagnosed with stress urinary incontinence and demonstrate a greater than or equal to 3g urine leakage and a less than or equal to 90g urine leakage ($\geq$3g and $\leq$ 90g) following a bladder-filling protocol and then a standardised stress test (provocative pad weight test) at the baseline assessment.
5. Subjects who score 9 or less ($\leq$9) out of 18 for the Urge Incontinence Questions and are confirmed as having predominant stress urinary incontinence on the Medical, Epidemiologic and Social Aspects of Aging Urinary Incontinence (MESA) Questionnaire completed at the screening assessment.
6. Subjects with a Body Mass Index of $\leq$ 35 kg/m^2.
7. Subjects of child-bearing potential who are using a highly effective contraceptive method (established use of oral, injected, implanted hormonal method of contraception or barrier method of contraception with spermicide).
8. Subjects who are willing not to seek any other treatment for stress incontinence during the study period.
9. Subjects who are able to give voluntary, written informed consent to participate in this study and from whom consent has been obtained.
10. Subjects who are able to understand this study and are willing to complete all the study assessments.

6.3 Exclusion Criteria

1. Subjects who have an existing medical condition that would compromise their participation in the study, e.g. reduced sensory perception in the contact area of the stimulation electrodes; scars or vaginal tissue wounds, lesions or inflamed/infected areas in the contact area of the stimulation electrodes; vaginal bleeding between menstrual periods; uncontrolled diabetes.
2. Subjects who have a physical condition that would make them unable to perform the study procedures, e.g. pelvic or hip surgery within the past 6 weeks.
3. Subjects who have been diagnosed with Chronic Obstructive Pulmonary Disease (COPD).
4. Subjects with a history of an underlying neurological condition, e.g. Multiple Sclerosis, Parkinson's disease, epilepsy.
5. Subjects with any bladder abnormality that would affect the urinary flow through the lower urinary tract including signs or symptoms of an active urinary tract infection, abnormal bladder capacity (e.g., >300 cc), post void residual volume >200 cc, spastic bladder, vesico-ureteral reflux or bladder stones.
6. Subjects with a blood clotting disorder or who are taking anti-coagulant medications.

7. Subjects who have previously had any uro-gynaecological related surgery that would affect the pelvic floor muscles or urinary flow through the urethra (excluding hysterectomy).
8. Subjects who have previously had pelvic floor radiation.
9. Subjects who have previously been treated for stress incontinence with injectable bulking agents and/or vaginal probes within the past 6 months.
10. Subjects with a clinical diagnosis of prolapse greater than Stage 2.
11. Subjects who are pregnant or could be pregnant.
12. Subjects who are less than 6 months post-partum or who are lactating.
13. Subjects who have any conductive intra-uterine devices or metal implants in the pelvic area, including hip and lumbar spine.
14. Subjects with pelvic pain or fibromyalgia or paravaginal defect.
15. Subjects with an active implanted medical device (i.e. pacemaker, insulin pump etc.) or conditions that may be adversely affected by electrical stimulation (e.g. cardiac arrhythmias).
16. Subjects with a current or active history of pelvic cancer and/or subjects with a life expectancy of less than 12 months.
17. Subjects who are currently involved in any injury litigation claims.
18. Subjects who have participated in a clinical study in the last 3 months or any previous clinical study with Bio-Medical Research Ltd.
19. Subjects who have been committed to an institution by virtue of an order issued either by the courts or by an authority.

6.4 Withdrawal Criteria

During the course of this study, subjects may be withdrawn, or may elect to withdraw through any of the listed following reasons below. However all subjects will be assessed on an individual basis when clarifying their withdrawal and for this reason, measurable parameters cannot be specifically defined for the withdrawal criteria below:

- Subject's rescission of consent.
- Any adverse event, related to the device or not, which may endanger the well-being of the subject if they were not withdrawn.
- Subject non-compliance or protocol violation.
- Subject unable to meet the protocol requirements.
- Development of a medical condition or illness which may compromise safety of the subjects or invalidate the results of the study.

The Investigator will clearly document the date and reason(s) for withdrawal in the Case Report Form.

All subjects discontinued from the study due to an adverse event will be followed up by the Investigator until resolution or condition has stabilised.

Subjects who are withdrawn prior to the completion of the baseline assessments only will be replaced.

6.5 Monitoring for Subject Compliance

Subject compliance will be based on three assessments, namely, the level of completion of patient 7-day voiding diary, attendance at scheduled follow-up visits plus evaluation of the internal memory of the Neurotech Vital Compact device and the itouch Sure Pelvic Floor Exerciser or the Device Record (diary) to check daily use parameters and schedules.

7 Study Treatments

One device will be issued to each randomized subject in a single-blinded manner. The investigator and those administering the 1-hour provocative stress test, evaluating adverse events and reviewing diary data are to remain blinded regarding treatment assignment.

7.1 Description

The Neurotech Vital Compact Device consists of a controller and a garment.

7.1.1 Neurotech Vital Compact Controller

The Neurotech Vital Compact Controller is a powered Neuromuscular Electrical Stimulation (NMES) device manufactured by Bio-Medical Research Ltd.

The Neurotech Vital Compact Controller is manufactured as a sealed, handheld portable unit containing electronics and a rechargeable battery with an LCD screen and keypad for interaction with the user (see Figure 1). The outer casing is manufactured from ABS resin and the device has been independently certified to comply with IEC60601-1-1 and IEC60601-2-10.

The Neurotech Vital Compact Controller is CE Mark approved as a Class IIa Device in Europe, in line with Medical Device Directive 93/42/EC as last amended by 2007/47/EC, and will be used in accordance with the Instructions for Use.

Figure 1. The Neurotech Vital™ Compact device Controller

The stimulation current is delivered to the body through an array of conductive adhesive electrodes (in accordance with the pre-defined parameters) which are held in place by a garment which wraps around the buttocks and thigh area (see Table 1). This ensures the current passes from the electrode set on one side of the body to the other and this approach has been found to be particularly effective in activating the pelvic floor muscles.

Table 1. Parameter Specifications on the Neurotech Vital Compact Controller

Duration of each session	Frequency	Pulse Width	Ramp-Up time	Contract Time	Ramp Down Time	Relax time
30 minutes	50Hz	620μs	0.5 seconds	5 seconds	0.5 seconds	5 seconds

The pulse is a conventional symmetric biphasic type with constant current control. The phase duration is 620μs and the maximum current amplitude is 120mA, leading to a maximum charge per pulse of 74 μC. The maximum rms current of this pattern is 30mA. The total power from the device at maximum output intensity setting with all electrodes active into a 500Ω load is 0.45 W. This maximum is comparable to the available power from several 8-electrode systems which are already cleared to market by the US Food and Drug Administration (FDA). For example Compex Sport (K011880) delivers up to 0.48W (100mA @ 120Hz, phase duration=400 μs).

Subjects will be at liberty to alter the intensity of the stimulation to the highest tolerable level and provided with guidance on the intensity of the muscle contraction to be achieved.

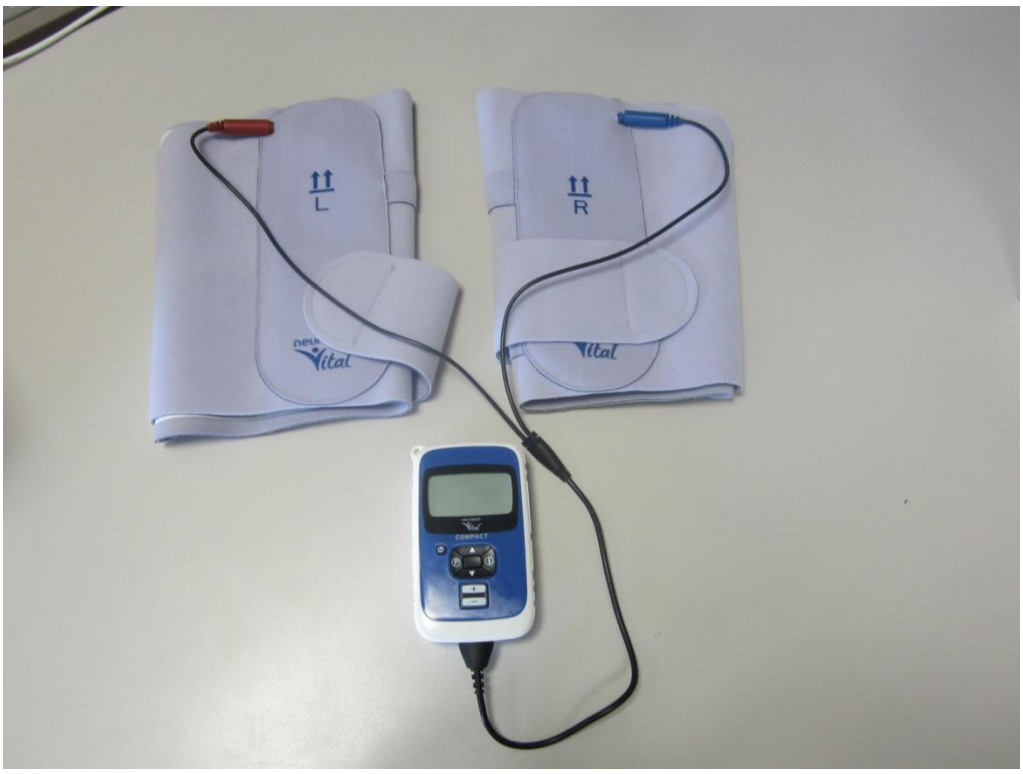
The Neurotech Vital Compact Controller will only permit stimulation if the garment is connected to the unit.

For purposes of this study, the Neurotech Vital Compact is to be used per the Instructions for Use (IFU) provided in Appendix XI. A Vital Compact Quick Start Guide is also included in Appendix XI.

7.1.2 Neurotech Vital Garment

The Neurotech Vital Compact Garment is intended for use with the Neurotech Vital Compact Controller to aid the placement of the electrodes and to help keep them securely in place (see Figure 2). The garment is made from an outer material which is 80% nylon, 20% elastane and a100% polyurethane inner. Fasteners are manufactured in nylon. All of these materials have been extensively used and documented for their biocompatibility with human skin. The garment will be used in accordance with the Instructions for Use.

Figure 2. The Neurotech Vital Compact device connected to the garment



7.1.3 Hydrogel Electrodes

The hydrogel electrodes are comprised of a three-layer conductive medium to deliver the electrical current. The electrodes are manufactured by Axelgaard (Fallbrook, C.A USA), a leading supplier to the medical device sector, and have undergone rigorous safety and biocompatibility testing. The double adhesive electrodes in the Neurotech Vital Compact device measure 15.0 by 10.5 cm and disperse the current over a large area of skin resulting in a low current density. The maximum current density remains low at less than 0.05 mA/cm^2 which is typical of TENS devices used in clinical practice.

The hydrogel electrodes are CE Mark approved as a Class I Device in Europe, in line with Medical Device Directive 93/42/EC as last amended by 2007/47/EC.

7.1.4 Pre-clinical Data

The Neurotech Vital Compact Controller has been tested by an independent test house (SGS, UK) and certified to be in conformance with the requirements of the IEC60601 series of standards. The controller is CE-marked under the European Medical Device Directive, authorised by the notified body, VDE Germany. The garment and electrode materials are certified to be in conformance with bio-compatibility standard ISO 14993.

There are no tissues of human or animal origin or any medicinal substances used in the garments, electrodes, or Neurotech Vital Compact device.

7.2 itouch Sure Pelvic Floor Exerciser

The itouch Sure Pelvic Floor Exerciser is manufactured by TensCare Ltd., 9 Blenheim Road, Longmead Business Park, Epsom, Surrey, KT19 9BE, UK.

This is an intravaginal device that will be used daily for 20 minutes. Further details on the itouch Sure Pelvic Floor Exerciser are presented in the 510(k) Summary (see Appendix II) and Instructions for Use (Appendix XII). The device will be used in accordance with the Instructions for Use provided for this study for treatment of stress incontinence.

7.2.1 Packaging and Labelling

The Neurotech Vital Compact device will be provided packaged, along with its electrode lead and hydrogel electrodes, in a box with an identifying serial number, part number and subject number. The device will also bear the CE mark.

The Neurotech Vital garments will be separately packaged and also will have their own identifiable lot numbers. Expiry dates will also be found on the electrode packaging.

The itouch Sure Pelvic Floor Exerciser will be provided packaged, along with vaginal lubricating gel, in a box with identifying serial number and subject number. The device will bear the CE mark.

Each device will be in packaging with a label with at least the following information:

For Clinical Trial Use Only

Study Number: BMR-13-1001
Contents: One Neurotech Vital Compact or itouch Sure Pelvic Floor Exerciser
Subject Number: XXXXX
Treatment Duration: 12 weeks at 30 minutes 5 days a week (Neurotech Vital Compact) or 12 weeks of 20 minutes 7 days a week (itouch Sure Pelvic Floor Exerciser)
Lot number: XXXXXXXX
Storage: Store at ambient (room) temperature
Study Sponsor and Manufacturer for Neurotech Vital Compact: Bio-Medical Research Ltd., Parkmore Business Park West, Galway, Ireland.
US Study Director Expedite Research, LLC, 15 Kerry LN, Phoenixville, PA 19460
Caution: The Neurotech Vital Compact is an investigational device limited by US Federal Law to be used by qualified Investigators only.

7.3 Device Storage and Accountability

Formal accountability will be performed for all devices. The Investigator will be provided with a Device Accountability Log to track disposition of all devices including the itouch Sure Pelvic Floor Exerciser, Neurotech Vital Compact devices, hydrogel electrodes and Neurotech Vital garments (left and right).

All devices must be stored in a secure place at ambient temperature. It is the responsibility of the Investigator to ensure that devices are stored correctly at the site. The Investigator must also make the devices, eCRFs, clinic notes and Investigator File available for inspection by the monitor upon request.

During this clinical study or upon its completion or termination, the Investigator will return all devices to Bio-Medical Research Ltd. Bio-Medical Research Ltd will keep a record of the number of devices provided and returned.

7.4 Device Training/Experience

At the initiation visit, the Principal Investigator and the research team will be provided with extensive training on the use of the Neurotech Vital Compact device and the itouch Sure Pelvic Floor Exerciser. The site will also be provided with training on how to train the subjects in the use of the devices in accordance with the Instructions for Use. All site and subject training will be documented.

7.5 Randomisation and Blinding

Subjects will be randomised to the Neurotech Vital Compact device or the itouch Sure Pelvic Floor Exerciser (1:1 ratio). They will know to which device they have been randomised since the two devices will be described in detail in the patient information sheet i.e., the Neurotech Vital Compact device delivers electrical stimulation through external electrodes and the itouch Sure Pelvic Floor Exerciser delivers electrical stimulation through an internal vaginal probe.

The site personnel who perform the device training at baseline and monitor the device compliance at the follow-up visits will not be blinded, but the personnel who perform the follow-up assessments will be blinded regarding device assignment.

Verification to ensure that this blinding is maintained will be assessed at the monitoring visits.

7.6 Concomitant Medication and/or Treatments

Subjects may use any medication that affects urinary output function if the medication has been used for at least 4 weeks prior to study enrolment and the medication regimen is not changed during the 12-week device treatment program

No device re-treatment will be allowed during the subject's participation in the study.

7.7 Treatment Compliance

Compliance will be assessed by reviewing the medical chart for information regarding the date and time of study visits. At each visit, information will be obtained from the devices (depending on the device) including treatment time, highest intensity reached and average intensity. In addition, subjects will be asked to complete a daily record of device use which will capture the duration of treatment and the maximum intensity reached during that session.

7.8 Unblinding/Breaking the Blind

The first course of treatment for any suspected device-related event or effect is to stop using the device. If necessary, the investigator may be made aware of the allocated treatment via the unblinded personnel at the site.

8 Study Procedures

8.1 Ethical and Regulatory Considerations

Prior to the study start relevant Institutional Research Board (IRB) approval will be obtained in writing and submitted to the Sponsor and no subjects will be recruited until a formal site initiation visit has been conducted.

This study will be conducted in compliance with:

- Study Protocol
- Applicable local IRB requirements
- US and international standards of Good Clinical Practice (FDA abbreviated IDE requirements set forth in 21 CFR 812.2(b), 21 CFR Part 50 and FDA guidance E6.
- Declaration of Helsinki as adopted by the 18th World Medical Assembly in 1964 and as revised in Tokyo (1975), Venice (1983), Hong Kong (1989), South Africa (1996), Edinburgh (2000), Washington (2002 note of clarification added), Tokyo (2004 note of clarification added), Korea (2008) and Brazil (2013).

Clinical study insurance and indemnity will be provided as required under local laws and practices.

Confidentiality of subject data will be maintained at all times. Subject anonymity will be guaranteed and all documentation relating to a subject will be kept in a secure location.

8.2 Regulatory Considerations

The Sponsor considers this study is a Nonsignificant Risk Study for the following reasons:

- In response to a written submission (Q 130879) filed by the company, giving details of the study design and the devices to be used, FDA has informed the sponsor in writing that this study may be considered a Nonsignificant Risk Study.
- The study does not meet the definitions for a Significant Risk Study.
- Non-implantable Electrical Incontinence Devices are classed by the FDA as an example of a nonsignificant risk device.
- The Neurotech Vital Compact included in this study is a Class II, CE marked medical device but has not been 510 (k) cleared by the FDA in the USA.
- The risks related to the use of the devices are minimal and the devices are being used under the supervision of the Investigator.

The study will therefore be conducted in accordance with the abbreviated Investigational Device Exemption (IDE) requirements set forth in 21 CFR 812.2(b).

The FDA also confirmed that the Neurotech Compact device can be classified as a Nonsignificant Risk device (19 September 13) since it met the definitions under 21 CFR 812.3(m).

8.3 Informed Consent

The Investigator will introduce the subject to the study by explaining the study procedures and objectives to the subject. The Investigator will then provide an information sheet describing the study, potential discomforts, risks and benefits of participation. The subject will have sufficient time to decide whether she wishes to participate in this study.

Any queries that subjects may have regarding this study will be addressed appropriately by the Investigator. Subjects will be instructed that they are free to obtain further information from the Investigator at any time, that they are free to withdraw their consent and to discontinue their participation in the study at any time without prejudice.

If the subject is willing to participate in the study, they must read, understand and sign the informed consent form. The Investigator will also sign this on the same occasion. The original copy of the signed consent form will be kept in the secure location at the study site, a copy provided to the subject and a copy filed in the medical records.

Written informed consent from the subject must be obtained before any clinical study related procedures are performed.

8.4 Study Start and Training

A summary of the schedule of events is provided in Appendix I. The study will not commence at a site until all the necessary approvals are in place and a formal study initiation visit has taken place. At the initiation visit, the monitor will ensure that all study personnel are fully aware of all study requirements and assessments. Extensive training on the use of the Neurotech Vital Compact device and the itouch Sure Pelvic Floor Exerciser will be provided as will training on how to train the subjects to use the devices correctly.

Study staff will document completion of protocol, device and study methodology training by signing the Study Training Log.

8.5 Study Recruitment

Subjects who attend the clinic for treatment of urinary stress incontinence will be approached by the Investigator to take part in the clinical study. Additionally, an approved advertisement will be made available to sites if they wish to advertise to recruit subjects into this clinical study.

8.6 Study Duration

Each subject will receive a 12-week period of treatment, which is preceded by a short period of time (2 to 4 weeks) for discussions of potential study involvement and provision of informed consent and formal evaluation of suitability for study inclusion.

Each subject will remain in the study for 14-weeks following completion of the 12 week treatment programme, therefore each subject will be involved for approximately 30 weeks.

8.7 Subject Eligibility

Once written informed consent has been obtained, the Case Report Form will be completed to document adherence to the inclusion and exclusion criteria.

Where a subject fails to fulfill any element of the inclusion and exclusion criteria, this will be documented and the signed consent form and completed inclusion/exclusion criteria retained by the Investigator. The subject will not be advanced further in the study.

When a subject is considered eligible for entry into the study, the subject will be randomized to the next available subject number (subject ID number). This number will be the unique identifier of the subject and written on each page of the Case Report Form and all other study documentation relating to the subject.

8.8 Randomisation

At the initiation visit, the designated personnel will be trained regarding how to conduct and document the randomisation of subjects enrolled into the study at that site.

The site will be provided with randomisation envelopes which will be used to allocate the devices. Access to these randomisation envelopes will be limited to the designated un-blinded personnel working on the study at the site.

When a subject has agreed to participate in the study, given informed consent, and is considered eligible with the inclusion/exclusion criteria, she will be entered into the study and only then will she be randomised to either device. The designated un-blinded personnel will train the subject according to which treatment has been allocated.

In the event of an emergency whereby it becomes necessary to know to which treatment the subject has been allocated, the investigator may be made aware of the allocated treatment via the unblinded personnel at the site. A documented procedure will be provided to the site before the study commences.

All baseline assessments must be completed prior to randomisation.

8.9 Screening Assessments – Visit 1

Each subject considered eligible for entry into this clinical study, and from whom written consent has been obtained, will have a screening assessment with the following information/procedures recorded (within 14 days of baseline assessment):

- Demographic data including height and weight.
- Medical history including details of stress urinary incontinence, previous bladder/kidney infections and any current/previous urological treatments.
- Physical examination including a detailed urological history to assess urinary symptoms and symptoms of bowel function, sexual function and pelvic organ prolapse.
- Details of all medication (over-the-counter and prescription) and dietary/herbal supplements in the previous 6 months.
- Urine pregnancy test to confirm subject is not pregnant (women of child-bearing potential only).
- Complete the Medical, Epidemiologic and Social Aspects of Aging Urinary Incontinence (MESA) Questionnaire (patient quality of life questionnaire).
- Complete a standardized stress test to evaluate amount of urine lost following a standardized bladder-filling protocol verified by ultrasound bladder scanning (provocative pad weight

test). The data from this test will not be used for analysis purposes, it is only to allow patients to practice the stress test. Further details of the stress test protocol and instructions for the Investigator and subject are provided in Appendix III.
- Record any cough or cold symptoms.
- Record any adverse events.

Prior to leaving the clinic, subjects will also be provided with the following:
- A 7-day voiding diary to complete seven days prior to the Visit 2 (baseline) appointment.
- Pre-weighed incontinence pads in a sealed bag to complete the 24-hour pad collection for three days prior to the Visit 2 (baseline) appointment.

The subject will then be asked to return the 7-day voiding diary and incontinence pads in the same sealed bag to the clinic at Visit 2. Any subjects menstruating during the three days prior to Visit 2 will also be asked to record this on the voiding diary. Any subjects who have sexual intercourse during this three day period will be asked to expel any fluid post-intercourse and also record this on the voiding diary.

8.10 Baseline Assessments – Visit 2

On the subject's return to the clinic to return the 7-day voiding diary and incontinence pads, the following information/procedures will be recorded:

- Complete the Incontinence Quality of Life Questionnaire (I-QOL) (patient quality of life questionnaire).
- Complete the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-IR).
- Complete a standardized stress test to evaluate amount of urine lost following a standardized bladder-filling protocol verified by ultrasound bladder scanning (provocative pad weight test). This assessment will be used to determine the subject's eligibility to participate. Further details of the stress test protocol and instructions for the Investigator and subject are provided in Appendix III.
- Number of incontinence episodes/day from 7-day voiding diary.
- Number of pads used/day from 7-day voiding diary.
- Mean weight of urine leaked during three consecutive 24-hour periods at home (difference in post- and pre-weight incontinence pads) (24-hour pad weight test). Severity score will be assessed as dry (less than 2g), mild (greater or equal to 2g and less than 10g), moderate (greater or equal to 10g and less than 50g) and severe (greater than 50g) (O'Sullivan, 2004).
- Record any medication use or changes in medication since the last visit.
- Record any cough or cold symptoms since the last visit.
- Record any adverse events since the last visit.

These assessments will be performed by the designated blinded site personnel only.

8.10.1 Device Training

Subjects will be briefed by the designated non-blinded site personnel on the set-up of the Neurotech Vital Compact device or the itouch Sure Pelvic Floor Exerciser (in accordance with the allocated treatment as per the randomisation schedule). Subjects will then be asked to follow

the set-up instructions and complete a 30 minute session with the Neurotech Vital Compact device or a 20 minute sessions with the itouch Sure Pelvic Floor Exerciser in accordance with the appropriate Instructions for Use. Subjects will be at liberty to alter the intensity of the stimulation to the highest tolerable level and will be advised on the importance of achieving a strong pelvic floor contraction. Guidance will be given on the typical minimum intensity setting to achieve this effect. Subjects will be advised that it not necessary to achieve this level in their first session but that they should gradually increase the setting in their first week of use.

All of the subject's training will be documented. Subjects unable to demonstrate competent use of the Neurotech Vital Compact device or the itouch Sure Pelvic Floor Exerciser will be withdrawn from the clinical study.

The subject will be provided with the Neurotech Vital Compact device or the itouch Sure Pelvic Floor Exerciser to take home with them. Details of all devices provided, including the serial/lot numbers, will be recorded.

8.10.2 Treatment Programme Schedule – Neurotech Vital Compact device

Subjects will be advised that they should empty their bladder prior to commencing the 30 minute session of the Neurotech Vital Compact device at home.

The subjects will be instructed to use the device at home once per day, in a therapeutic position, for five days each week with two rest days taken within a 7 day week period, for the 12-week period. Each treatment cycle is fixed at 30 minutes and the device will alert the subject when the cycle is completed.

Subjects will be advised that during the 12-week treatment programme not to do any new pelvic floor exercises.

8.10.3 Treatment Programme Schedule – itouch Sure Pelvic Floor Exerciser

Subjects will be advised that they should empty their bladder prior to commencing the 20 minute session of the itouch Sure Pelvic Floor Exerciser at home.

In accordance with the instructions for use for the device, the subjects will be instructed to use the device at home once per day for the 12-week period. Each treatment cycle is fixed at 20 minutes and the device will alert the subject when the cycle is completed.

Subjects will be advised that during the 12-week treatment programme not to do any new pelvic floor exercises.

8.10.4 Prior to Leaving Clinic

Prior to leaving the clinic, subjects will also be provided with the following:

- A 7-day voiding diary to complete seven days prior to Visit 3 appointment.
- A device record form to record device use each day.
- Pre-weighed incontinence pads in a sealed bag to complete the 24-hour pad collection for three days prior to the Visit 3 appointment.

The subject will then be asked to return the 7-day voiding diary, device record and incontinence pads in the same sealed bag to the clinic at Visit 3. Any subjects menstruating during the three days prior to Visit 3 will also be asked to record this on the voiding diary. Any subjects who have sexual intercourse during this three day period will be asked to expel any fluid post-intercourse and also record this on the voiding diary

Subjects will be advised they can telephone the clinic at any time to discuss any concerns.

8.11 Assessments During 12-Week Treatment Programme – Visit 3 and Visit 4

8.11.1 Early Termination

If a subject starts treatment discontinues before completing all study visits, she is to be asked to return to the clinic to complete a Visit 4 visit as an early termination visit (if prior to that visit) or a Visit 5 visit (if after Visit 4 has taken place).

8.11.2 Telephone Contact

The subjects will be contacted via telephone at one week (Week 1) following Visit 2 to assess if there are any issues with the treatment, if they are using the device as per the Instructions for Use and to assess if there are any adverse events and/or changes to medication.

8.11.3 Timing of Visit Assessments (+/- 7 days)

Patients included in the clinical study will return for follow-up visits at 4 weeks (Visit 3) and 12 weeks (Visit 4) during the 12-week treatment programme.

8.11.4 One Week Prior to Visit

Approximately 7 days before each of the planned assessments, subjects will be contacted by telephone to remind them that their follow-up appointment is due and that they should start completing the 7-day voiding diary they have been provided which collects information on number of leaks and number of pads used per day. They will also be reminded that they should also start using their pre-packaged pads to complete the 24-hour pad collection 3 days prior to their appointment and remind them to bring the diary, pads and device back to the clinic.

8.11.5 Assessments

At each visit the following information/procedures will be recorded by the designated blinded site personnel:

- Urine pregnancy test to confirm subject is not pregnant (women of child-bearing potential only) (Week 4 only).
- Complete the Incontinence Quality of Life Questionnaire (I-QOL) (patient quality of life questionnaire).
- Complete the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-IR) (Week 12 only).
- Complete the Patient Global Impression of Improvement (PGI-I) (Week 12 only).
- Complete a standardized stress test to evaluate amount of urine lost following a

standardized bladder-filling protocol verified by ultrasound bladder scanning (provocative pad weight test). Further details of the stress test protocol and instructions for the Investigator and subject are provided in Appendix III.

- Number of incontinence episodes/day from 7-day voiding diary.
- Number of pads used/day from 7-day voiding diary.
- Mean weight of urine lost during a three day 24-hour period at home (difference in post- and pre-weight incontinence pads) (24-hour pad weight test).
- Record any medication use or changes in medication since the last visit.
- Record any cough or cold symptoms since the last visit.
- Record any adverse events since the last visit.

At this visit the following information/procedures will be recorded by the designated unblinded site personnel only:

- Hydrogel electrodes will be checked and replaced with new electrodes if required (Neurotech Vital Compact device only).
- Data from the device will be recorded to determine stimulation parameters and duration of treatments that were completed according to the planned treatment programme. If usage information has been inadvertently erased, the device record provided by the patient may be used to provide compliance data.

At Visit 3 and Visit 4 subjects will be provided with a 7-day consecutive voiding diary and pre-weighed incontinence pads in a sealed bag to complete prior to the next visit. Subjects will be reminded to return the 7-day voiding diary and incontinence pads in the same sealed bag to the clinic at the next visit. Any subjects menstruating during the three days prior to the next visit will also be asked to record this on the voiding diary. Any subjects who have sexual intercourse during this time will be asked to expel any fluid post-intercourse and will be asked to record this on the voiding diary.

8.12 Pelvic Floor Exercises – Visit 4 Only

At Visit 4, the subjects will be provided with a set of instructions for pelvic floor exercises (Kegel exercises as outlined in Appendix IV). Subjects will be advised to perform Kegel exercises daily from 12 weeks to the 26 weeks follow-up. The device and all study-related equipment must be returned to the clinic at this visit.

8.13 Assessments Following Treatment Programme – Visit 5

The same assessments as detailed in Section 9.9.3 and 9.9.4, apart from any assessments related to the devices will be performed at 6 months (+/- 14 days) (Visit 5).

8.14 Adverse Event Reporting – All Visits

All subjects will be evaluated throughout the study for adverse events. All adverse events, including the following, will be assessed by the Investigator, and recorded in the subject Case Record Form including:

- Observed or volunteered problems
- Complaints

- Physical signs and symptoms
- Medical condition which occurs during the study, having been absent at baseline

The need to capture adverse events is not dependent upon whether or not the clinical event is associated with the use of the device. The Investigator will take all appropriate and necessary therapeutic measures required for resolution of the adverse event.

The Investigator should institute appropriate therapeutic and follow-up measures in accordance with good medical practice but should notify the monitor of such actions and record them in the subject's Case Report Form.

Further details on adverse events including definitions are provided in Section 10.0.

Each adverse event must be described in detail including the date of onset, date of resolution, severity, anticipated/unanticipated, frequency of the event (single episode, intermittent, continuous), action taken (none, medical and/or surgical), outcome, relationship to device/procedure, device details (type no./lot no./device status) and if defined as serious must be recorded. Each adverse event must be recorded separately.

Severity will be assessed using the following definitions:

Mild	Aware of sign or symptom, but easily tolerated
Moderate	Discomfort enough to cause interference with usual activity
Severe	Incapacitating with inability to work or do usual activity

The relationship to the device will be assessed by the Investigator using the following definitions:

Not Related	Evidence exists that the adverse event definitely has a cause other than the study device (e.g. pre-existing condition or underlying disease, current illness, or concomitant medication) and does not meet any other criteria listed.
Possibly Related	A temporal relationship exists between the event onset and administration of device. Although the adverse event may appear unlikely to be related to the study device, it cannot be ruled out with certainty; and or the event cannot be readily explained by the subject's clinical state or concomitant therapies.
Probably Related	A temporal relationship exists between the event onset and administration of device, and appears with some degree of certainty to be related based on known mechanism of action of the device. It cannot be readily explained by the subject's clinical state or concomitant therapies.
Definitely Related	Strong evidence exists that the device caused the adverse event. There is a temporal relationship between the event onset and administration of the device. There is strong mechanistic evidence that the event was caused by the device. The subject's clinical state and concomitant therapies have been ruled out as a cause.

9 Adverse Events and Device Deficiencies

9.1 Adverse Events Definitions

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

Adverse Device Effects:
An adverse event related to the use of a medical device.

Device Deficiency:
An inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Device deficiencies include malfunctions, user errors and inadequate labelling.

Collection of Adverse Events:
Adverse events will be collected for randomized subjects only.

Serious Adverse Events (SAE):
An adverse event that:

- Led to death,
- Led to a serious deterioration in the health of a subject, that resulted in 1) a life threatening illness or injury, or 2) a permanent impairment of a body structure or a body function, or 3) in patient or prolonged hospitalisation or 4) medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function
- Led to foetal distress, foetal death or a congenital abnormality or birth defect

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

9.2 Anticipated Adverse Events

There are a number of known potential adverse events that have been documented, or are theoretically potential adverse events with Neuromuscular Electrical Stimulation (NMES).

Potential anticipated adverse events inherent to the use of Neuromuscular Electrical Stimulation (NMES) including:

- Temporary skin reaction (irritation, redness and/or inflammation) at or near the stimulation site during and following periods of stimulation;
- Discomfort and pain (including throbbing pain) at or near the stimulation site;
- Stomach ache;

- Change in bowel habits;
- Twitching, numbness, muscular contraction, tightening, aching;
- Use of excessive intensity or usage time can cause muscle injury;
- On very rare occasions, some patients have reported feeling light-headed or faint, so it is recommended that patients have somewhere to sit nearby should this happen.

Potential anticipated adverse events specifically related to the use of the Neurotech Vital Compact device:

- Develop a sensitivity to the hydrogel electrodes

Potential anticipated adverse events specifically related to the use of the itouch Sure Pelvic Floor Exerciser:

- Abdominal cramps
- Vaginal irritation or infection.

9.3 Reporting to Bio-Medical Research Ltd

ALL SERIOUS ADVERSE EVENTS, SERIOUS ADVERSE DEVICE EFFECTS, UNANTICIPATED ADVERSE DEVICE EFFECTS AND/OR ANY DEVICE DEFICIENCIES MUST BE REPORTED TO BIO-MEDICAL RESEARCH LTD OR ITS AGENT WITHIN 24 HOURS OF BECOMING AWARE OF THE EVENT TO ENSURE THE NECESSARY VIGILANCE PROCEDURES/REPORTING REQUIREMENTS AT BIO-MEDICAL RESEARCH LTD CAN BE MET.

Expedite Research, LLC must be contacted on the following numbers:

Contact Name:	Barbara Powers
Telephone Number:	1-484-686-0545
Fax Number:	1-610-933-1284
Email:	Barbara.Powers@ExpediteResearch.com

The Vigilance Department at Bio-Medical Research Ltd must also be contacted on the following numbers:

Contact Name:	Brendan McCormack, Quality Manager
Telephone Number:	011-35391-774300
Fax Number:	011-35391-774301
Email:	quality@bmr.ie

9.4 Institutional Review Board (IRB) Reporting

All serious adverse events, unanticipated adverse device effects and/or device deficiencies will be reported to the Institutional Review Board in accordance with the local site requirements and to Bio-Medical Research Ltd in accordance with the Study Specific Procedure for the study.

9.5 Food and Drug Administration (FDA) Reporting

This study is considered a Nonsignificant Risk Device Study and is being conducted in accordance with the abbreviated Investigational Device Exemption (IDE) requirements set forth in 21 CFR 812.2(b).

All necessary reporting to the FDA as outlined in FDA guidance (Records under 812.140(b) 4 and 5 and Reports under 812.150(b) 1-3 and 5-10) will be followed.

10 Statistical Analysis

This section describes the statistical methods to be used for the analysis and reporting of data collected under BMR-13-1001. Additional details will be provided in the statistical analysis plan (SAP).

10.1 Analysis Populations

The primary analysis population will be the intent to treat (ITT) population. This will include all randomized subjects. Patients will be summarized according to their randomized assignment.

A per-protocol (PP) population will also be evaluated for the primary endpoint. The PP population will consist of the following subjects and may be further defined in the Statistical Analysis Plan (SAP):

- Signed informed consent
- Meet inclusion/exclusion criteria
- Treated per randomized assignment
- 12 week outcome data available

The Safety population will include all randomized subjects who used the device at least once. Patients will be summarized according to the actual device used, rather than the randomized assignment.

10.2 Sample Size

Sample size calculations were performed using the NQuery Advisor® version 5.0, under a two group test of proportions.

Research suggests that the response rates for Neurotech Vital and itouch Sure at 12 weeks will be 71% and 46%, respectively (itouch success rate based on Sand, 1995).

The sample size calculation is based on the assumption that the itouch Sure Pelvic Floor Exerciser success rate is 52% and the Neurotech Vital Control success rate is 71%. A sample size of 87 subjects per group will provide 90% power using a one-sided Type I error rate of 0.025, and a non-inferiority margin of 5%. A randomization allocation of 1:1 was also assumed. For practical reasons, the sample size has been increased to a recruitment of 180 patients (90 patients per treatment group).

10.3 Statistical Methods

10.3.1 General Statistical Considerations

Data will be summarized using descriptive statistics. For continuous measures this will include mean, standard deviation, median, and range. For categorical measures, counts and percentages will be provided. Data will be summarized separately for each randomized arm under the principles of intent to treat, unless otherwise noted.

10.3.2 Primary Endpoint

The primary endpoint is defined as the proportion of subjects considered to have achieved 'significant improvement' following a provocative pad weight test at 12 weeks compared to baseline.

'Significant improvement' is defined as a greater than 50% reduction in pad weight from baseline.

10.3.3 Hypothesis test

The primary hypothesis that will be tested is that the proportion of patients who respond (i.e. have achieved 'significant improvement') using Neurotech Vital Compact is not less than 5% worse than the itouch Sure Pelvic Floor Exerciser (i.e. the lower bound of the confidence interval about the difference between device groups should be greater than - 5%).

Using a one-sided 2.5% level significance test:

$$H_0: p_{\text{Neurotech Vital Compact}} - p_{CONTROL} \leq -5\%$$

$$H_1: p_{\text{Neurotech Vital Compact}} - p_{CONTROL} > -5\%$$

Where $p_{\text{Neurotech Vital}}$ is the proportion of patients who respond on receiving Neurotech Vital Compact and similarly $p_{CONTROL}$ for the itouch Sure Pelvic Floor Exerciser.

If the primary non-inferiority endpoint is met, a hierarchically nested test of superiority will be performed. The hypothesis test for the assessment of superiority is as follows, using a one-sided 2.5% level significance test:

$$H_0: p_{\text{Neurotech Vital Compact}} - p_{CONTROL} \leq 0\%$$

$$H_1: p_{\text{Neurotech Vital Compact}} - p_{CONTROL} > 0\%$$

Where $p_{\text{Neurotech Vital}}$ is the proportion of patients who respond on receiving Neurotech Vital Compact and similarly $p_{CONTROL}$ for the itouch Sure Pelvic Floor Exerciser.

10.3.4 Analysis Methods

For the primary analysis variable (proportion of patients who respond at Week 12) the difference in the proportions of responders and a 95% CI of the difference in proportion of responders will be calculated using the normal approximation to the binomial distribution. The ITT population will serve as the primary analysis population, with PP population analyses serving as supportive. For the ITT analysis, if a subject does not complete the 12 week assessment, their outcome will be imputed using multiple imputations. Non-inferiority will be claimed if the lower limit of the 95% CI is greater than -5%.

The total number of successes in each study arm will be summarized, along with the corresponding proportions and 95% CIs. The difference between proportions will also be summarized with its corresponding 95% CI.

Sensitivity analyses will be performed to assess the impact of missing data on the primary endpoint results. These analyses will be based on the ITT population. A last observation

carried forward (LOCF) method will be used to account for all missing data. A tipping point analysis will also be performed (Campbell et al., 2011 and Yan X. et al., 2009).

10.3.5 Key Secondary Endpoints

The key secondary endpoints listed below will be tested only if the primary efficacy endpoint is met. These endpoints will each be tested at a 5% two-sided significance level. In order to control the type I error rate the endpoints will be analysed in the following hierarchy. If an endpoint in the sequence fails to show a statistically significance then no further testing of the subsequent endpoints in the hierarchy will be performed.

1. Between group comparison of mean change, with respect to baseline, in urine leakage in a provocative pad weight test at Week 12;
2. Within Neurotech Vital Compact group estimate of mean change, with respect to baseline, in urine leakage in a provocative pad weight test at Week 12;
3. Between group comparison of mean change, with respect to baseline, in urine leakage in the 24-hour pad weight test at Week 12;
4. Within Neurotech Vital Compact group estimate of mean change, with respect to baseline, in urine leakage in the 24-hour pad weight test at Week 12;
5. Between group comparison of mean change, with respect to baseline, in the number of incontinence episodes/day recorded using a 7-day voiding diary at Week 12;
6. Within Neurotech Vital Compact group estimate of mean change, with respect to baseline, in the number of incontinence episodes/day recorded using a 7-day voiding diary at Week 12;
7. Between group comparison of the mean improvement, with respect to baseline, in Incontinence Quality of Life Questionnaire (I-QOL) score at Week 12;
8. Within Neurotech Vital Compact group estimate of mean improvement, with respect to baseline, in Incontinence Quality of Life Questionnaire (I-QOL) score at Week 12;
9. Between group comparison of mean change, with respect to baseline, in the number of pads used/day recorded using a 7-day voiding diary at Week 12;
10. Within Neurotech Vital Compact group estimate of mean change, with respect to baseline, in the number of pads used/day recorded using a 7-day voiding diary at Week 12;
11. Between group comparison of the proportion of subjects achieving dryness at Week 12 (<1g on the provocative pad weight test).

10.3.6 Hypothesis tests

The key-secondary hypothesis for the between group tests (1, 3, 5, 7 and 9 in the hierarchy listed above) is that the key-secondary endpoints of Neurotech Vital Compact is not equal to the itouch Sure Pelvic Floor Exerciser.

Using a two-sided 5% level significance test:

H_0: $\mu_{\text{Neurotech Vital Compact}} = \mu_{\text{CONTROL}}$

H_a: $\mu_{\text{Neurotech Vital Compact}} \neq \mu_{\text{CONTROL}}$

Where μNeurotech Vital Compact and μCONTROL are the mean responses for the key-secondary variable for Neurotech Vital Compact and the itouch Sure Pelvic Floor Exerciser, respectively.

The hypothesis for key-secondary endpoint 11 is as follows, using a one-sided 2.5% level significance test:

H_0: $p_{\text{Neurotech Vital Compact}} - p_{CONTROL} \leq 0\%$

H_1: $p_{\text{Neurotech Vital Compact}} - p_{CONTROL} > 0\%$

Where $p_{\text{Neurotech}}$ Vital is the proportion of patients who become dry on receiving Neurotech Vital Compact and similarly $p_{CONTROL}$ for the itouch Sure Pelvic Floor Exerciser.

The key-secondary hypothesis for the within-group tests (2, 4, 6, 8 and 10 in the hierarchy listed above) is that the key-secondary endpoints of Neurotech Vital Compact are not equal to 0.

Using a two-sided 5% level significance test:

H_0: $\mu_{\text{Neurotech Vital Compact}} = 0$

H_a: $\mu_{\text{Neurotech Vital Compact}} \neq 0$

Where $\mu_{\text{Neurotech Vital Compact}}$ is the mean responses for the key-secondary variable for Neurotech Vital Compact.

10.3.7 Analysis Methods

Analysis of secondary endpoints will be based on the ITT population. All available data will be used, and no imputation is planned for missing data. The Week 12 summaries for each device group will include the number of observations, mean, median, standard deviation, minimum, maximum, and 95% confidence interval. The difference between device groups will be summarized using mean change, standard deviation, and 95% confidence interval of the difference. P-values will be obtained from two-sample t-tests for key-secondary endpoints 1, 3, 5, 7, and 9. For key-secondary endpoint 11, the proportion and counts of subjects achieving dryness at Week 12 will be summarized by group, along with 95% confidence interval. The difference between device groups will be summarized with the 95% confidence interval for the difference. The p-value from the comparison will be based on a chi-square test. One-sample t-tests will be used for key-secondary endpoints 2, 4, 6, 8, and 10. In the event that data are highly non-normal, non-parametric methods may be employed (i.e. signed-rank test, rank-sum test).

10.3.8 Other Secondary Endpoints

Additional secondary endpoints will be summarized using descriptive statistics. There are no formal statistical tests associated with these endpoints, and no claims for labelling will be made.

The secondary endpoints that will be evaluated at 4 weeks and 26 weeks are as follows:

- Proportion of subjects considered to have achieved significant improvement, defined as a greater than 50% reduction in pad weight, from baseline on the provocative pad weight test;
- Urine leakage on the provocative pad weight test (following standardized bladder-filling protocol);
- Urine leakage experienced by the subject at home in the 24-hour pad weight test;
- Incontinence episodes/day recorded using a 7-day voiding diary;
- Proportion of subjects achieving dryness (<1g on the provocative pad weight test);

- Improvement in quality of life assessed using the Incontinence Quality of Life Questionnaire (I-QOL);
- Number of pads/day recorded using a 7-day voiding diary; and
- Dryness, defined as a pad weight of less than 1.3g on the 24-hour pad weight test (including an evaluation at 12 weeks).
- Proportion of subjects considered to have achieved significant improvement, defined as a greater than 50% reduction in pad weight, from baseline on the 24-hour pad weight test (including an evaluation at 12 weeks).

Other secondary measures to be evaluated are as follows:

- Proportion of subjects achieving dryness at Week 12 in each group (<1g on the provocative pad weight test).
- Within Neurotech Vital Compact group estimate of mean change, with respect to baseline, in sexual function as measured by the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-IR) at Week 12;
- Between group comparison of mean change, with respect to baseline, in sexual function as measured by the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-IR) at Week 12;
- Within Neurotech Vital Compact group estimate of patient response to the Patient Global Impression of Improvement (PGI-I) at Week 12.
- Between group comparison of patient response to the Patient Global Impression of Improvement (PGI-I) at Week 12;
- Safety in relation to adverse events and device deficiencies reported;
- Evaluation of reduction in urine leakage on the provocative pad weight test in relation to the mean intensity of the stimulation delivered during the 12-week treatment programme;
- Evaluation of the reduction in urine leakage on the provocative pad weight test at Week 12 in relation to the BMI category (underweight/normal/overweight/obese) of the subjects;
- Evaluation of the reduction in urine leakage on the provocative pad weight test at Week 12 in relation to the baseline severity of stress urinary incontinence of the subjects;
- Device compliance of the Neurotech Vital Compact device with the treatment protocol during the 12-week treatment programme;
- Device compliance of the itouch Sure Pelvic Floor Exerciser with the treatment protocol during the 12-week treatment programme;

10.3.9 Safety

Safety analyses will be performed on the Safety population.

Adverse events will be summarized overall, by severity, seriousness and by relationship to investigational device. Adverse device effects and early withdrawals due to adverse events will be listed and summarised separately. Adverse events will be collected for randomized subjects only.

Ninety-five percent confidence intervals may also be provided for the comparison of serious adverse event rates between randomized arms.

10.3.10 Interim Analysis for Futility

An interim analysis for futility will be conducted when 90 patients have Visit 4 (12 week) data available. The analysis will be conducted by an independent statistician. A conditional power will be calculated based on projecting the observed trend of the difference between the two groups in the primary efficacy parameter for patients completing the study. If the analysis indicates that the conditional power for a positive outcome of non-inferiority is less than 30%, the independent statistician will communicate to a designated sponsor's representative that the study is unlikely to meet its primary objective. The sponsor may evaluate additional information and make a final decision regarding continuation of the study. The interim analysis will not be used to stop the study early for a positive outcome; therefore, no adjustment to the Type-1 error is indicated (Lachin, 2005). Details of the interim analysis for futility will be specified in the Statistical Analysis Plan.

10.3.11 Poolability Analysis

A poolability analysis will be performed on the primary endpoint to test for a differential treatment effect across study centres. The primary endpoint will be summarized by study centre. Poolability will be assessed using a logistic regression model. The logistic regression model will include a covariate for the treatment arm, study centre, and interaction effect of treatment by centre. The p-value for the interaction effect will be provided.

Analyses will be performed for both the ITT and PP population.

10.3.12 Subgroup Analyses

Subgroup analyses will be performed on the primary endpoint to test for differential treatment effects across baseline subgroups. At a minimum, subgroups will be derived for the following parameters: race, BMI, and baseline pad weight. Descriptive statistics will be provided for the primary endpoint success rate for each subgroup.

Logistic regression models will be used to statistically evaluate the effect of the subgroups on the primary endpoint. Specifically, the logistic regression model will include a covariate for the treatment arm, subgroup, and interaction effect of treatment by subgroup. The p-value for the interaction effect will be provided.

Analyses will be performed for both the ITT and PP population.

10.3.13 Software

All analyses will be performed using SAS, version 9.3 or later. In the event an analysis is required that is better suited for a statistical package other than SAS, this other package (e.g. R) will be used.

11 Investigator Responsibilities

11.1 Investigator Responsibilities

11.1.1 Informed Consent
The investigator is responsible for obtaining informed consent under 21 CFR Part 50.

11.1.2 Records
Clinical investigators must maintain the records of each subject's case history and exposure to the device under §812.140(a)(3)(i). Case histories include case report forms and supporting data, including signed and dated consent forms and medical records, including progress notes of the physician, the individual's clinical records(s), and the nurses' notes (where applicable to healthy volunteers). Records must include documents demonstrating informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent. The case history of each individual must document that informed consent was obtained prior to participation in the study.

11.1.3 Reports
Clinical investigators must make the following required reports when applicable:
- Unanticipated Adverse Device Effects [§812.150(a)(1)]
- Withdrawal of IRB Approval [§812.150(a)(2)]
- Informed consent [§812.150(a)(5)]
- Other reports requested by a reviewing IRB or FDA [§812.150(a)(7)]

11.1.4 Financial Disclosure
Because the data in this study is planned to be submitted in a marketing application, then 21 CFR 54, Financial Disclosure, applies. The Investigator must disclose to the Sponsor sufficient accurate financial information to allow the IDE applicant (or sponsor) to submit certification or disclosure of financial interests. The investigator must update the information if any relevant changes occur during the course of the study and for one year following completion of the study (§ 812.110).

11.1.5 Investigator Qualifications and Training

The Investigators have been selected to participate in this study due to their extensive experience and publications in the field of Women's Health/Urology/Urogynecology/ and study of investigational medical devices.

11.1.6 Financial Considerations and Support

Details of financial support provided by Bio-Medical Research Ltd for the conduct of the study will be addressed in the Investigator Agreement.

11.2 Data Collection

11.2.1 Completion of Case Report Forms

An electronic case report form (eCRF) will be utilised for this study. Prior to the start of the clinical study, the eCRF provider will provide the site with appropriate log-in credentials for the Investigator, study personnel (blinded and unblinded). The Investigator will be responsible for the accuracy and completeness of the eCRF for each individual subject and be responsible for completing the eCRF in a timely manner. The personal data recorded on all documents will be regarded as confidential.

The Investigator must record the subject's participation in this clinical study in the subject's clinic notes. In addition, the Investigator must keep a separate Subject Identification Log of all subjects entered into the clinical study showing each subject's name, date of birth and assigned subject number for identification purposes.

11.3 Review and Return of Completed Documentation

The Investigator will make the original source documentation available to the Sponsor's designated monitor at each visit. At the conclusion of the clinical study, completed eCRFs will be electronically signed by the Investigator. A copy of the eCRF will be provided to the site at the conclusion of the study.

11.4 Retention of Documentation

The Investigator will retain all copies of the records for a period of 15 years from the discontinuation of the clinical study. In all cases, the Investigator must contact the Sponsor prior to disposing of any records related to the clinical study. Included in records to be maintained are signed Study Protocol, copies of the Case Report Forms, signed consent forms, ethics committee approval letters, device accountability records, correspondence concerning the clinical study and any other documents to identify the subjects.

In addition, if the Investigator leaves the position, etc., he/she should provide Bio-Medical Research Ltd with the name and address of the person who will be responsible for the clinical study related records.

11.5 Maintenance of Randomisation and Blinding

A randomisation schedule will be provided. The randomisation schedule is in a permuted block-format randomisation, stratified by study site, to ensure that the subject allocation at the sites remains balanced.

The Subject ID number, randomisation date and patient initials will be recorded along with the allocated treatment.

It is not anticipated that there will be any need to unblind (break the randomisation code) of any subject participating in the study because of an adverse event/adverse device effect, however, the information will be available at the site via the unblinded personnel.

One member of the investigational site team will be responsible for patient training and will consequently be unblinded to required treatment instructions for training. A different member of the team will be responsible for all other patient assessments and CRF completion.

11.6 Data Management

All required data will be entered into the electronic Case Record Forms (eCRF) by designated site personnel. The data will be maintained securely within the database by means of password protection and other security measures with restricted access as detailed by the data management company.

Database validation will have been carried out prior to inclusion of study data and once verified an appropriate documentation trail will be maintained to include details of initial entry, data validation checks, query resolution and database amendment.

The database will be subject to quality control checks and the resulting output will be used to raise any data queries, after reference to the eCRF throughout the study. All data queries will be resolved with the assistance of monitoring staff and according to the Data Management Plan.

On resolution of all data queries, the database will be closed and data listings, summary tables, graphical output and descriptive statistics produced.

12 Sponsor Responsibilities

The Sponsor agrees to adhere to the ICH Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95, Jan.97) and US FDA Regulations. It is the Sponsor's responsibility to obtain appropriate regulatory approval to perform the trial (if applicable). The Sponsor should notify promptly all concerned investigator(s), IRB(s)/IEC(s) and the Regulatory Authority of findings that could adversely affect the health of the patients/ subjects, impact on the conduct of the trial or alter the Regulatory Authority's authorization to continue the trial. If it is necessary to change, or deviate from the protocol to eliminate an immediate hazard to the subjects the Sponsor will notify the relevant regulatory authority and relevant IRB/IEC of the new events, the measures taken and the plan for further action as soon as possible. This will be by telephone in the first instance followed by a written report.

On completion of the trial, the Sponsor will inform the regulatory authority that the trial has ended. If the study is terminated for any reason the Sponsor will provide a written statement to the relevant regulatory authority and the IRB/IEC with the reasons for termination of the trial. This will be conducted within 15 days of the decision to terminate the trial. The Sponsor will report in an expeditious manner all suspected unexpected serious adverse reactions (SUSARs) to the relevant regulatory authority and IRBs/IECs, as required.

12.1 Indemnity

The Sponsor will provide "no-fault" compensation insurance against any risk incurred by a subject as a result of participation in this trial. The Sponsor will indemnify the Investigator as detailed in a separate document.

12.2 Study Monitoring

The Investigator will permit a designated representative of Bio-Medical Research Ltd to inspect all Case Report Forms and corresponding subject's clinic records at regular intervals throughout the clinical study. These monitoring visits are for the purpose of verifying adherence to the Study Protocol and the completeness and accuracy of the data being entered on the Case Report Forms and will be conducted in accordance with an approved monitoring plan.

The monitor will be responsible for securing the compliance of the Investigator to the signed agreement, the Study Protocol and requirements of FDA abbreviated IDE requirements set forth in 21 CFR 812.2(b) and international standards of Good Clinical Practice (FDA guidance E6). Assessments will also be made regarding the subjects' protection and safety, as well as the quality, completeness, and integrity of the data.

Subject diaries, device records and questionnaires completed by the subject will be classified as source data. All other study data should have alternative identifiable source documents agreed by the Investigator and Bio-Medical Research Ltd prior to the start of the study, in the subject notes.

The planned extent of source data verification will be documented in a monitoring plan which is agreed and signed off by the Study Manager prior to the commencement of the first monitoring visit.

12.3 Final Report

Statistical analyses for the final report will be carried out when all subjects have completed the study or withdrawn from the study and the database has been locked.

12.4 Publications

The results of this clinical study may be submitted for publication. Details of publications will be addressed in the Investigator Agreement.

12.5 Quality Control and Quality Assurance

Investigators are reminded that in agreeing to participate in this clinical study and by signed agreement of the Study Agreement documentation, they will seek to ensure that all subjects included in the study are compliant with the requirements of the study at the point of entry and remain so during their participation in the study.

Repeated and serious failures in subject compliance will be addressed as they have the potential to affect both patient safety and study outcome and where necessary corrective and preventative actions will be taken.

12.6 Termination Procedure

The clinical study will be stopped when the risk benefit profile of the study becomes negative caused by the occurrence of unexpected serious adverse device effects or lack of performance.

If such action is taken, the Sponsor/Coordinating Investigator will discuss the reasons with the Investigator.

If the study is terminated or suspended due to safety reasons, the Sponsor/Coordinating Investigator will inform research ethics committee promptly and provide the reason(s) for the suspension or termination.

13 References

1. Ashton-Miller J, Howard D, DeLancey JO. The functional anatomy of the female pelvic floor and stress incontinence control system. Scan J Urol Nephrol Suppl 2001, Supplement 207: 1-7.
2. Bo, K. Pelvic Floor muscle training is effective in treatment of female stress urinary incontinence, but how does it work? Int Urogynecol J Pelvic Floor Dysfunct 2004, 15(2): 76-84.
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4. Castro RA, Arruda RM, Zanetti MRD, Rotta AL, Santos PFD, Sartori MGF, Girão MJBC. Single blind, randomized, controlled trial of pelvic floor muscle training, electrical stimulation, vaginal cones and no active treatment in women with stress urinary incontinence. Clinics 2008; 63(4):465-72.
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6. Maher R.M, Crowe L. The impact of surface neuro muscular electrical stimulation (NMES) on stress urinary incontinence patient outcomes. University College Dublin, 2008.
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8. R.O'Sullivan, *et al* "Definition of Mild, Moderate and Severe Incontinence on the 24-hour pad test". BJOG, International Journal of Obstetrics and Gynecology. August 2004. Volume III, pgs. 859-862.
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10. Yalcin I, Bump R. Validation of two global impression questionnaires for incontinence. Am J Obstet Gynecol 2003;189:98-101
11. Yan X, Lee S, Li N Missing data handling methods in medical device clinical trials J. Biopharm. Stat. 2009: 19; 1085-1098

14 Appendices

14.1 Appendix I. Schedule of Events

		12-week treatment programme with Neurotech Vital Compact device or itouch Sure Pelvic Floor Exerciser				Kegel Exercises Week 12 to 26
	V1	V2	Telephone	V3	V4	V5
Assessments	Screening	Baseline	Week 1	Week 4	Week 12	Week 26 (6 months)
Patient Consent	X					
Demographics	X					
Medical History/Physical Examination	X					
Medication Use (or change of medication)	X	X	X	X	X	X
Record cough/cold symptoms	X	X		X	X	X
Adverse Events	X	X	X	X	X	X
Pregnancy Test (pre-menopausal subjects only)	X			X		
Subject device training		X				
Stress test following standardised bladder filling (provocative pad test)	X Practice test	X To determine eligibility		X	X	X
24-h pad weight test (3 days prior to visit)		X		X	X	X
7-day voiding diary (prior to visit)		X		X	X	X
Incontinence Quality of Life Questionnaire (IQOL)		X		X	X	X
Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-IR)		X			X	
Patient Global Impression of Improvement (PGI-I)					X	
MESA questionnaire	X					
Telephone Contact			X			
Download compliance data; review device record				X	X	
Kegel exercise instructions					X	

14.2 Appendix II. itouch Sure Pelvic Floor Exerciser 510k Summary

See Itouch Sure Pelvic Floor Exerciser 510K letter from the FDA dated June 21 2011.

K103698
pg 1/3

510(k) Summary

JUN 2 1 2011

Date of Summary prepared: April 27th, 2011

Submitter : Tenscare Ltd
Address : 9 Blenheim Road, Longmead Business Park, Epsom, Surrey, KT19 9BE, United Kingdom
Tel : +44(0)1372 723 434
Fax : +44(0)1372 745 434
E-Mail : sales@tenscare.co.uk
FDA Establishment registration no: 3003446042
Contact person: Andrew Brown

Address of the manufacturing facility:
EasyMed Instrument Ltd
5F/6F, Block A, Gupo Gongmao Building,
Fengxin Road, Fangxiang Industrial District,
Datiang, Shunde, Foshan, Guangdong,
China,
Zip: 528300
FDA Establishment registration no: 3004049909

Address of American Representative:
DEBORAH IAMPIETRO
QRC CONSULTING ASSOCIATES
130 Gotzens Rd
Conway, NH 03818
Phone: 603 4476086 ext
Fax: 734 4236086
Email: qrcassoc@aol.com

Submitted Device:

Generic name: Pelvic Floor Stimulator
Trade name: TensCare itouch Sure
Common name: itouch Sure Pelvic Floor Exerciser
Classification name: Stimulator, Electrical, Non-implantable, for Incontinence – Title 21, Code of Federal Regulations Sec.876.5320 ProCode: 78 KPI
Device Classification: Class II
Predicate Devices: Innova Pelvic Floor Stimulation System by EMPI. K941911
Kegel 8 Pelvic Muscle Trainer by NE Services. K81480

The class of the predicate Devices: Class II

Device Description:
The itouch Sure is a small lightweight battery powered single channel neuromuscular stimulation device supplied with a vaginal two electrode stimulation probe.
The probe connects to the control unit by cable and plug.

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14.3 Appendix III. Stress Test Protocol

Where possible the assessment will be performed by the same examiner each time for the duration of the study, for a given subject, as follows:

Balance Calibration

- All pad weights will be weighed using a balance supplied by the Sponsor.
- On each day of the assessments and prior to the weighing of the pads, the balance will be calibrated using calibration weight supplied by the Sponsor and the details recorded to verify the balance is operational.
- All zip-lock freezer bags will be weighed in a container to minimise any weight fluctuations.

Bladder Filling Protocol

- Prior to the stress1h pad test, a pad (moderate POISE) is placed in a zip-lock bag (Weight A).
- Subjects are advised to attend the clinic with a comfortably full bladder.
- Following the pregnancy test, the subject voids the bladder and then drinks 500 mL of water.
- The subject is instructed not to go to the toilet and waits for 1 hour.
- After approximately 1 hour, the Investigator will check that natural diuresis has resulted in a bladder volume of more than 250mL as confirmed by ultrasound or other appropriate method.
- If the bladder volume is not 250mL or more, the subject will be instructed to wait for approximately 30 minutes when it will be re-checked. The exact bladder volume will be recorded.
- On confirmation the bladder volume is 250mL or more, the pad is handed to the subject in the bag and the subject is instructed to attach the pad in their underwear and put the packaging and pad liner back in the zip-lock freezer bag.

Stress Test Protocol is a modified version of the provocative test determined by Bo, 1999.

- The metronome is set to 132bpm.
- The subject is instructed not to contract their pelvic floor muscles but to ‘leak’ as usual.
- The subject is then instructed to run on the spot (with their knees bent) for 30 seconds followed immediately by 30 seconds of jumping jacks (with their arms straight and legs as wide as they can).
- The subject will be encouraged to keep pace with the metronome during the test. If the subject cannot, it will be documented how much of the protocol was completed to establish their baseline. This exact test must then be used in subsequent follow up visits.
- The subject will be asked to sit and stand 10 times from a chair, (the same chair to be used in repeated tests)
- The subject will cough forcefully 10 times
- The subject will pick an object, e.g a pencil, off the floor 5 times.
- The subject then places the pad in the ziplock freezer bag which is weighed (Weight B)
- The weight of urine loss during the stress test is then calculated (Weight B – Weight A)
- All timings will be conducted using a stop-watch or smart phone.

14.4 Appendix IV. Pelvic Floor Exercises

How to do Kegel exercises
It takes diligence to identify your pelvic floor muscles and learn how to contract and relax them. Here are some pointers:

Find the right muscles
To make sure you know how to contract your pelvic floor muscles, try to stop the flow of urine while you're urinating. If you succeed, you've got the basic move. Or try another technique: Insert a finger inside your vagina and try to squeeze the surrounding muscles. You should be able to feel your vagina tighten and your pelvic floor move upward. Then relax your muscles and feel your pelvic floor move down to the starting position. As your muscles become stronger — and you become more experienced with the exercises — this movement will be more pronounced.

But don't make a habit of starting and stopping your urine stream. Doing Kegel exercises with a full bladder or while emptying your bladder can actually weaken the muscles. It can also lead to incomplete emptying of the bladder, which increases your risk of a urinary tract infection.

Perfect your technique
Once you've identified your pelvic floor muscles, empty your bladder and lie down. Then:

- Contract your pelvic floor muscles.
- Hold the contraction for three seconds then relax for three seconds.
- Repeat 15 times.
- Once you've perfected three-second muscle contractions, try contracting it for four seconds at a time, alternating muscle contractions with a four-second rest period.
- Work up to keeping the muscles contracted for 10 seconds at a time, relaxing for 10 seconds between contractions.

To get the maximum benefit, focus on tightening only your pelvic floor muscles or isolating your pelvic floor muscles. Be careful not to flex the muscles in your abdomen, thighs or buttocks. Also, try not to hold your breath. Just relax, breathe freely and focus on tightening the muscles around your vagina and rectum.

Repeat twice a day
Perform 3 sets of 15 Kegel exercises twice a day. The exercises will get easier the more often you do them. You might make a practice of fitting in a set every time you do a routine task, such as checking e-mail or commuting to work.

14.5 Appendix V. Incontinence Quality of Life (I-QOL) Questionnaire

PLEASE WRITE IN TODAY'S DATE: ___ _____ ____
Day Month Year

PARTICIPANT ID:

PLEASE READ THIS CAREFULLY

ON THE FOLLOWING PAGES YOU WILL FIND SOME STATEMENTS THAT HAVE BEEN MADE BY PEOPLE WHO HAVE URINARY INCONTINENCE (LEAKING URINE WHEN YOU DON'T WANT TO).

PLEASE CHOOSE THE RESPONSE THAT APPLIES BEST TO YOU RIGHT NOW AND CIRCLE THE NUMBER OF YOUR ANSWER.

IF YOU ARE UNSURE ABOUT HOW TO ANSWER A QUESTION, PLEASE GIVE THE BEST ANSWER YOU CAN. **THERE ARE NO RIGHT OR WRONG ANSWERS.**

YOUR ANSWERS WILL BE KEPT STRICTLY CONFIDENTIAL.

IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT:

INCONTINENCE – QUALITY OF LIFE

Your Feelings

(Please circle the number of your answer)

1. I worry about not being able to get to the toilet on time

   1 EXTREMELY
   2 QUITE A BIT
   3 MODERATELY
   4 A LITTLE
   5 NOT AT ALL

2. I worry about coughing or sneezing because of my urinary problems or incontinence.

   1 EXTREMELY
   2 QUITE A BIT
   3 MODERATELY
   4 A LITTLE
   5 NOT AT ALL

3. I have to be careful standing up after I've been sitting down because of my urinary problems or incontinence.

   1 EXTREMELY
   2 QUITE A BIT
   3 MODERATELY
   4 A LITTLE
   5 NOT AT ALL

4. I worry about where toilets are in new places.

   1 EXTREMELY
   2 QUITE A BIT
   3 MODERATELY
   4 A LITTLE
   5 NOT AT ALL

5. I feel depressed because of my urinary problems or incontinence.

   1 EXTREMELY
   2 QUITE A BIT
   3 MODERATELY
   4 A LITTLE
   5 NOT AT ALL

INCONTINENCE – QUALITY OF LIFE

(Please circle the number of your answer)

6. Because of my urinary problems or incontinence, I don't feel free to leave my home for long periods of time.

   1 EXTREMELY
   2 QUITE A BIT
   3 MODERATELY
   4 A LITTLE
   5 NOT AT ALL

7. I feel frustrated because my urinary problems or incontinence prevents me from doing what I want.

   1 EXTREMELY
   2 QUITE A BIT
   3 MODERATELY
   4 A LITTLE
   5 NOT AT ALL

8. I worry about others smelling urine on me.

   1 EXTREMELY
   2 QUITE A BIT
   3 MODERATELY
   4 A LITTLE
   5 NOT AT ALL

9. My urinary problems or incontinence is always on my mind.

   1 EXTREMELY
   2 QUITE A BIT
   3 MODERATELY
   4 A LITTLE
   5 NOT AT ALL

10. It's important for me to make frequent trips to the toilet.

    1 EXTREMELY
    2 QUITE A BIT
    3 MODERATELY
    4 A LITTLE
    5 NOT AT ALL

INCONTINENCE – QUALITY OF LIFE

(Please circle the number of your answer)

11. Because of my urinary problems or incontinence, it's important to plan every detail in advance.

    1 EXTREMELY
    2 QUITE A BIT
    3 MODERATELY
    4 A LITTLE
    5 NOT AT ALL

12. I worry about my urinary problems or incontinence getting worse as I grow older.

    1 EXTREMELY
    2 QUITE A BIT
    3 MODERATELY
    4 A LITTLE
    5 NOT AT ALL

13. I have a hard time getting a good night of sleep because of my urinary problems or incontinence.

    1 EXTREMELY
    2 QUITE A BIT
    3 MODERATELY
    4 A LITTLE
    5 NOT AT ALL

14. I worry about being embarrassed or humiliated because of my urinary problems or incontinence.

    1 EXTREMELY
    2 QUITE A BIT
    3 MODERATELY
    4 A LITTLE
    5 NOT AT ALL

15. My urinary problems or incontinence makes me feel like I'm not a healthy person.

    1 EXTREMELY
    2 QUITE A BIT
    3 MODERATELY
    4 A LITTLE
    5 NOT AT ALL

INCONTINENCE – QUALITY OF LIFE

(Please circle the number of your answer)

16. My urinary problems or incontinence makes me feel helpless.

1 EXTREMELY
2 QUITE A BIT
3 MODERATELY
4 A LITTLE
5 NOT AT ALL

17. I get less enjoyment out of life because of my urinary problems or incontinence.

1 EXTREMELY
2 QUITE A BIT
3 MODERATELY
4 A LITTLE
5 NOT AT ALL

18. I worry about wetting myself.

1 EXTREMELY
2 QUITE A BIT
3 MODERATELY
4 A LITTLE
5 NOT AT ALL

19. I feel like I have no control over my bladder.

1 EXTREMELY
2 QUITE A BIT
3 MODERATELY
4 A LITTLE
5 NOT AT ALL

20. I have to watch what or how much I drink because of my urinary problems or incontinence.

1 EXTREMELY
2 QUITE A BIT
3 MODERATELY
4 A LITTLE
5 NOT AT ALL

INCONTINENCE – QUALITY OF LIFE

(Please circle the number of your answer)

21. My urinary problems or incontinence limit my choice of clothing.

1 EXTREMELY
2 QUITE A BIT
3 MODERATELY
4 A LITTLE
5 NOT AT ALL

22. I worry about having sex because of my urinary problems or incontinence.

1 EXTREMELY
2 QUITE A BIT
3 MODERATELY
4 A LITTLE
5 NOT AT ALL

14.6 Appendix VI. PISQ-IR questionnaire

Appendix A:
PISQ-IR: Sexual Function for Women with: POP, Urinary Incontinence and/or Fecal Incontinence

IUGA
international urogynecological association

For More Information or Questions
Email: survey@iuga.org

Q1 Which of the following best describes you:

Not sexually active at all	1 ☐ ➜	Go to item Q2 (Section 1)
Sexually active with or without a partner	2 ☐ ➜	Skip to item Q7 (Section 2)

Section 1: For those who are not Sexually Active

☞ If you engage in sexual activity please check this box ☐ and skip to Page 3

Q2 The following are a list of reasons why you might not be sexually active, for each one please indicate how strongly you agree or disagree with it as a reason that you are not sexually active.

	STRONGLY AGREE	SOMEWHAT AGREE	SOMEWHAT DISAGREE	STRONGLY DISAGREE
a No partner	☐1	☐2	☐3	☐4
b No Interest	☐1	☐2	☐3	☐4
c Due to bladder or bowel problems (urinary or fecal incontinence) or due to prolapse (a feeling of or a bulge in the vaginal area)	☐1	☐2	☐3	☐4
d Because of my other health problems	☐1	☐2	☐3	☐4
e Pain	☐1	☐2	☐3	☐4

Q3 How much does the fear of leaking urine and/or stool and/or a bulging in the vagina (either the bladder, rectum or uterus falling out) cause you to avoid or restrict your sexual activity?

1 ☐ Not at All
2 ☐ A Little
3 ☐ Some
4 ☐ A Lot

Q4 For each of the following, please circle the number between 1 and 5 that best represents how you feel about your sex life.

		RATING					
a.	Satisfied	1	2	3	4	5	Dissatisfied
b.	Adequate	1	2	3	4	5	Inadequate

PISQ-IR 2

Q5 How strongly do you agree or disagree with each of the following statements:

	STRONGLY AGREE	SOMEWHAT AGREE	SOMEWHAT DISAGREE	STRONGLY DISAGREE
a. I feel frustrated by my sex life	☐1	☐2	☐3	☐4
b. I feel sexually inferior because of my incontinence and/or prolapse	☐1	☐2	☐3	☐4
c. I feel angry because of the impact that incontinence and/or prolapse has on my sex life	☐1	☐2	☐3	☐4

Q6 Overall, how bothersome is it to you that you are not sexually active?

1 ☐ Not at All
2 ☐ A Little
3 ☐ Some
4 ☐ A Lot

End of Items for Not Sexually Active

PISQ-IR 3

Section 2: For Those Who are Sexually Active

The remaining items in the survey are about a topic that one is not often asked to report on in a survey please answer as honestly and clearly as you possibly can.

Q7 How often do you feel sexually aroused (physically excited or turned on) during sexual activity?

1 ☐ Never
2 ☐ Rarely
3 ☐ Sometimes
4 ☐ Usually
5 ☐ Always

Q8 When you are involved in sexual activity, how often do you feel each of the following:

	NEVER	RARELY	SOMETIMES	USUALLY	ALMOST ALWAYS
a. Fulfilled	☐[1]	☐[2]	☐[3]	☐[4]	☐[5]
b. Shame	☐[1]	☐[2]	☐[3]	☐[4]	☐[5]
c. Fear	☐[1]	☐[2]	☐[3]	☐[4]	☐[5]

Q9 How often do you leak urine and/or stool with <u>any type</u> of sexual activity?

1 ☐ Never
2 ☐ Rarely
3 ☐ Sometimes
4 ☐ Usually
5 ☐ Always

Q10 Compared to orgasms you have had in the past, how intense are your orgasms now?

1 ☐ Much less intense
2 ☐ Less intense
3 ☐ Same intensity
4 ☐ More intense
5 ☐ Much more intense

PISQ-IR 4

Q11 How often do you feel pain during sexual intercourse? (If you don't have intercourse check this box ☐ and skip to the next item.)

1 ☐ Never
2 ☐ Rarely
3 ☐ Sometimes
4 ☐ Usually
5 ☐ Always

Q12 Do you have a sexual partner?

1 ☐ Yes ➜ Go to Q13
2 ☐ No ➜ Skip to Q15

Q13 How often does your partner have a problem (lack of arousal, desire, erection ,etc.) that limits your sexual activity?

1 ☐ All of the time
2 ☐ Most of the time
3 ☐ Some of the time
4 ☐ Hardly ever/Rarely

Q14 In general, would you say that your partner has a positive or negative impact on each of the following:

	VERY POSITIVE	SOMEWHAT POSITIVE	SOMEWHAT NEGATIVE	VERY NEGATIVE
a. Your sexual desire	☐1	☐2	☐3	☐4
b. The frequency of your sexual activity	☐1	☐2	☐3	☐4

Q15 When you are involved in sexual activity, how often do you feel that you want more?

1 ☐ Never
2 ☐ Rarely
3 ☐ Sometimes
4 ☐ Usually
5 ☐ Always

Q16 How frequently do you have sexual desire, this may include wanting to have sex, having sexual thoughts or fantasies, etc.?

1 ☐ Daily
2 ☐ Weekly
3 ☐ Monthly
4 ☐ Less often than once a Month
5 ☐ Never

PISQ-IR 5

Q17 How would you rate your level (degree) of sexual desire or interest?

1 ☐ Very high
2 ☐ High
3 ☐ Moderate
4 ☐ Low
5 ☐ Very low or none at all

Q18 How much does the fear of leaking urine, stool and/or a bulging in the vagina(prolapse) cause you to avoid sexual activity?

1 ☐ Not at All
2 ☐ A Little
3 ☐ Some
4 ☐ A Lot

Q19 For each of the following, please circle the number between 1 and 5 that best represents how you feel about your sex life.

		RATING					
a	Satisfied	1	2	3	4	5	Dissatisfied
b	Adequate	1	2	3	4	5	Inadequate
c	Confident	1	2	3	4	5	Not Confident

Q20 How strongly do you agree or disagree with each of the following statements:

	STRONGLY AGREE	SOMEWHAT AGREE	SOMEWHAT DISAGREE	STRONGLY DISAGREE
a. I feel frustrated by my sex life	☐[1]	☐[2]	☐[3]	☐[4]
b. I feel sexually inferior because of my incontinence and/or prolapse	☐[1]	☐[2]	☐[3]	☐[4]
c. I feel embarrassed about my sex life	☐[1]	☐[2]	☐[3]	☐[4]
d. I feel angry because of the impact that incontinence and/or prolapse has on my sex life	☐[1]	☐[2]	☐[3]	☐[4]

PISQ-IR 6

14.7 Appendix VII. Medical, Epidemiologic and Social Aspects of Aging Urinary Incontinence (MESA) Questionnaire

If you have any urine leakage, the questions below will be asking you about urination and activities that cause some people to lose urine. Please place a tick in the box that best describes you and your situation.
STRESS INCONTINENCE QUESTIONS

1)	Does coughing gently cause you to lose urine?	☐ Often (3) ☐ Sometimes (2) ☐ Rarely (1) ☐ Never (0)
2)	Does coughing hard cause you to lose urine?	☐ Often (3) ☐ Sometimes (2) ☐ Rarely (1) ☐ Never (0)
3)	Does sneezing cause you to lose urine?	☐ Often (3) ☐ Sometimes (2) ☐ Rarely (1) ☐ Never (0)
4)	Does lifting things cause you to lose urine?	☐ Often (3) ☐ Sometimes (2) ☐ Rarely (1) ☐ Never (0)
5)	Does bending over cause you to lose urine?	☐ Often (3) ☐ Sometimes (2) ☐ Rarely (1) ☐ Never (0)
6)	Does laughing cause you to lose urine?	☐ Often (3) ☐ Sometimes (2) ☐ Rarely (1) ☐ Never (0)
7)	Does walking briskly cause you to lose urine?	☐ Often (3) ☐ Sometimes (2) ☐ Rarely (1) ☐ Never (0)
8)	Does straining, if you are constipated, cause you to lose urine?	☐ Often (3) ☐ Sometimes (2) ☐ Rarely (1) ☐ Never (0)
9)	Does getting up from a sitting to standing position cause you to lose urine?	☐ Often (3) ☐ Sometimes (2) ☐ Rarely (1) ☐ Never (0)

If you have any urine leakage, the questions below will be asking you about urination and activities that cause some people to lose urine. Please place a tick in the box that best describes you and your situation.
URGE INCONTINENCE QUESTIONS

1)	Some people receive very little warning and suddenly find that they are losing, or about to lose, urine beyond their control. How often does this happen to you?	☐ Often (3) ☐ Sometimes (2) ☐ Rarely (1) ☐ Never (0)
2)	If you can't find a toilet or find the toilet is occupied, and you have an urge to urinate, how often do you end up losing urine or wetting yourself?	☐ Often (3) ☐ Sometimes (2) ☐ Rarely (1) ☐ Never (0)
3)	Do you lose urine when you suddenly have the feeling that your bladder is full?	☐ Often (3) ☐ Sometimes (2) ☐ Rarely (1) ☐ Never (0)
4)	Does washing your hands cause you to lose urine?	☐ Often (3) ☐ Sometimes (2) ☐ Rarely (1) ☐ Never (0)
5)	Does cold weather cause you to lose urine?	☐ Often (3) ☐ Sometimes (2) ☐ Rarely (1) ☐ Never (0)
6)	Does drinking cold beverages cause you to lose urine?	☐ Often (3) ☐ Sometimes (2) ☐ Rarely (1) ☐ Never (0)

I confirm that this has been completed by patient ID no _____ **Study Site Staff Initials:**	Date Completed (dd/mm/yy):

Total Urge Score =	☐☐ **(maximum score =18)**
Urge Score Ratio x 100% =	☐☐.☐ **%**
Total Stress Score =	☐☐ **(maximum score =27)**
Stress Score Ratio x 100% =	☐☐.☐ **%**
Predominance =	☐ **Stress incontinence** ☐ **Urge incontinence** ☐ **Neither**

14.8 Appendix VIII. 7-Day Voiding Diary and Device Record

Bio-Medical Research Ltd Version: 2.0 25MAR2015

Neurotech Vital – Compact RCT USA **Study Number: BMR-13-1001**	**Voiding Diary**
Subject Initials: ____ ____ ____ **Subject ID No: S** ____ ____ - ____ ____ ____ **Subject ID No.:** ____ ____ - ____ ____ ____ *(after randomization)*	**Starting Date:** ☐☐/☐☐/☐☐ M M / D D / Y Y

YOUR DAILY BLADDER DIARY ***Please fill out this diary for SEVEN consecutive days and bring it with you to your next appointment with your used/unused pads and other study supplies.***

Date (month/day/year)	How many pads used during this 24h period? If none, write zero.	How many leaks during this 24h period? If none, write zero.	Were you menstruating during this 24h period? (Yes or No)	Did you have intercourse during this 24h period? (Yes or No)

I confirm that I completed this form (Subject signature/date):

I confirm that I have reviewed this form (staff signature/date):

Bio-Medical Research Ltd Version: 2.0 13MAR2015

Neurotech Vital – Compact RCT USA **Study Number: BMR-13-1001**	**Device Record**
Subject Initials: ____ ____ ____	**Subject ID No:** ____ ____ - ____ ____ ____

<u>YOUR DAILY Device Record:</u> ***Write the date, duration of use and the stimulation intensity; bring it with you to your next appointment with your used/unused pads, device and other study supplies.***

Starting Date (month/day/year) ___ / ___ / ___	Duration of use (minutes) (write ND if did not use device on this date)	Maximum Stimulation Intensity (write ND if did not use device on this date)
Month/Day		
I confirm that I completed this form (Subject initials):		
I confirm that I have reviewed this form (staff signature/date):		

14.9 Appendix IX. Patient Global Impresssion of Improvement – Incontinence (PGI-I)

The PGI-I is a transition scale that is a single question asking the patient to rate their urinary tract condition now, as compared with how it was prior to before beginning treatment on a scale from 1. Very much better to 7. Very much worse (Yalcin & Bump, 2003).

14.10 Appendix X. Sample Informed Consent

Sample Consent to Participate in Research Study BMR-13-1001
(May be revised with Sponsor consent if required by local IRB)

A single-blind, multi-centre, randomised controlled, non-inferiority clinical study to assess the safety and performance of the Neurotech Vital Compact device compared to the itouch Sure Pelvic Floor Exerciser for the treatment of stress urinary incontinence in female subjects.

Study to be conducted at: [Insert Site Name]

Sponsor Name: Bio-Medical Research Ltd, Parkmore Business Park West, Galway, Ireland

Principal Investigator: [Insert Principal Investigator Name and Address, Telephone]

Further information and contact details:
For more information concerning this study and research-related risks or injuries, or to give comments or express concerns or complaints, you may contact the principal investigator, xxxx, MD. You may also contact a representative of the Institutional Review Board XXXXXX for information regarding your rights as a participant involved in a research study or to give comments or express concerns, complaints or offer input. You may obtain the name and number of this person by calling xxxxx.

Introduction:
You are being asked to participate in a research study. However, before you choose to be a research participant, it is important that you read the following information and ask as many questions as necessary to be sure that you understand what taking part in this research study will involve. Your signature on this consent form will acknowledge that you received all of the following information and explanations verbally and have been given an opportunity to discuss your questions and concerns with the Investigator.

What is the purpose of the study?
The purpose of this study is to determine whether the safety and performance profile of the Neurotech Vital Compact (delivering electrical stimulation through external electrodes) is equivalent to the itouch Sure Pelvic Floor Exerciser (delivering electrical stimulation through an internal vaginal probe) over a 12-week treatment period with a 14-week follow-up period.

What are the devices that are being used in the study?
Neurotech Vital™ Compact: The Neurotech Vital Compact device is considered by the US FDA to be an investigational product currently under development by the Sponsor of this clinical research study, Neurotech Group, a division of Bio-Medical Research (BMR) Ltd (Bio-Medical Research Ltd, Parkmore Business Park West Galway, Ireland). The Neurotech Vital Compact device uses neuromuscular electrical stimulation (NMES) to activate the pelvic floor muscles. A small electrical current is delivered to the muscles via electrodes contained within a pair of wrap-around garments that will be positioned in specific areas on the outside of your body around your pelvic area. The product is intended to strengthen the pelvic floor muscles of women who have stress urinary incontinence (SUI). The Neurotech Vital Compact device is on the market in Europe but it is not approved in the US.

itouch Sure Pelvic Floor Exerciser®: The itouch Sure Pelvic Floor Exerciser is manufactured by TensCare Ltd., 9 Blenheim Road, Longmead Business Park, Epsom, Surrey, UK. The itouch Sure Pelvic Floor Exerciser sends an electrical stimulation to the pelvic floor muscles through a probe inserted into the vagina. The product is intended to strengthen the pelvic floor muscles of women who have stress urinary incontinence (SUI). The itouch Sure Pelvic Floor Exerciser is marketed in Europe and approved in the USA. This product is being used as a comparator in this study.

Which device will I be given?

If you choose to participate in this study and meet the eligibility requirements, you will be given either the Neurotech Vital Compact device or the itouch Sure Pelvic Floor Exerciser and instructed on its use. Which device you will be given will be randomly determined (like a flip of a coin) at the start of the study. You have an equal chance of receiving either device (ratio 1:1).

You and the study staff member who shows you how to use the assigned device will know which device you have been given. If you have any questions or concerns about the device or using it, you can discuss your questions with this staff member openly at any time.

The study staff who will care for you (including the doctor) throughout the study will not know which device you have been given so it is important you do not discuss the device you are using with them at any time.

The study will compare the results of the two devices and see if there are any differences in the treatment of stress urinary incontinence if the electrical stimulation is delivered through electrodes placed on the outside of the body (Neurotech Vital Compact device) or electrical stimulation delivered through an internal vaginal probe (the itouch Sure Pelvic Floor Exerciser).

Why have I been invited to participate?

You have been invited to take part in this study because you are female, you are over eighteen and less than 66 years of age and you have been diagnosed with stress urinary incontinence. If you suffer from a different form of incontinence (for example as a result of damaged nerves), if you are pregnant or lactating, if you had a heart attack or stroke, if you have implants like a pacemaker or suffer from a serious illness like cancer, you may not participate in the study. Your study team will personally discuss the requirements for study participation with you.

Do I have to take part?

No. It is up to you to decide. The study procedures and devices will be described to you, and you and a member of the study team will review this consent sheet together. You will have the chance to meet with the doctor and ask any questions you have about the study, the devices, and your stress urinary incontinence condition. If you agree to take part in this study and fully understand all the information, we will ask you to sign this consent form to show you have agreed to take part. You are free to withdraw your consent at any time, without giving a reason. You will receive a copy of this signed form. Your study records cannot be reviewed or released for research purposes unless you agree. If you do not agree to this use, you will not be able to participate in this study.

What are my responsibilities?

If you participate, you must follow the instructions of the Investigator, agree to participate in the below-mentioned examinations, come to the clinic for the required visits and use the device as directed for 12 weeks. Additionally, you have to report to your Investigator/study team any new

problems or health issues that might arise with the device or your health, even if you do not think they are related to the device or the study procedures.

What is involved and how long will I be in the study?
The study is being carried out in clinics in the USA. You will be required to attend the clinic for this screening visit then five study visits which will take about two hours each time, and be available for contact by telephone on one occasion which will take up approximately 5 minutes of your time. Participation will be required for the full 26 weeks (6 months).

During the study you will be asked to complete a 12-week treatment programme with your allocated device. You will be asked to use the device according to the manufacturer's instructions for use.

The Neurotech Vital Compact device is used once-a-day for five (5) days each week with each daily session lasting 30 minutes for the 12-week period. The itouch Sure Pelvic Floor Exerciser is used once-a-day for seven (7) days each week with each daily session lasting 20 minutes during the 12-week period.

It is important that during the 12-week treatment program you do not begin any new pelvic floor exercises.

Following completion of the 12-week treatment programme, you will be asked to continue in the study by performing Kegel exercises to maintain your pelvic floor tone for another 14 weeks.

What will happen to me if I take part?
If you agree to take part, we will check whether you meet the study requirements. If you meet these criteria, you will be need to give written consent to participate in the study. If you are of childbearing potential you will take a urine pregnancy test to ensure your maximum safety to enter the study.

A summary of what will happen at each visit follows:

<u>Screening Assessment – Visit 1 (up to 2 weeks before enrolling)</u>
At this visit we will review the study with you to see if you are eligible and review and sign this informed consent. We will then ask you a series of questions about your medical history, what medications you are taking, measure your weight and height and perform a urine pregnancy test if you are of childbearing potential. You will complete a questionnaire called the Medical, Epidemiologic and Social Aspects of Aging Urinary Incontinence Questionnaire (MESA). This questionnaire takes about 5 minutes to complete and asks you questions about your incontinence.

You will then complete a 1-hour Pad Weight Test. For this test, you will drink 500mL (about 16 ounces) of water, and wait one hour without going to the toilet. An ultrasound examination of your bladder will check if your bladder is full. If not, you will have to wait for your bladder to fill.

When your bladder is full, you will complete a 1-minute exercise routine. This will be 30 seconds of running on the spot, 30 seconds doing jumping jacks, coughing, standing up from a chair 10 times and picking up a small object off the floor while wearing a pre-

weighed pad so that we see how much urine you leak while performing those tests. During this test it is important that you do not contract your pelvic floor muscles to try to withhold passing any urine, but while you carry out the routine you 'leak' as usual.

If you leak a sufficient amount, at the end of the visit, you will be given a diary to complete at home for 7 days before your next visit. In the diary you will write down the number of drinks you have, how many times you go to the toilet (urinate), and if you accidentally leaked urine from your bladder. You will be given pre-weighed pads, and we will ask you wear these pads and collect them for 3 days before the next visit so we can measure the urine leaked. If you have sexual intercourse during the three day period while wearing the pads, it is important that you expel any fluid following intercourse and write this on your diary. In addition, if you are menstruating during this pad test it is important you record this on the diary. We will try to schedule pad collections when you are not expected to be menstruating.

Visit 2 (Baseline, within 2 weeks of your initial visit)
At this visit, we will collect the voiding diary and the pads you have used as instructed. We will also ask you how you are feeling, what medications you are taking and perform a urine pregnancy test if you are of childbearing potential.

You will complete a questionnaire called the Incontinence Quality of Life Questionnaire (I-QOL). This 10-minute, written questionnaire rates the effect of your condition on your quality of life. You will also be asked to complete a Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-IR), which asks questions about whether your stress urinary incontinence has affected your ability to have a satisfying sex life.

We will ask you to repeat the 1-hour Pad Weight Test during which you will drink 500mL of water, wait one hour without going to the toilet, have the bladder ultrasound performed to show that your bladder is full and then complete the 1-minute exercise, stand up from a chair and cough routine.

We will then re-check you meet all the criteria for entry into the study. If you meet all the study criteria, you will then be randomly allocated to one of the devices and trained how to use it.

What will happen if I get the Neurotech Vital Compact Device?
You will be given instructions about how to put on and take off the device. All training and instructions will be given in a private treatment room at the clinic. Application of the garments will require you to take off your clothes below the waist to expose your buttocks and inner thighs. The garment will be attached to your thighs, hips and bottom with special gel electrodes. The garment will be connected to a control unit (called the Neurotech Vital Compact controller) that has buttons which control the intensity of stimulation. The unit will be turned on and the intensity of the electrical current will be gradually increased until you begin to feel the sensation (many users say they feel a tingling sensation). If you are comfortable, you may increase the intensity. Stimulation will continue for 30 minutes. You will dictate the level of intensity (how strong the stimulation is) and at no stage will you be required to attain a level of stimulation that feels too strong to you. During this training period you may be asked questions of a sensitive nature, for example where you can feel the stimulation on your thighs, hips and bottom and be in your underwear covered by a sheet for the duration of the treatment session.

If you are comfortable with using the device and putting on the garment, you will be given the Neurotech Vital Compact device to take home to begin a 12-week treatment programme using the device for 30 minutes a day at home, 5 days a week, for 12 weeks. Remember to empty your bladder before starting each session. You will also be given sealable baggies with pre-weighed pads to wear during the 3 days prior to your next clinic visit, and a 7-day diary to be completed during the 7 days prior to your next clinic visit. Please bring your device, garment, diary pages and all pads to your next clinic visit.

What will happen if I get the itouch Sure Pelvic Floor Exerciser?

You will be given training and instructions about how to use the device in a private treatment room at the clinic. Application of the device will require you to take off your clothes below the waist, lie down on an examination table and be covered with a sheet. A special gel is provided to lubricate the vaginal probe. You will insert the lubricated probe into your vagina. The vaginal probe will be connected to a control unit (the itouch Sure) that has buttons which control the intensity of stimulation. Increasing stimulation will be applied through the vaginal probe until you begin to feel the effect and then continued for 20 minutes. You will dictate the level of intensity (how strong the stimulation) is and at no stage will you be required to attain a level of stimulation that feels too strong to you. During this training period you may be asked questions of a sensitive nature, for example where you can feel the stimulation and be without clothes below the waist covered by a sheet for the duration of the treatment session.

If you are comfortable with using the device and inserting it into your vagina, you will be given the itouch Sure Pelvic Floor Exerciser to take home to begin the 12-week programme using the device for 20-minutes a day at home, each day, for the 12 weeks. Remember to empty your bladder before starting each session. You will also be given sealable baggies with pre-weighed pads to wear during the 3 days prior to your next clinic visit, and the 7-day diary to be completed during the 7 days prior to your next clinic visit. Please bring your device, diary pages and all pads to your next clinic visit.

How much time do I need?

It is really important that you have the time and are willing to perform the entire 12-week programme with the assigned device, otherwise we will not be able to analyse the results of the study. It is also important you bring the device to each visit so we can check how you are positioning the device at home. Both devices track how many sessions have been completed as well as the intensity level of the device.

<u>Telephone Call (1 Week after Baseline Visit 2)</u>

Arrangements will be made to contact you for a follow-up telephone call about one week following your baseline visit to see if you have questions or concerns with the treatment and how you are feeling.

<u>Visit 3 (4 Weeks after Visit 2) + Visit 4 (12 Weeks after Visit 2)</u>

The same procedures as were performed at the Baseline visit will be performed during this visit. Before the visit, drink normally so when you arrive at the clinic you have a comfortably full bladder.

At Visit 3 and 4 we will collect the voiding diary and the pads you have used as instructed. We will also ask you how you are feeling and what medications you are taking. At Visit 3 a urine pregnancy test will be performed if you are of childbearing potential.

At Visit 4, we will ask you to complete the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-IR) and the Patient Global Impression of Improvement (PGI-I).

At the end of visits 2, 3 and 4, you will be provided with a voiding diary to complete at home for 7 days before your next visit and pre-weighed pads. We will ask you to collect the pads you wear for 3 days before the next visit so we can measure the urine lost.

You will be asked to return the device to the clinic at the end of Visit 4.

Also at Visit 4 you will be instructed regarding how to perform Kegel exercises to perform daily at home for the next 14 weeks. These are exercises that will teach you how to contract and relax your pelvic floor muscles and detailed instructions will be available for you to take home.

Visit 5 (26 Weeks after Visit 2)
At this visit we will collect the voiding diary and the Kegel exercise diary and the pads you have used as instructed. We will also ask you how you are feeling and what medications you are taking.

You will also be asked to complete the 1-hour Pad Weight Test in which you will drink 500mL of water, wait one hour without going to the toilet, have the bladder ultrasound performed to confirm your bladder is full and then complete the 1-minute exercise, stand up from a chair and cough routine. You will complete the I-QOL questionnaire. At this point you will have completed all the visits for the study.

What are the possible risks associated with participation in the study?
Both devices in this study have been determined by FDA to be "nonsignificant risk" devices. The risks associated with participation in the study are minimal. There are no anticipated additional risks to involvement in this clinical study than would be expected for normal treatment of this condition with alternative NMES devices with the possible, but unlikely, exception of patient sensitivity to the fabric/materials of the garment or its electrodes. However, there is no reason to suspect that any reaction would occur or that there would be any subsequent long term health problems. All of these materials have been extensively used and documented for their biocompatibility with human skin. The garment and devices will be used in accordance with the Instructions for Use.

The Neurotech Vital Compact device is a CE-marked device which means it is approved for use in Europe and has been available to use in Europe for several years, but is not approved for use in the US. The itouch Sure Pelvic Floor Exerciser is CE-marked and is cleared for use in the USA.

People with implanted electronic devices (like pacemakers or defibrillators), other heart problems (like arrhythmia or heart disorder) or insulin pumps are excluded from this study and should not get stimulation because the electronic signals might lead to health problems like ventricular fibrillation or other cardiac arrhythmias.

It is also unknown whether electrical stimulation has any effect on an unborn child. To ensure maximum safety, if you could be pregnant then you are not allowed to take part in the study and we will check if you are pregnant by conducting a pregnancy test at each visit. Women of childbearing potential must use safe contraception (oral contraception, hormonal contraceptive)

and you must provide details of this method to the study team at the start of the study. If you become pregnant during the study you must inform the study team immediately.

Adverse effects that have occurred with use of Neuromuscular Electrical Stimulation (NMES) (both devices) include:

- Temporary skin/surface reaction (irritation, redness and/or inflammation) at or near the stimulation site during and following periods of stimulation;
- Discomfort and pain (including throbbing pain) at or near the stimulation site;
- Stomach ache;
- Change in bowel habits;
- Twitching, numbness, muscular contraction, tightening, aching;
- Muscle injury caused by use of excessive intensity or usage time.

Potential anticipated adverse events specifically related to the use of the Neurotech Vital Compact device:

- On very rare occasions, some patients have reported feeling light-headed or faint, so it is recommended that patients have somewhere to sit nearby should this happen;
- Develop sensitivity to the hydrogel electrodes.

Potential anticipated adverse events specifically related to the use of the itouch Sure Pelvic Floor Exerciser:

- Abdominal cramps;
- Vaginal irritation or infection.

In summary, if you experience any adverse reactions while using the device, or after using the device, you should stop using the device immediately and notify the study team.

What should I expect while using the device?

Neurotech Vital Compact Device: During the study you will be applying electrical muscle stimulation to your body which is similar to regular exercise. Electrical stimulation works by activating the muscles, and slight muscle pain/discomfort is a known after-effect, especially when first starting to use the device. Increase stimulation levels gradually over the period of a week or so to avoid this effect. When you first turn on the unit, you will increase the intensity until you feel a mild tingling in the buttocks area. As you increase the intensity level, the feeling gradually moves to the area between the legs and you will experience a strong contraction of your pelvic muscles. The treatment goal is to get to a level of 75 units within a few weeks after starting treatment, and to maintain this level for the remainder of the 12 weeks. If you must pause the treatment during a 30-minute session, turn the intensity back to zero. The treatment is conducted in a standing position, and you may move around a little bit during the treatment as long as you do not dislodge the electrodes. You may also lie on your back with knees bent if more comfortable for you.

The electrodes are designed to be sticky to ensure good skin contact, and mild skin irritation and pain/discomfort have been reported following their use, however, this reaction is usually temporary and quickly subsides. It is also possible that you may become sensitive to the electrodes during the study – this will be monitored at every visit and any such reaction will be discussed with the Investigator and appropriate action will be taken and documented. It is important not to attach the electrodes to other body parts. Avoid any usage of ointments or skin

creams on the buttocks or upper thighs during the study, as the electrical conductivity of the skin will be decreased.

On very rare occasions, some participants have reported feeling light-headed or faint during the treatment, so have somewhere to sit nearby should this happen during your treatment.

itouch Sure Pelvic Floor Exerciser:
The muscle contractions caused by electrical stimulation can lead to training aches which usually disappear within a week. After treatment tingling sensations may continue or your skin may feel numb which is normal. Use of excessive intensity or usage time can cause muscle injury. Always increase intensity gradually. If stimulation causes pain reduce intensity or stop treatment.

You will increase the intensity until you feel the sensation but it is not overly painful. It is important to be conservative upon initial use. As long as you can feel the contraction, itouch sure is working. You can build up the strength slowly over a number of days. The intensity increases in steps of 0.5 and the range is 0 to 99.5. If you experience discomfort reset the intensity down one step. During use you may feel cramping. If this happens, stop using the itouch sure until the cramping goes away, then start again using a lower intensity.

If you must pause the treatment during a 30-minute session, turn the intensity back to zero. The treatment is conducted while you are lying down. Your head may be propped on a pillow, but you may not move around during the treatment. If you have a urinary infection or any surface irritations in the vagina, you are not recommended to use the device.

What are the possible benefits of taking part in this research study?
It is hoped you will get some benefit from participation in this study with an improvement in your stress urinary incontinence symptoms such as not leaking as much or being able to stop using pads. We cannot promise this study will help you, but the information we get from this study will help improve the treatment of people like you who suffer from stress urinary incontinence.

Are there any alternative treatments?
One alternative treatment available for women who suffer from stress urinary incontinence is oral medications, which affect the nervous system of the bladder. Another alternative is surgical intervention (implanting medical products or surgery). Another is to work with a physical therapist to strengthen your pelvic floor muscles. You can discuss all advantages and disadvantages of alternative treatments with your Investigator if you wish.

What happens when the research study stops?
After completing your 12-week treatment programme, you will be trained, then asked to perform standard Kegel exercises each day for 14-weeks then visit the clinic for a final assessment. The study team will discuss with you at this final contact how you are feeling and what other treatments may be available to you, if needed.

What happens if the study ends early?
If you or the study team observe unanticipated adverse device effects, if your health condition worsens or if you do not follow the instructions of the study team, your study participation may be ended early. You can also decide to withdraw your consent early. If this situation should arise, the next visit should still preferably be conducted, as some safety examinations will be

done during the visit. But if you do not agree, the routine standard treatment for people with your condition will be offered to you.

Authorization to use and disclose (release) medical information:
As part of this research study, your study doctor and the research team will keep records of your participation in this study. These study records may be kept on a computer and will include all information collected during the research study, and any health information in your medical records that is related to the research study. Your study doctor and research team will use and disclose (release) your information in an anonymous manner as they conduct this study. To evaluate the results of the study and for compliance with federal and state law, your health information may be examined and copied by the Food and Drug Administration (FDA), other governmental regulatory agencies, the Institutional Review Board of the study or Hospital System, the study sponsor and the sponsor's authorized representative(s). This study may result in scientific presentations and publications, but steps will be taken to make sure you are not identified.

Under federal privacy laws, your study records cannot be used or released for research purposes unless you agree. If you sign this consent form, you are agreeing to the use and release of your health information. If you do not agree to this use, you will not be able to participate in this study.

The right to use your health information for research purposes does not expire unless you withdraw your agreement. You have the right to withdraw your agreement at any time. You can do this by giving written notice to your study doctor. If you withdraw your agreement, you will not be allowed to continue participation in this research study. However, the information that has already been collected will still be used and released as described above. You have the right to review your health information that is created during your participation in this study. After the study is completed, you may request this information. Once your health information has been released, federal privacy laws may no longer protect it from further release and use.

If you have any questions about the privacy of your health information, please ask your study doctor. All data from the study will be handled confidentially. Data collected for analysis will not carry your name or your address or other information that can identify you. This information will also be sent to the sponsor's agent for data analysis. At the beginning of the study you will be assigned a participant number which will be noted on all documentation. It will not be possible to identify you outside the department. The collected data may be transferred to any of the Sponsor offices including, but not limited to, the Sponsor head-office (Parkmore Business Park West, Galway, Ireland). The information may be recorded by the sponsoring company in paper form or in a computer database. However, they will obtain only your participant number. Your name and your address will be removed from all data being transferred outside the department to ensure that you cannot be identified.

***Compensation for Injury as a Result of Study Participation*:**
We will provide you with the care needed to treat any injury or illness that directly results from taking part in this research study. Your insurance company or other third parties may be responsible for the care you get for an injury. You may also be responsible for these costs. For example, if the care is billed to your insurer, you will be responsible for the payment of any deductibles and co-payments required by your insurer or even possibly the entire cost of the service.

Injuries sometimes happen in research even when no one is at fault. The study sponsor, the clinic or hospital or the investigators as part of this study have no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form. If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible.

What if new information becomes available?
Sometimes we get new information about the treatment being studied. If this happens, your Investigator will tell you and discuss whether this affects your personal situation and whether you should continue in the study. A new written informed consent may become available which you would have to sign to participate further in the study. If you decide not to carry on, the Investigator will make arrangements for your care to continue.

If the study is stopped for any other reason, we will tell you and arrange your continuing care.

Who has reviewed the study?
The clinical study presented here has been looked at and approved by a duly-constituted Institutional Review Board (IRB) in compliance with the law.

What will happen to the results of the study?
The results will be analysed and a report will be written and may be submitted for publication in a scientific journal. This report will not contain any information that could be used to identify you in any way.

***Who is organising and funding the research*?**
Bio-Medical Research Ltd. is the Sponsor and will pay the investigator (doctor) and study team for including you in this study.

Expenses and payments:
There is no cost to you to participate in this study. Study funds will pay for the study device, incontinence pads and all study-related examinations that are provided to you. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff.

Payment for participation:
You will be paid to participate in this study. You will be paid up to a total of $TBD depending on how many study visits you complete. You will be eligible to receive your payments after the completion of all functional tests and questionnaires required at each data collection appointment. If you do not complete the required tests and questionnaires at your appointments, you will not receive the payment for that visit.

CONSENT TO PARTICIPATE

My study doctor, _____, has explained the nature and purpose of this study to me. I have been given the time and place to read and review this consent form and I choose to participate in this study. I have been given the opportunity to ask questions about this study and my questions have been answered to my satisfaction. I agree that my health information may be used and disclosed (released) as described in this consent form. After I sign this consent form, I understand I will receive a copy of it for my own records. I do not give up any of my legal rights by signing this consent form.

Printed Name of Participant _____

Signature of Participant _____

Date _____Time _____

Signature of Witness _____

Date _____Time_____

INVESTIGATOR STATEMENT

I have carefully explained to the participant the nature and purpose of this study. The participant signing this consent form has (1) been given the time and place to read and review this consent form; (2) been given an opportunity to ask questions regarding the nature, risks and benefits of participation in this research study; and (3) appears to understand the nature and purpose of the study and the demands required of participation. The participant has signed this consent form prior to having any study-related procedures performed.

Investigator Print Name: _____

Investigator Signature: _____

Date _____Time_____

14.11 Appendix XI. Neurotech Vital™ Compact Instructions for Use and Quick Start Guide

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SAFETY INFORMATION

Validity

This manual is intended for the correct application of the product. The information and technical data contained in this document relates to the Vital Compact muscle stimulator provided with this manual. It is proprietary to Bio-Medical Research Ltd. and may be used and disseminated only for the purposes of and to the extent specifically authorised in writing by the company. Each Vital Compact controller is assigned a unique serial number, which is located on the back of the controller.

Important: The product should not prescribed for use by a patient until the clinician has received full training on its correct usage from an authorised **neurotech**® representative.

Restrictions

The sale and/or operation of this equipment is subject to law in various countries. Compliance with this legislation rests with the importer, dealer or user of the equipment as appropriate.

Intended Use:

- Vital Compact is intended for rehabilitation of the pelvic floor muscles in stress urinary incontinence

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Neuromuscular Electrical Stimulation (NMES)

NMES may be defined as the application of electrical stimulation of the peripheral nervous system to contract a muscle either through the direct activation of the motor neurons in the mixed peripheral nerve, or indirectly through reflex recruitment.

Vital Compact treats the following conditions:

Stress Urinary Incontinence
Stress urinary incontinence is described as the leakage of urine associated with an increase in intra-abdominal pressure, for example, during a cough, sneeze, laugh or physical exertion.

CONTRAINDICATIONS, WARNINGS & PRECAUTIONS

Contraindications:
- Do not use this device if you have a cardiac pacemaker, implanted defibrillator, or other implanted electronic device because this may cause electric shock, burns, electrical interference, or death.
- Do not use this device if you are pregnant. The safety of electrical stimulation during pregnancy has not been established.
- Do not use the device if you have any implanted metal devices in the abdominal or pelvic areas, for example hip prostheses.

Warnings:
- Stimulation should not be applied across or through the head, directly on the eyes, covering the mouth, on the front of the neck, (especially the carotid sinus), or from electrodes placed on the chest and the upper back or crossing over the heart.
- Application of electrodes near the thorax may increase the risk of cardiac fibrillation.
- Do not apply stimulation across the chest, because the introduction of electrical current into the chest may cause rhythm disturbances to the heart, which could be lethal.
- Do not apply stimulation over open wounds or rashes, or over swollen, red, infected, or inflamed areas or skin eruptions (e.g. phlebitis, thrombophlebitis, varicose veins).
- Do not apply stimulation over, or in proximity to, cancerous lesions.
- Do not apply stimulation in the presence of electronic monitoring equipment (e.g. cardiac monitors, ECG alarms), which may not operate properly when the electrical stimulation device is in use.
- Do not apply stimulation when in the bath or shower.
- Do not apply stimulation while driving, operating machinery, cycling or during any activity in which electrical stimulation can put the patient at risk of injury.
- Do not use in close proximity to shortwave or microwave therapy equipment which may produce instability in the stimulator output.
- Wireless communication equipment such as wireless home network devices, mobile phones, cordless telephones , base stations and walkie-talkies of between 1W to 10W can affect this equipment and should be kept a distance of least 2.3 to 7.3 metres away from the device.
- Use this device only with the garments, leads, electrodes, and accessories recommended by the manufacturer.
- Always ensure that the charger/power supply is positioned so that it is easy to unplug the power supply from the socket.
- To isolate this equipment from the mains, the charger/power supply plug should be removed from the socket.
- Apply stimulation only to normal, intact, clean, healthy skin.
- Do not attach any cables or connectors to Vital Compact, other than those supplied by **neurotech**®. Never connect any computer leads to the controller.

Precautions:
- The long-term effects of electrical stimulation are unknown.
- Since the effects of stimulation of the brain are unknown, stimulation should not be applied across the head and electrodes should not be placed on opposite sides of the head.
- Some patients may experience skin irritation or hypersensitivity due to the electrical stimulation or the electrical conductive medium.
- Patients with suspected or diagnosed heart disease should follow precautions recommended by their clinician.
- Patients with suspected or diagnosed epilepsy should follow precautions recommended by their clinician.

- Use caution if you have a tendency to bleed internally, such as following an injury or fracture.
- Use caution following recent surgical procedures when stimulation may disrupt the healing process.
- Use caution if stimulation is applied over areas of skin which lack normal sensation.
- Keep this device out of the reach of children.
- Due to the risk of strangulation, keep the device away from children.
- Due to the risk of small parts which may be broken off and cause a choking hazard, keep the device away from children.
- Keep this device out of the reach of pets or pests.
- Use this device only under the continued supervision of a licensed practitioner.
- The size, shape, and type of electrodes may affect the safety and effectiveness of electrical stimulation and recording.
- Using stimulation electrodes which are too small or incorrectly applied could result in discomfort or skin burns.
- You should contact the manufacturer of this electrical stimulator if you do not know if the electrodes you have can be used with this stimulator.
- Electrodes and garments should not be shared with other people. To prevent cross-infection, each person should have their own set of electrodes and garments.
- Replace the electrodes if they no longer stick to your skin properly. See the advice on electrode maintenance (Page 5).

Additional Warnings and Precautions:

- Please wait before using Vital Compact product until:
  - At least six weeks after the birth of your baby (consult a clinician first).
  - At least three months after having a Caesarean section (consult a clinician first).
  - The heavy days of your period have finished.
- Do not use the Vital Compact stress programs if you have had an IUD fitted, which is made from any electrically conductive material such as copper. Please consult your doctor in this instance.
- Stimulation should not be applied over the carotid sinus nerves, particularly in patients with a known sensitivity to the carotid sinus reflex.
- Although compliant with applicable EMC requirements, this device may still interfere with more sensitive equipment, please move away or switch off this device if necessary.
- Specific patient groups (e.g. the elderly) may require further attention and care.
- Before using the equipment, a visual inspection must be performed (check for a broken enclosure, damaged connector or exposed wires). If there is any doubt, the equipment must not be used.
- Once the treatment has ceased, always remember to switch off the controller.
- If in doubt, always seek medical advice.
- Medical advice must be obtained before use on persons who are insulin dependent diabetics or for persons who are under medical supervision for any cognitive dysfunction.
- When repositioning electrodes during treatment, always pause or stop the controller first.
- Simultaneous connection of a patient to high frequency surgical equipment may result in burns at the site of the stimulator electrodes and possible damage to the stimulator.
- This device can deliver current densities in excess of 2mA/cm² when used at a high intensity with small electrodes.
- Do not use the device with the electrodes positioned on injection sites (of medications/drugs), such as hormone treatment sites.
- Do not touch the electrodes, connectors or lead pins with your fingers while the stimulation session is in progress. Always pause or switch off the controller before handling the electrodes.
- The device must not be used with any other unit which delivers electrical current to the body (e.g. interferential or another muscle stimulator).
- It is advised that the patient use the bathroom before starting each treatment session.
- Always check the product leads before use and do not use if they are damaged in any way.

Adverse Reactions:

- A small number of isolated skin reactions have been reported by people using muscle stimulation devices, including allergies, a prolonged reddening of the skin and acne.
- On very rare occasions, first-time users of NMES have reported feeling light-headed or faint. In this event, we recommend that the patient switches off the unit and sits down until they are feeling better. They may then resume the treatment.
- Patients should stop using the device and should consult their clinician if they experience adverse reactions from the device.

Notes:
- The patient should only run one full treatment session per day to reduce the potential for muscle fatigue. A treatment session is defined as 30 minutes of treatment, even if this is broken down into shorter 10- or 15-minute sessions. This restriction may be changed depending on the prescribing clinician.
- An effective treatment should not cause undue discomfort.

Important:
- The safety information provided in this User Manual must be followed.
- The unit should only be set-up and operated according to the instructions laid-out in this manual.
- The patient should always cease using the unit and consult their doctor if they are feeling light headed or faint.
- **neurotech**® will not accept responsibility if the guidelines and instructions supplied with this unit are not followed.

IMPORTANT

- **NEVER** connect leads or wires from other equipment such as computers, games, cameras etc. to the controller.
- **NEVER** connect the leads provided with Vital Compact to any other equipment.
- If in doubt, contact **neurotech**®.

CARING FOR YOUR NEUROTECH VITAL™ ELECTRODES

IMPORTANT ELECTRODE INFORMATION

In order to prolong the life of the electrodes, after every few treatment sessions, the patient should sprinkle a few drops of clean water over the adhesive surface of each electrode with their fingertips and then gently rub it over the complete surface of the electrode. This will clean away debris and help to rehydrate the adhesive surface.
Note: This should only be done with the side of the electrode which adheres to the skin. The side of the stress electrode which adheres to the garments should be left affixed to the garment.

- The electrodes are for single person use only.
- You should always ensure your skin is clean and free from oils, creams and other lotions before use.
- The durability and effectiveness of the electrodes depends entirely on the proper use, storage and care on the part of the user, certain skin types and the type, duration, number of sessions, intensity used and site of stimulation.
- Ensure your hands are clean before handling electrodes. You should avoid touching the skin-side of the electrodes with your fingers as much as possible when applying or removing the garments or electrodes, as this can transfer oils and skin particles to the electrodes' surface.
- After use, replace the liners on the adhesive side of the electrodes and store your unit in a cool, dry place until the next use.
- Electrodes will need to be replaced periodically as the surface picks up skin debris and becomes dry over time.

VITAL COMPACT PACK CONTENTS

The picture below shows the complete Vital Compact kit. Your clinician may have prescribed just a part of this kit, depending on the type of treatment you require.

1. Vital Compact Controller
A portable neuromuscular electrical stimulator that generates signals which are sent, via electrodes and garments, to activate the muscles. It is rechargeable and will take approximately 5 hours to fully charge. It is designed for home use.

2. Left Stress Garment
This conductive garment fastens around the left thigh and buttock area. It has a ***blue*** connector pin, which is plugged into the stress lead.

3. Right Stress Garment
This conductive garment fastens around the right thigh and buttock area. It has a ***red*** connector pin, which is plugged into the stress lead.

4. Battery Charger
Vital Compact is supplied with a power supply for charging the battery. Country-specific adaptors (2-pin and 3-pin) are included to permit use in your country of residence (see page 10).

5. Stress Lead
This connects the controller to the stress garments.

6. Stress Electrodes
These 8 electrodes are for use on the stress garments only.

7. Lanyard:
The lanyard clips to the unit to let it be worn around the neck.

8. Instruction Manual
The detailed guide you are currently reading for setting-up and using Vital Compact.

9. Quick Start Guide
This is an additional guide, which illustrates how to set up and apply the stress garments.

English

DESCRIPTION OF THE VITAL COMPACT CONTROLS

1. On/Off/Pause Button ( )
Press this button to switch your controller on. Press and hold it for 2 seconds to switch the controller off. During a treatment, pressing this button briefly will Pause/Unpause the treatment.
Note: You cannot switch the unit on while the battery is charging.

2. Up Intensity Button ( )
Press this button to increase the stimulation intensity during treatment.

3. Down Intensity Button ( )
Press this button to decrease the stimulation intensity during treatment.

4. Program Button (P)
The Program Button is used to select the treatment type required:
Program 1 = P1 - Stress Urinary Incontinence Treatment
The Program Button is deactivated while a session is running.
Important:
For Clinical Trial BMR-13-1001, only Program 1 is active.

5. Information Button (/)
Press this button to see various items of information and treatment results from the sessions you are running or have completed (see page 14-15).

6. Scroll Up Button (▲)
This button is used to scroll up through the information relating to individual treatment sessions.

7. Scroll Down Button (▼)
This button is used to scroll down through the information relating to individual treatment sessions.

VITAL COMPACT SOCKETS

1. Battery Charger Socket
Connect the battery charger to this socket and plug it into an electrical socket. You should charge the battery for approximately 5 hours. It is fully charged when all 5 bars of the battery icon on the display are visible ( ).

2. PC Connector Socket
The software option is not available on this version of the unit. Do not insert anything into this socket.

3. Treatment Lead Socket
You must connect the treatment lead to this socket in order to run a treatment program.

4. Socket Isolators
These sliders ensure that the Vital Compact unit cannot be connected to the patient and to an electrical power source at the same time. To charge the unit, these must be slid inwards to cover the Treatment Lead Socket (Fig. 1). To run a treatment program, they must be slid outwards to cover the Battery Charger Socket and PC Connector Socket (Fig. 2).

Fig. 1

Fig. 2

CONTROLLER DISPLAY ICONS

The following icons may appear on the display at various times during the operation of the unit.

The Battery symbol displays the amount of charge the battery has left. It is visible whenever the unit is switched on or is being charged.

This is a Warning Indicator. It flashes whenever the unit detects poor contact between the unit and electrodes or between the electrodes and the skin. It also flashes to indicate other errors.

The Keylock symbol appears when Keylock has been activated to indicate that the intensity cannot be accidentally increased or decreased.

The Mute symbol indicates when the unit sound has been switched off.

This symbol appears when viewing the number of treatment sessions a patient has run to date.

The Treatment Timer appears when viewing the Total Treatment Time (all sessions to date) or when viewing the duration of an individual treatment session.

The Maximum Intensity symbol is displayed when viewing the highest intensity reached to date or the highest intensity reached in a particular treatment session.

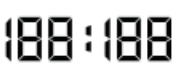
The Average Intensity indicator is displayed when viewing the average intensity of all treatment sessions run to date.

The Pause symbol appears whenever a treatment session has been paused.

The Program Indicator displays which program is currently selected.

The Individual Session Indicator displays each session (from 1 - 90) which can be selected to review its treatment data.

The Intensity Indicator appears each time the unit transmits a contraction.



The Intensity/Time Indicator displays various information data (e.g. intensity from each channel, treatment time remaining etc.)

The Unit Indicators indicate which type of information is being displayed by the Intensity/Time Indicator.

The Pad Contact Indicator shows the user which electrode(s) is/are in poor contact with either the skin or with the treatment garment (see page 9).

English

ELECTRODE DETECTION FUNCTION

During a treatment session, the controller continuously monitors its connection with the electrodes and can detect if they are in proper contact with a patient's skin. If the controller detects a poor quality contact, it alerts the user that there is a problem. This can be caused by one of the following:

- An electrode is missing from the garment(s).
- An electrode is not covering its silver stud on the garment(s).
- Poor contact between the electrode(s) and the skin.
- Poor electrode condition (i.e. with damaged and/or dry surface following too many sessions).

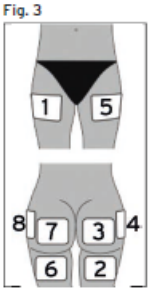
If any of these issues are detected, the controller will:

- Highlight the specific electrode(s) at fault. Please note that there may be more than one electrode concerned.
- Stop the stimulation until the problem is fixed.
- Beep repeatedly until the controller is switched off or the problem is fixed.
- The warning symbol (⚠) will flash until the problem is corrected.

CHECKING / FIXING ELECTRODE FAULTS

Stress Treatment Session
If an electrode detection fault occurs during a **Stress Treatment Session**, the controller will highlight the faulty electrode(s) with the numbers 1 to 8. The numbers 1 to 8 relate to specific electrodes on each garment, so you know which electrode(s) should be checked. The specific electrode numbers are shown in Fig. 3.

Fig. 3



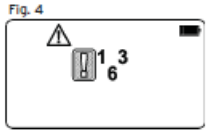
If the unit detects a contact fault:

1. The unit will cease stimulation and indicate which electrode(s) have a problem (Fig. 4).

2. Switch off the controller. Disconnect the stress lead connectors from the garment plugs.

3. Carefully remove the garment(s), as described on Page 12 and move or replace the electrode(s) causing the problem. Make sure none of the liners have been left on the electrodes.

Fig. 4

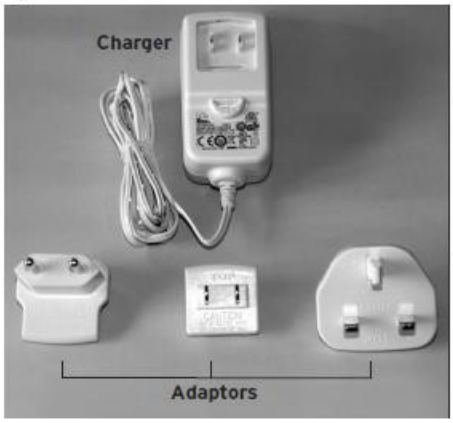


4. Then put the garment(s) back on and press the whole surface of each electrode firmly against the skin. Reconnect the stress lead to the garments and begin the treatment again.

5. If the screen still indicates the same electrode(s) as being faulty, you should try another set of electrodes. If this still doesn't fix the problem, you may have a faulty lead or garment and should contact **neurotech**ₘ or your local distributor for advice.

THE BATTERY CHARGER

Fig. 5



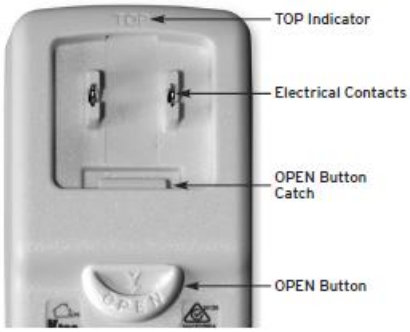
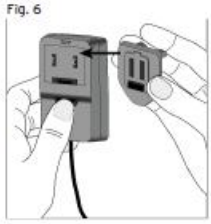


Fig. 6



ASSEMBLING THE CHARGER

Your battery charger is supplied with a number of different adaptors for use in different countries (Fig. 5). Before charging the battery, you must connect whichever adaptor is suitable for your area.

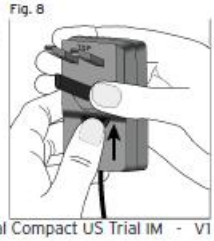
1. Align the adaptor with the charger (Fig. 6). The word "TOP" is embossed on the charger and the adaptors to show the correct orientation.

Fig. 7

2. Press the button marked "OPEN" and slide it away from adaptor recess (Fig 7).

3. Place the "TOP" end of the adaptor into the adaptor recess and then press the other end firmly into the recess while at the same time releasing the "OPEN" button (Fig. 8). There is a catch on each adaptor which the "OPEN" button latches onto to hold the adaptor in place. You must ensure that this catch has been engaged correctly before plugging the charger into an electrical outlet.

Fig. 8



Important:

- When disconnecting the adaptor from the charger, always hold the adaptor before disengaging the "OPEN" button to stop the adaptor springing away from the charger.

English

PROGRAM 1: STRESS URINARY INCONTINENCE

PREPARING THE STRESS GARMENTS

- Please note that this will only be required for running program 1.

Note:
We recommend wearing high-thigh underwear (e.g. a thong), which leaves the buttocks exposed, because the electrodes need to make contact with the lower buttocks and hips.

1. Prepare the skin for treatment. Clean the skin thoroughly where treatment will be applied. The electrodes will not adhere properly if any dirt, oils, creams or other cosmetics are on the skin. Use warm, soapy water to clean the skin. Dry the skin thoroughly after cleaning.

2. Place the stress garment for the right-leg on a flat surface with the inner surface facing upwards.

3. Remove the covers from the ***patterned side*** of the electrodes (Fig. 9). Do not remove the covers from the ***black*** side of the electrodes yet.

4. Place the electrodes on the garment in either position A or B, as determined in conjunction with the **Sizing Guide**. Press the whole surface of each electrode firmly onto the garment to ensure they adhere properly.

5. Repeat these steps with the stress garment for the left-leg.

6. Remove the covers from the ***black side*** of the electrodes. Do not throw these covers away as you have to put them back on the electrodes at the end of the session. With the electrodes facing the body, wrap the right stress garment firmly around the right leg and fasten. Please refer to the separate **Quick Start Guide** for more detail. Then repeat the same steps, wrapping the left stress garment around the left leg and fasten.

Note:
- The whole surface of each electrode must be in contact with the skin to ensure a successful treatment.

7. When the garments are placed on the body, the electrodes should lie on the quadriceps, hamstrings and gluteal muscles of both legs as per Fig. 10, 11 and 12.

Note:
- Only use electrodes specified for use with Vital Compact.

Important
You should consult your clinician before using this device and ensure that you have been given full instructions on how to use it correctly.

Fig. 9

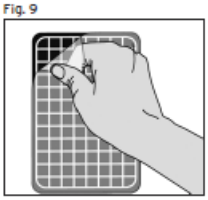


Fig. 10

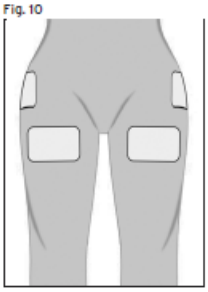


Fig. 11

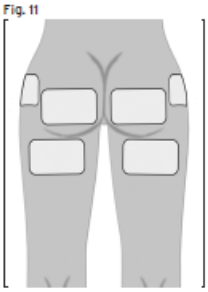
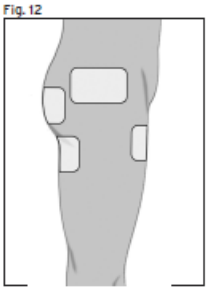


Fig. 12



RUNNING PROGRAM 1

1. Ensure the battery is sufficiently charged. If the battery charge is low, connect the charger to the unit (Fig. 13) and plug it into an electrical socket. You should charge the battery for approximately 5 hours. It is fully charged when all 5 bars of the battery symbol ( ) on the display screen are visible.

Important:
Once the battery is fully charged, let the unit cool down for a couple of minutes as the battery heats-up during charging.

Warning: For all users, including those with impaired sensory capabilities:
The controller should not be handled at any time during the charge cycle. If the charge cycle is terminated early, please do not handle the controller for at least 1 hour, as surfaces may be hot.

Fig. 13

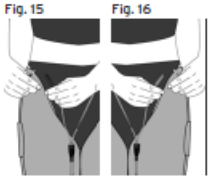
2. Ensure the electrodes and garments are positioned correctly.

3. Connect the stress lead to the connector socket on the controller (Fig. 14).

Fig. 14

4. Connect the stress lead to the garments by inserting the ***blue*** plug on the ***left*** garment into the ***blue*** connector on the stress lead (Fig. 15) and the ***red*** plug on the ***right*** garment to the ***red*** connector on the stress lead (Fig. 16).

Fig. 15 Fig. 16

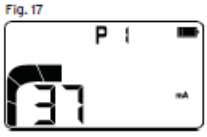


5. Switch on the unit by pressing the On/Off Button ( ). Start the treatment session by pressing the **Up Intensity Button** ( ). You will begin to feel the stimulation and the Intensity Indicator will rise on-screen. The intensity level appears beside Intensity Indicator (Fig. 17). The Intensity Buttons increase/decrease the intensity in single increments. The intensity range for the stress treatment is **0 - 120.** If you keep the intensity button pressed, the intensity will begin to increase at a faster rate. As the intensity increases, you should begin to feel a strong muscle contraction, first in the buttock area and then, as the intensity increases, the contraction between the legs becomes apparent.

6. You should continue to increase the Intensity until you feel a good, strong but comfortable contraction in your pelvic floor, or until you reach your target intensity level (pre-defined by your clinician). It may take a few minutes to become accustomed to the strong sensation. Once the intensity is set, the treatment timer starts to count down from 30 minutes as the program is running (Fig. 18).

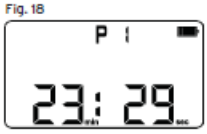
During each contraction, the stimulation will ramp-up to the selected intensity level, stay at that intensity through the contraction phase and then ramp-down to the relaxation phase. The treatment runs through pre-set contraction and relaxation phases until the timer counts down to zero, at which point the stimulus is reduced to zero and the program stops.

Fig. 17



Important:
Once the unit is set up and the program has started, you can clip the lanyard onto the unit to hang it around your neck if you wish. To optimise the results from a treatment session, it is recommended that you stand with your feet flat on the ground and your hands resting on a stationary object, such as a table. You may move a little during the treatment to help you remain comfortable, but you should avoid moving too much as this may interfere with the effectiveness of the treatment. However, if you wish to move to a different location, you should pause the session, move to the new location and then unpause the session.

Fig. 18

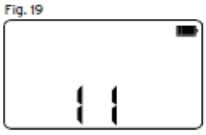


For patients unable to stand continuously for 30 minutes the treatment session can be broken-up into shorter sessions, which can be done more frequently e.g. 15 minutes done twice daily or 10 minutes done 3 times per day. The goal is to amass a cumulative 30 minutes use per day. Patients unable to stand for 30 minutes can also complete their session by lying down with their knees bent. See Quick Start Guide for details.

- Don't be concerned if you cannot reach the intensity level recommended by your clinician in your first session. It may take several sessions to reach this level.
- Never exceed the intensity level set by your clinician.
- Never exceed your comfort level. Effective stimulation should never be painful.

PAUSING A TREATMENT SESSION

Fig. 19

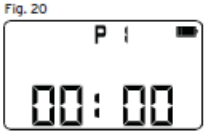


If you wish to pause a session before it is finished, simply press the on/off button briefly. The stimulation will stop and the display will indicate that the unit is paused (Fig. 19). To resume the session, briefly press the on/off button again. The display will return to the timer countdown and the stimulation will begin again. However, if the session is paused for 2 minutes or more, the intensity will be halved when the session is unpaused. This is a safety feature to ensure that the intensity you had previously reached is not excessive once you have become unaccustomed to the sensation.

You may switch off your unit at any time during a session by pressing the on/off button for two seconds.

CONCLUDING PROGRAM 1

Fig. 20



1. The treatment session is completed when the counter reaches zero. The display will flash "00:00" (Fig. 20), stimulation is reduced to zero and the controller will beep to indicate the end of the session.

2. Once the session is complete, switch the controller off by pressing the on/off button for two seconds and disconnect the stress lead from the left and right garments.
Note: If you do not switch the controller off, it will do so automatically after 30 seconds. However, if another button is pressed within this 30-second period, the controller will remain on for 2 minutes, at which point it will switch off automatically.

3. If you are using the lanyard, remove the unit from around your neck, lay it carefully on a flat surface and disconnect the leads from the garments.

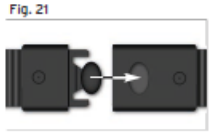
4. Unfasten and then slowly and carefully remove the garment from your left leg. First, peel the garment from the front of the leg until it is half detached and then peel the other end from the rear. Then unfasten and slowly remove the garment from your right leg in the same way.

5. Lay the garments on a flat surface and replace the covers on the ***black side*** of the 8 electrodes, then pack everything away until the next session.
Important: You should only fold the garments once in half, which allows the electrodes to remain flat between sessions.

Note: Always replace the covers on the black side of the electrodes after use. The electrodes can remain affixed to the garment in between treatment sessions.

USING THE LANYARD

Fig. 21



1. When using the lanyard, attach it to the lanyard clip at the top of the unit (see page 7). Ensure the unit is attached with the screen facing away from your body.

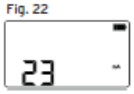
2. The lanyard is equipped with a safety-clip which pops open if there is a sudden, forceful pull on the lanyard. If this happens, align the two halves of the clip and simply push them back together until the oval button clicks into place (Fig. 21). If it does not "click" together, you may have one side of the clip back-to-front. Turn it around and try again.

INFORMATION BUTTON

The Information Button is used to display various information about your current and previous treatment sessions. Each time you press the button a new element of your treatment progress is displayed on screen. This information remains on screen for 3 seconds and will then revert back to the countdown timer unless you press the Information Button again. The information is displayed in the following sequence:

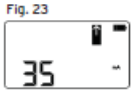
1 Press: Displays your current intensity level (Fig. 22).

Fig. 22



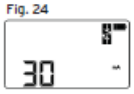
2 Presses: Displays the maximum intensity reached during any session to date (Up to 90 sessions - Fig. 23)

Fig. 23



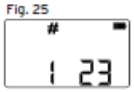
3 Presses: Displays the average intensity of all sessions completed to date (Up to 90 sessions - Fig. 24)

Fig. 24



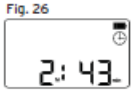
4 Presses: Displays the total number of sessions completed to date, up to 2000 sessions. This includes partial sessions, where the full 30 minutes were not completed (Fig. 25).

Fig. 25



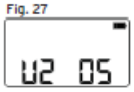
5 Presses: Displays the total amount treatment time completed to date, up to 199 hours and 59 minutes (Fig. 26)

Fig. 26



6 Presses: Displays the treatment code for this particular unit. You should check that your unit displays U205. If another code is displayed, you should contact Neurotech or your local distributor for advice (Fig. 27).

Fig. 27



Pressing the Information Button a 7th time will bring you back to the treatment timer screen.

English

IN-PROGRAM INFORMATION (Scroll Buttons)

Note:
Review the instructions below with your clinician. If any of these instructions are not clear, contact Neurotech for assistance.

Your Vital Compact unit stores three pieces of data from each session you run, to allow your clinician to monitor your treatment progress; a) the maximum intensity for each session, b) the average intensity for each session and c) the duration of each session. This information can be reviewed in 2 different ways - either by individual session or by specific parameter.
Note:
The scroll buttons are deactivated so this information can not be accessed while a program is running.

Review by Session

1. Access the list of treatment sessions by pressing either the Up or Down Scroll Buttons. By pressing the Up Scroll Button (▲), you will access the list of sessions in ascending order, highlighting session #1, then #2, #3 etc. By pressing the Down Scroll Button (▼), you will access the list of sessions in descending order, highlighting the last session completed, then the session before that, etc.
2. When you have highlighted the session you wish to review, press the Information Button to see the maximum intensity for that session (Fig. 28. This information remains on screen for 3 seconds and will then revert back to the start screen, unless you press the Information Button again.
3. Press the Information Button twice to display the average intensity of the selected session (Fig. 29).
4. Press the Information Button three times to display the duration of the selected session (Fig. 30).

Fig. 28

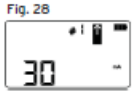


Fig. 29

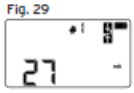


Fig. 30

Review by Parameter

1. Access the list of treatment sessions by pressing either the Up or Down Scroll Buttons. By pressing the Up Scroll Button (▲), you will access the list of sessions in ascending order, highlighting session #1, then #2, #3 etc. By pressing the Down Scroll Button (▼), you will access the list of sessions in descending order, highlighting the last session completed, then the session before that, etc.
2. When you have highlighted the session you wish to review, press the Information Button until you find the parameter you wish to review (e.g. Fig. 31 shows maximum intensity in session #1).
3. Next, press the Up Scroll Button to display the same parameter in the next session (e.g. Fig. 32 and Fig. 33 shows maximum intensity in sessions #2, #3 etc.). Or press the Down Scroll Button to display the same parameter in the previous session.

This information remains on screen for 3 seconds and will then revert back to the start screen, unless you press the Scroll Buttons or the Information Button again.

Fig. 31

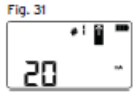


Fig. 32

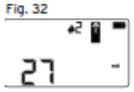


Fig. 33

ADDITIONAL FUNCTIONS

Mute Function
If you want to switch off your unit's sound effects, press and hold both the Up and Down Scroll Buttons for 1 second (Fig. 34). This will activate the Mute Function. The Mute Function remains active indefinitely unless manually changed. Deactivate the Mute Function by again pressing both the Up and Down Scroll Buttons for 1 second.
Note:
The Mute Function is overruled if there is a pad contact problem (see page 9) or if there is a unit error message (see page 17).

Fig. 34

Keylock Function
When you have set the intensity to a level you find comfortable, press and hold the Information Button for two seconds (Fig. 35) to activate the Keylock Function. This "locks" the Up and Down Intensity Buttons, so the intensity cannot be changed accidentally. The other buttons will still function as normal. If you wish to increase or decrease the intensity, you can deactivate the Keylock Function by again pressing the Information Button for two seconds. This function only remains active during the session in which it is activated. Once the treatment session is complete, the Keylock Function deactivates automatically.
Note:
Keylock cannot be activated while the uinit is paused.

Fig. 35

Reset Data
The Vital Compact controller can store the data from 90 treatment sessions. Upon completion of 90 sessions, you can bring your controller to your clinician so they can review your treatment progress data. Once this is done, the controller can be reset and the data cleared by pressing and holding the Down Intensity Button and the Information Button for 4 seconds (Fig. 36). After 2 seconds, the Total Treatment Time will begin to flash on screen and when this resets to 00:00, your data has been cleared. This function will not work while a treatment session is in progress.

If you don't reset the data after 90 sessions, you can still continue to use your unit. What happens in this instance is that the data from the 91st and subsequent sessions is written over the data for session #1, #2 etc.

Important:
Do not reset your data unless you have been advised to do so by your clinician.

Fig. 36

English

Problem Solving Guide

The following is a list of issues which may arise when using Vital Compact and how to deal with each one.

Problem	Possible Cause	Solution
The display does not come on and there is no signal	Battery discharged	Recharge battery
Battery symbol flashing	The battery is low	Recharge the battery
Increasing intensity causes unpleasant sensation	Electrode(s) incorrectly positioned	Reposition the garment or electrode(s) to ensure the electrodes are correctly positioned
	Electrode surface is dry	Moisten the surface of the electrodes
	Possible oils, creams or lotions, pigment marks, dry marks or other factors on the skin	Wash any oils, creams or lotions, from the skin
The Pad Contact symbol (⚠) is flashing and the controller is beeping	Liner left on one or more electrodes	Remove liners from all electrodes
	Poor electrode contact with the skin	Ensure each electrode is in full contact with skin. Press each one firmly against the skin
	Lead not properly connected	Ensure lead is properly connected to controller and garments/electrode
	Electrode(s) faulty	Replace the electrode(s)
	Faulty lead assembly	Check connections, replace if broken
	Broken wire within garment	Replace the garment
Program number is flashing on the display	Incorrect treatment lead connected to the controller	Ensure the correct lead for the selected program is connected
Screen goes blank during a session	Battery discharged	Recharge battery
	Unit fault	Switch off the controller and then switch it back on again. If the error persists, contact **neurotech**®
The Pad Contact symbol (⚠) is flashing, the controller is beeping and E 'XXX' appears on screen *	Unit error	Switch off the controller and then switch it back on again. If the error persists, contact **neurotech**®

(* 'XXX' = 001, 002, 003 etc.)

PRODUCT MAINTENANCE

If you drop your Vital Compact controller and there is any visible damage or any indication of loose/dislodged internal components as a result, please return the controller to **neurotech**®.

Cleaning Instructions
Never let the controller get wet. However, it can be cleaned using a soft cloth, lightly dampened in soapy water. Do not use the unit is it gets wet.

Washing Instructions
Important: Detach the Controller and Stress Lead from the Garments before cleaning. Before washing, remove all eight electrodes. We recommend that it be washed when you are replacing the electrodes.

You should wash the Garments in a receptacle which allows you to lay them flat (e.g. a bath or tub). NEVER wring the Garments during or after washing. This protects the internal composition of the Garment from damage.

Always follow the instructions on the label when washing the Garments.


Never machine wash the Garments. Always handwash them in lukewarm water.


Do not use any bleach when washing your Garments.


Do not dry clean your Garments.


Do not tumble dry your Garments. The Garments should be hung up to dry. Do not dry over anything hot (e.g. a radiator or any other direct heat source). Ensure the Garment is completely dry before use. Do not fold while drying.


The Garments should not be ironed.

Note: Replace the Garment if the material is damaged and exposes the wiring within.

Garment materials
Outer material: 100% Nylon; Inner Material: 100% Polyurethane; Fastening: 100% Nylon

Battery Power
Your unit is powered by a rechargeable battery. The full performance of a new battery is achieved only after two or three complete charge cycles (fully charged and discharged).

The battery symbol is displayed in the upper-right corner of the screen. When the battery is fully charged, the battery symbol will have 5 bars. If the battery depletes completely, the controller will beep and the battery will begin flashing. Use the battery only for its intended purpose. Never use any charger or battery which is damaged. If the unit has not been used for a significant period of time and the battery is completely discharged, it may take a few minutes before the charging indicator appears on the display. Charging may take longer than normal in this instance.

Unplug the charger from the electrical socket and the device when it is not in use. Do not leave a fully charged battery connected to a charger, since overcharging may shorten its lifetime. If left unused, a fully charged battery will loose its charge over time.

Leaving the battery in hot or cold places, such as in a closed car in summer or winter conditions, will reduce the capacity and lifetime of the battery. Always try to keep the battery between 15ºC and 25ºC (59ºF and 77ºF). A device with a hot or cold battery may not work temporarily, even when the battery is full charged. Battery performance is particularly limited in temperatures well below freezing. Do not dispose of batteries in a fire as they may explode. Batteries may also explode if damaged. Dispose of batteries according to local regulations. Please recycle when possible. Do not dispose as household waste.

This product is intended for continuous operation. i.e. operation in normal use, for an unlimited period of time, without the specified limits of temperature being exceeded.

Disposal of Batteries and Electrodes
Used electrodes and battery packs must never be disposed of in a fire, but in accordance with your country's national or state laws governing the disposal/recycling of such items.

REPLACING THE BATTERY

The battery can be charged and discharged hundreds of times, but it will eventually wear out. To ensure optimum battery performance you should use your device regularly e.g. perform 1 session a day, 5 days per week. New batteries are available from Neurotech. To install a new battery, follow the steps below:

1. On the back of the unit is a small rubber plug (Fig. 37). Remove this and unscrew the back of the unit.

Fig. 37

2. Carefully unplug the battery connector from its socket and remove the battery pack (Fig. 38).

Fig. 38

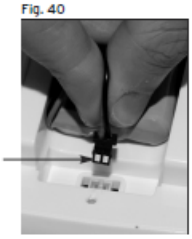
3. Insert the new battery pack with the connector lead towards the bottom of the unit (Fig. 39).

Fig. 39

4. Plug the battery connector into its socket, ensuring the 2 silver contacts are facing **AWAY FROM** the battery pack (Fig. 40).

5. Replace back of the unit. Re-attach to the unit by inserting the screw and screwing it in. Re-insert the small rubber plug.

Fig. 40



TECHNICAL SPECIFICATIONS

TREATMENT PROGRAM INFORMATION

Table 1: Treatment Parameters - Stress

Prog	Frequency Hz	Pulse Width µS	Contraction (Sec.)	Relaxation (Sec.)	Treatment Time (Mins.)
1	50	620	5	5	30

GENERAL SPECIFICATIONS

Product Type: 205

Classification: Internally powered equipment, Class II charger, and Type BF applied parts.
This unit is not suitable for use in an oxygen-rich environment.

Intended use: Electrical muscle stimulator.

Waveform: Symmetrical bi-phasic square current waveform.
This product is intended for continuous operation.
This product has an IP rating of 22.
To isolate the system from the mains, remove the charger from the wall socket.

PCB Fuses:
- F1: 1 Amp, fast-acting, max. Voltage Rating (V): 50, Interrupting Rating (AC/DC): 50A@50VDC/50A@VAC.
- F2:1 Amp, fast acting, max. Voltage Rating (V): 50, Interrupting Rating (AC/DC): 50A@50VDC/50A@VAC.

ELECTRICAL SPECIFICATIONS

The output current reading displayed on the screen indicates the peak current for a 500ohm resistive load only. The actual current value delivered, may be lower due to varying impedance levels within users. See table below for measured values at different resistive values.

Rated Outputs - Voltage/Currents

Parameters	500Ω	1KΩ	1.5KΩ
Output RMSA	17.9mA	14.5mA	10.8mA
Output RMSV	8.9V	14.5V	16.2V
Output Frequency	50HZ	50HZ	50HZ
DC component	0V	0V	0V
Pulse Width	620µS	620µS	620µS
Max Output Current (peak)	120mA	100mA	70mA

Environmental Specifications:

Operating Range:	Temperature: 5 to 40°C Humidity: 15 to 93 % RH (non condensing) Atmospheric Pressure: 70 to 106kPa
Transport & Storage Range:	Temperature:-25 to +70° C Humidity: 10 to 93% RH (non condensing) Atmospheric Pressure: 50-106kPa

CARING FOR YOUR UNIT

Your unit should not be allowed to get wet or be left in excessive sunlight. It may be cleaned regularly using a soft cloth, lightly dampened in soapy water. Do not allow the interior of your unit to become wet. Do not use detergents, alcohol, spray aerosols or strong solvents on your unit.

Access to the interior of the unit is not required for maintenance purposes. If your unit is damaged, you should not use it but should return it to neurotech or your local distributor for replacement or repair. Repairs, service and modifications may not be carried out by anyone other than qualified service personnel authorised by neurotech.

If required, always seek assistance to set-up, use or maintain your Vital Compact from your clinician or neurotech.

You should report any unexpected operation or event to your clinician or neurotech.

Important:
Under no circumstance should anything other than the correct type of battery pack - (rechargeable batteries 1 x 7.2 (6 x 1.2 AAA) volt (NiMH) DC battery pack) be used with your unit. These can be purchased from the Neurotech careline.

ACCESSORIES

Under no circumstances should anything other than neurotech accessories be used with your Vital Compact unit (Type 205). Any others may not be compatible with your unit and could degrade the minimum safety levels. You can purchase all accessories neurotech

Vital Compact Left Leg Garment (S) - 1220-0811
Vital Compact Right Leg Garment (S) - 1220-0812
Vital Compact Left Leg Garment (M) - 1220-0813
Vital Compact Right Leg Garment (M) - 1220-0814
Vital Compact Left Leg Garment (L) - 1220-0815
Vital Compact Right Leg Garment (L) - 1220-0816

Vital Compact Stress Electrodes - Type 729

Battery pack - 1 x 7.2V (6 x 1.2 AAA) (NiMH) - 3924-0310

Power Supply (2504-0806)
Input: 100-240V ~ /50-60Hz/400mA
Output: 12V DC / 1.0A
Important: Do not use any other chargers or Power Supplies

EXPECTED SERVICE LIFE

Controller: 5 years
Garment: 3 years
Battery Pack: 2 years
Battery Charger: 2 years
Electrodes: 20 uses

DESCRIPTION OF THE CONTROLLER'S SYMBOLS

There are a number of technical markings on your controller. These can be explained as follows:

The controller and garments are manufactured for:
Bio-Medical Research Ltd, Parkmore Business Park West, Galway, Ireland.

The controller requires 1 x 7.2V (6 x 1.2 AAA) (NiMH) DC battery pack; DC is indicated by the symbol: ⎓

Power (**P**): Maximum power output measured in Watts (W) into a 500Ω load.

Frequency (**F**): Number of pulses output by the controller per second, measured in Hertz (Hz).

IP22: Ingress Protection Rating

VXX: Software version.

These symbols mean "Attention, read the accompanying documents".

This symbol means type BF applied parts (electrodes).

CE 0366 This symbol on your unit is to indicate conformity to the requirements of the Medical Device Directive (93/42/EEC). 0366 is the number of the notified body (VDE).
The CE mark applied also indicates that this equipment complies with the requirements of the ROHS Directive (2011/65/EU) for the Restriction of Hazardous Substances in Electrical and Electronic Equipment.

SN stands for 'serial number'. On a label on the underside of the controller and cradle are the serial numbers specific to those items. The letter preceding the number indicates the year of manufacture, where "T" denotes 2014, "U" denotes 2015 etc.

The garments' batch number is represented on its packaging, by the number corresponding with the LOT symbol.

At the end of the product lifecycle, do not throw this productor the batteries into the normal household garbage, but bring it to a collection point for the recycling of electronic equipment.

Some product materials can be re-used if you bring them to a recycling point. By re-using some parts or raw materials from used products you make an important contribution to the protection of the environment. Please contact your local authorities if you need more information about collection points in your area.

Waste Electrical and Electronic Equipment can have potentially harmful effects on the environment. Incorrect disposal can cause harmful toxins to build up in the air, water and soil and can be harmful to human.

WARRANTY

Bio-Medical Research Limited (BMR Ltd.) warrants (a) that your Vital Compact controller will be free from defects in material and workmanship for a period of two years from the date of original purchase and (b) that the Vital Compact garments will be free from defects in material and workmanship for a period of six months from the date of original purchase. These warranties do not apply to the batteries supplied with your product and exclude consumables such as the electrodes.

Should your controller or either garment develop a fault within the warranty period, BMR Ltd. will replace or repair it/them free of charge, provided the controller and/or garment:

- have been used for their intended purpose and in the manner described in this instruction manual;
- have not been connected to an unsuitable power source;
- have not been subjected to misuse or neglect;
- have not been modified or repaired by anyone other than an approved **neurotech**® distributor or agent.

This warranty complements existing applicable national guarantee obligations and does not affect a consumers statutory rights.

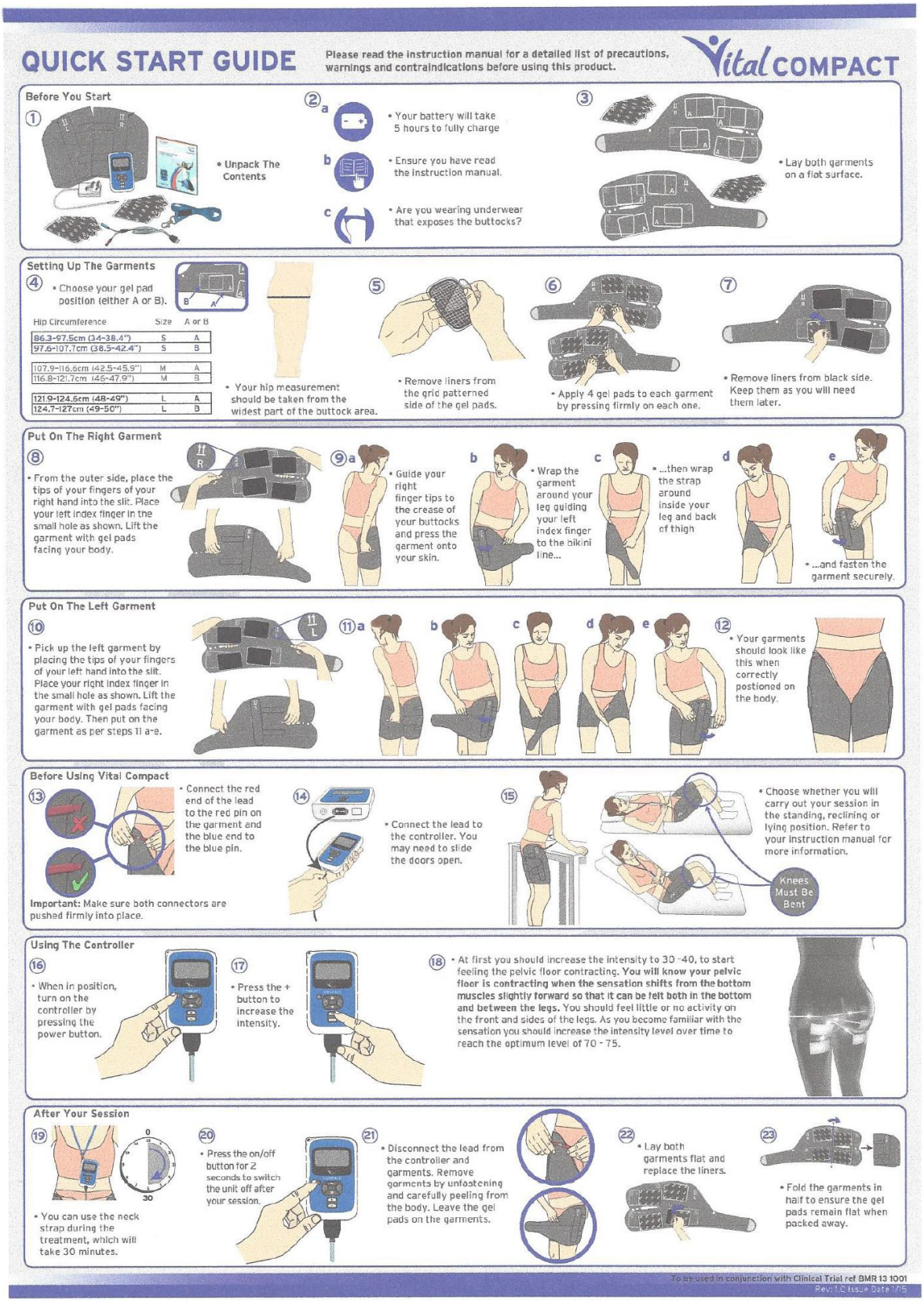
English

Assistance:
If you have any problems with your device please contact your study doctor whose contact details are on the Informed Consent form you received at the beginning of the study. For further assistance you may contact:

Expedite Research, LLC
15 Kerry Lane
Phoenixville, PA 19460-2771
Office 610 933 1529

These instructions for use were created specifically for study BMR-13-1001 by:
Bio-Medical Research Ltd.,
Parkmore Business Park West,
Galway, Ireland.

For Investigative Purposes Only. For Use in Clinical Trial BMR-13-1001.
NT Vital Compact US Trial IM - V1


QUICK START GUIDE
Please read the instruction manual for a detailed list of precautions, warnings and contraindications before using this product.
Vital COMPACT
Before You Start
• Unpack The Contents
• Your battery will take 5 hours to fully charge
• Ensure you have read the instruction manual.
• Are you wearing underwear that exposes the buttocks?
• Lay both garments on a flat surface.
Setting Up The Garments
• Choose your gel pad position (either A or B).
Hip Circumference | Size | A or B
86.3-97.5cm (34-38.4") | S | A
97.6-107.7cm (38.5-42.4") | S | B
107.9-116.6cm (42.5-45.9") | M | A
116.8-121.7cm (46-47.9") | M | B
121.9-124.6cm (48-49") | L | A
124.7-127cm (49-50") | L | B
• Your hip measurement should be taken from the widest part of the buttock area.
• Remove liners from the grid patterned side of the gel pads.
• Apply 4 gel pads to each garment by pressing firmly on each one.
• Remove liners from black side. Keep them as you will need them later.
Put On The Right Garment
• From the outer side, place the tips of your fingers of your right hand into the slit. Place your left index finger in the small hole as shown. Lift the garment with gel pads facing your body.
• Guide your right finger tips to the crease of your buttocks and press the garment onto your skin.
• Wrap the garment around your leg guiding your left index finger to the bikini line...
• ...then wrap the strap around inside your leg and back of thigh
• ...and fasten the garment securely.
Put On The Left Garment
• Pick up the left garment by placing the tips of your fingers of your left hand into the slit. Place your right index finger in the small hole as shown. Lift the garment with gel pads facing your body. Then put on the garment as per steps 11 a-e.
• Your garments should look like this when correctly postioned on the body.
Before Using Vital Compact
• Connect the red end of the lead to the red pin on the garment and the blue end to the blue pin.
Important: Make sure both connectors are pushed firmly into place.
• Connect the lead to the controller. You may need to slide the doors open.
• Choose whether you will carry out your session in the standing, reclining or lying position. Refer to your instruction manual for more information.
Knees Must Be Bent
Using The Controller
• When in position, turn on the controller by pressing the power button.
• Press the + button to increase the intensity.
• At first you should increase the intensity to 30 -40, to start feeling the pelvic floor contracting. You will know your pelvic floor is contracting when the sensation shifts from the bottom muscles slightly forward so that it can be felt both in the bottom and between the legs. You should feel little or no activity on the front and sides of the legs. As you become familiar with the sensation you should increase the intensity level over time to reach the optimum level of 70 - 75.
After Your Session
• You can use the neck strap during the treatment, which will take 30 minutes.
• Press the on/off button for 2 seconds to switch the unit off after your session.
• Disconnect the lead from the controller and garments. Remove garments by unfastening and carefully peeling from the body. Leave the gel pads on the garments.
• Lay both garments flat and replace the liners.
• Fold the garments in half to ensure the gel pads remain flat when packed away.
To be used in conjunction with Clinical Trial ref BMR 13 1001
Rev: 1.0 Issue Date: 7/15

14.12 Appendix XII. itouch Sure Pelvic Floor Exerciser Instructions for Use

itouchsure
PELVIC FLOOR EXERCISER

IMPORTANT: Read this manual carefully before starting to use your itouch sure Pelvic Floor Exerciser. INAPPROPRIATE OR INCORRECT USE COULD BE UNSAFE.

This user manual is provided to you as part your participation in a clinical study. Please only use the iTouch sure as directed by your study doctor

Caution: U.S. Federal Law restricts this device to sale by or on the order of a licensed healthcare practitioner.

Support
Please call your study doctor if you have any questions.

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CONTENTS OF PACKAGE

Itouch Sure Control Unit
itouch sure Electrode
Connecting lead wire
Four AA batteries
Instruction booklet
Storage pouch

Before you use itouch sure for the first time

An examination of the vaginal tissue should be completed prior to initial treatment to rule out any contraindications, establish the baseline tissue condition and assess the physiology discussed below. Pelvic floor stimulation may not be successful if the urethra has excessive scarring or if there is significant denervation of the pelvic floor. The neuromuscular structures involved in urine storage must also be at least partially preserved. Patients with intact sacral reflex arcs and some innervation of the pelvic floor may benefit from pelvic floor stimulation.

The itouch sure unit must only be used in accordance with the advice of your treating physician. Be sure to read the instructions included in this booklet to supplement the information provided to you by your physician.

CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS

Contraindications

Should not be used if you have any of the following conditions:
If you have a heart pacemaker or a rhythm problem
If you are pregnant or trying to become pregnant
If you have been diagnosed or treated for cervical, or any pelvic, cancer
If you have, or have had epilepsy
While driving, or during any activity in which involuntary muscle contractions may put the user at undue risk of injury
If you have:
An active urinary tract infection
Recent history of vaginal bleeding between menstrual periods
Infections or lesions in the area of electrode placement
Diminished sensory perception
Inability to understand the directions of use or operate the device correctly
History of urinary retention or post-void residual volume greater than 200 cc If any discomfort occurs when inserting the electrode consult your study doctor.

Warnings

The patient should discontinue use and immediately consult the clinician if irritation, pain or unusual bleeding occurs.
Keep out of reach of children.
Do not use in water (for example, while bathing) or device may shock user.
This equipment is not rated for use while immersed or under dripping water.
Do not use simultaneously with high frequency hospital diagnostic/therapeutic equipment. Doing so may result in burns at the site of the electrodes and possible damage to the device.
Do not use simultaneously with patient monitoring equipment such as EKG monitors without investigating the possibility of output from the device causing erroneous monitor readings.
Do not carry batteries in a pocket, purse or other place where the terminals could become short circuited, (e.g. by way of a coin or paperclip). Intense heat could be generated and injury may result.

The long term effects of chronic electrical stimulation are unknown.
Do not use with products other than those recommended by your treating clinician.

Precautions
Review the following precautions before using:
It is not recommended to use the device while under the influence of alcohol or other substances, such as sleeping pills or tranquilizers, which could affect the patient's ability to operate the system correctly.
Removing or inserting the electrode while the system is on could result in discomfort.
Use while operating hazardous equipment, machinery or motorized vehicles could cause abrupt changes in stimulation which can startle the patient and create a hazard.
Do not use in close proximity (e.g. <3ft.) to transmitting cellular (wireless) telephones or two-way radios. This equipment may produce instability in the stimulatory output. Sudden unexpected changes in output could startle the patient and create a hazard.
Use while sleeping is not recommended.
The patient should discontinue use and consult a clinician if a significant change in the stimulation sensation occurs without changing the intensity settings. It is normal to feel a difference in sensation when changing positions during stimulation.
Caution should be used following recent surgical procedures when muscle contraction may disrupt the healing process.

ITOUCH SURE INDICATIONS FOR USE

Your physician has prescribed the use of the itouch sure Pelvic Floor Exerciser for the treatment of your urinary incontinence symptoms. itouch sure is indicated for the rehabilitation and strengthening of weak pelvic floor muscles in the treatment of stress, urge, and mixed urinary incontinence.

TREATING URINARY INCONTINENCE

You have been selected for this study because you suffer from Stress Urinary Incontinence and the iTouch sure is indicated for the treatment of this condition. The device may also be used for other forms of incontinence however in this study you will only be using the Stress treatment.

Please always ensure that the letters "STRES" are displayed at the top of the screen during treatment. If the words URGE, MIXD or TONE are displayed then you are using the wrong program. Press button P until STES appears on the screen and continue treatment

Please follow the instructions for use given to you by your study physician. The initial electrode fitting and the treatment session should be done under medical supervision by study staff.

You should experience the sensation of a muscular contraction in the vagina when using itouch sure.

HOW TO SET UP AND USE itouch sure

Setting up and using the itouch sure Pelvic Floor Exerciser is very simple.

Step 1: Before you use itouch sure for the first time, clean the Probe gently with soap and water (do not immerse).

Step 2: Insert two AA batteries into the Control Unit (see "Inserting the Batteries"). To test that the batteries have been inserted correctly and that the unit is working, press and hold the "ON" button for three seconds. The screen will light up and you will hear a beep.

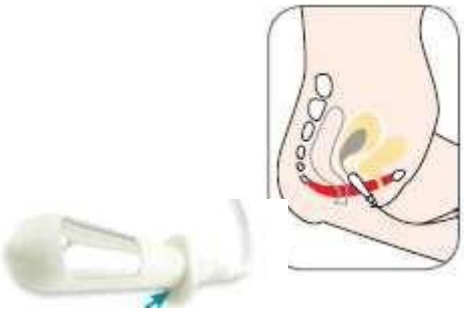
Step 3: Insert the two prongs of the lead wire into the matching receptacle end of the itouch sure Probe wire.

Step 4: Plug the USB port end of the lead wire directly into the bottom of the itouch sure Control Unit as shown.

Step 5: Before you insert the itouch sure Electrode, empty your bladder (urinate), and **make sure the itouch sure Control Unit is switched OFF**.

Step 6: Lubricate the itouch sure Probe with the conductive gel provided.

Step 7: After the wires are securely connected, insert the Probe into the vagina, in the same way you would a tampon, until only the flange at the end is visible.
The Probe will naturally position itself with the widest part of the flange vertically (see diagram).



Note: The flange should not be inserted into the vagina and should remain outside of the vagina at all times.

It is important to relax and choose a comfortable position - such as a semi-reclined pose - or to lie down on a bed or couch when performing this step.

Step 8: Turn the itouch sure ON by pressing the ON button (↑) for three seconds. When the unit is switched ON an audible "beep" will be heard.

Step 9: You will be using the STRES program in this study. The P Button is used to change the program. Please do not change the Program. If you accidentally change it you can get the STRES program back again by pressing the P button a few times.

Step 10: After insertion, adjust the strength by pressing the strength (⇈) button. The selected intensity will appear on the display. Begin to increase the strength to a level where you feel the sensation but is not overly painful. You may not feel any sensation until the strength reaches a certain level. This level may vary based on individual use and any pre-existing physical conditions, but stimulation occurs as soon as the strength is registered above 0.

Note: It is important to be conservative upon initial use. As long as you can feel the contraction, itouch sure is working. You can build up the strength slowly over a number of days.

During use you may feel cramping. If this happens, stop using the itouch sure until the cramping goes away, then start again using a lower strength.

Step 11: To decrease intensity, press the strength down (⌄⌄) button.

NOTE: itouch sure cycles between active stimulation and periods of rest to allow your muscles to recover between contractions. It is normal to feel the stimulation ramp down, stop briefly, and then ramp back up again during treatment. (During the "rest" period, the strength display flashes "0.0".)

Step 12: The length of each session has been set at 20 minutes. Please do not change the preset time.

Step 13: When the timer reaches zero, your session is complete. Press and release the OFF button once to turn off the power or it will automatically turn off.

Step 14: Remove the itouch sure Probe from your vagina by grasping the probe flange and gently pulling outward. It is important that you do not pull from the wires, as it may become disconnected at the two-prong connection.

Step 15: Wash and thoroughly dry the itouch sure Probe before placing it and the itouch sure Control Unit into the storage pouch.

Note: As with any new exercise regimen, with the first few sessions your muscles may be a bit sore the next day.

Note: The next time you turn on the unit, it will default to the mode last used but at half strength. Thus, it may be beneficial for you to adjust the intensity to the desired setting for your next treatment session prior to turning off the itouch sure Pelvic Floor Exerciser.

iTOUCH SURE "SMART FEATURES"

itouch sure Pelvic Floor Exerciser is designed with state-of-the art electronic features including:

Controllable Stimulation

The strength of the stimulation is under your control. You can gradually increase or decrease the intensity whenever you want to make sure the stimulation always feels comfortable.

Easy Start - One Touch Memory

The itouch sure has intelligent memory that enables the unit to remember the last settings you used, and return to similar settings at your next use.

•Automatic Safety Shutoff

This feature automatically turns the device off after 20 minutes of use to protect the pelvic floor muscles from being overworked. If your physician recommends sessions that are longer than 20 minutes, you can adjust the device to override the safety shutoff and allow a longer session.

ITOUCH SURECONTROLS

To turn itouch sure ON: Press and hold the ON button **for three seconds.**
When the unit turns on, you will hear a beep.

Memory Start

If you turned the unit off before completing the session, it will automatically start in the program you used last, at about 50% of the strength level you were using. This way you can adjust the strength comfortably for each new session.

Strength UP (⌃⌃) Button

To increase strength: Press and hold the Strength UP button until your desired strength is displayed on the screen. You may not feel any initial sensation, as it is a gentle increase of intensity. To increase the strength, press and release the button until you reach your required level. The strength will increase in 0.5 increments up to a maximum of 99.5.

Strength DOWN (⌄⌄) Button

To decrease strength: Press and hold the Strength DOWN button until the desired strength is achieved. To decrease the strength, press and release the button until you reach your desired level.

Program (P) Button

itouch sure has four preset programs which appear as STRES, URGE, MIXD and TONE on the screen. You will be only using the STRES program in this study. The P Button is used to change the program. Please do not change the Program. If you accidentally change it you can get the STRES program back again by pressing the P button a few times.

Lock Button

The Lock button can be used to lock all the controls except for the strength down and OFF buttons. This way you won't accidentally change the settings while you use the unit, but you still have the ability to decrease the strength at any time. To lock the unit, press and hold down the Lock button for three seconds until LOCK is displayed on the screen. To unlock the unit, simply repeat.

Time Selector Button

The itouch sure Pelvic Floor Exerciser counts down the minutes of your session. This countdown is displayed on the screen. When the count reaches zero, the unit will automatically turn off.

Each time you switch on the itouch sure, the time selector will be set at 20 minutes which is the treatment time for this study. Please do not change the timer setting.

To PAUSE the session - in case you need to suspend the treatment session and resume later - hold down the Time Selector button for three seconds. The display will read "PAUSE".

To return to the main screen, press any other key and you will return to the settings where you left off.

OFF Button

To turn itouch sure OFF: Press the OFF button. You will hear a double beep.

NOTE: Always make sure the unit is OFF before removing the itouch sure Probe from your vagina.

SCREEN DISPLAYS

The screen lights up whenever a button is pressed.

LEADS ALARM

itouch sure monitors the contact between you, the Probe, and the itouch sure Control Unit. If either of these go outside of a standard range, while the strength is above 20.0, the uni t will flash "LEADS", beep three times, and return strength to zero.

The most common causes are:
Poor contact with your vaginal walls.
•A broken lead wire.
•A faulty connection at the USB port or at the dual probe connectors.

If the LEADS alarm sounds, make sure the wires are connected properly. If that doesn't solve the problem:

Change the position of the probe in the vagina; or
Change your body position; or
Add lubrication to the itouch sure Probe so that it can make a better contact with the vaginal tissue.

If you have taken the above steps above and the alarm still shows, please refer to Troubleshooting section for further information.

Treatment

Please follow the instructions for use given to you by your study physician. The initial electrode fitting and the treatment session should be done under medical supervision by study staff.

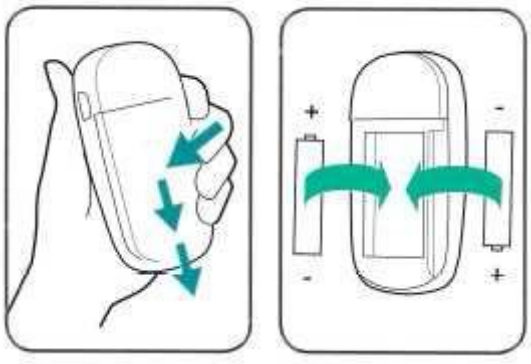
Set the strength level to that prescribed by your study doctor. If you experience discomfort reset the intensity down one step. Don't "overdo" it early on. As long as you can feel the contractions, itouch sure is working properly. You can build up slowly over a number of sessions.

Your muscles may be sore the next day- the same reaction you would get with any new exercise - and you may need to stop using your itouch sure for a day or two until the soreness goes away, and then start again using a lower strength and shorter treatment time. As the pelvic floor muscles get stronger, you will be able to increase your strength level and time.

NOTE: itouch sure cycles between active stimulation and periods of rest. It is normal to feel the stimulation ramp down, stop briefly and then ramp back up again during treatment.

BATTERY USE

Inserting the Batteries



Open the battery cover:

Press down in centre of battery cover and slide the cover downwards in the direction of the raised arrows.

Insert the batteries in the direction shown inside the case. Make sure that the ribbon goes behind the batteries, which makes them easier to remove later. When the batteries are running low, a low battery indicator will show on the screen (battery symbol) and the display will begin to fade. The intensity of your workout, however, will stay the same until the battery runs out and the unit shuts off.

Battery removal and replacement:

When the batteries need to be changed the low battery sign, " BATT", will be displayed on the screen. To remove batteries, pull gently on the ribbon behind them. Remove batteries from your itouch sure unit if the unit is unlikely to be used for a long period.

Battery type:

ONLY use either AA alkaline batteries. . DO NOT mix batteries of different types. Do not try to recharge alkaline batteries. Properly dispose of used batteries, as batteries should not be disposed of with household waste.

Warning:
Keep batteries out of the reach of small children
If battery leakage occurs and comes in contact with the skin or eyes, wash thoroughly with lots of water.
Do not attempt to revive alkaline batteries by heating, charging or other means
Never put batteries in a fire nor try to disassemble them

ITouch SURE CLEANING AND STORAGE

Cleaning the Probe

It is important to clean the itouch sure Probe after each use to prevent bacterial growth that could possibly lead to an increased risk for infection. Wash the probe with warm soapy water and then wipe the probe with an alcohol wipe, and dry thoroughly.
DO NOT immerse the probe under water, or in boiling water, as this will damage it.

The Probe that is supplied with the itouch sure Pelvic Floor Exerciser is intended strictly for one person's use. Do not let anyone else use your itouch sure.

Cleaning the itouch sure Control Unit

Clean the itouch sure Control Unit weekly with a cloth or paper towel dampened with soapy water, but DO NOT immerse it under water. Dry it with a clean cloth and make sure it is fully dry before storing the unit in its pouch.

Storing Your itouch sure Pelvic Floor Exerciser

Store itouch sure in its pouch.
Do not store at high temperatures or in damp conditions.
Do not store or use near a microwave oven.
Remove batteries if storing for more than 30 days

TROUBLESHOOTING

If you have problems with the operation of your itouch sure Pelvic Floor Exerciser, follow these directions:

Fading display or no display -
The display will begin to fade as the batteries run low, and there will be nothing on the display when there is no power left in the batteries. Make sure the batteries are charged and inserted correctly. If necessary, replace them. (For more information, see " Battery Use" on page 19)

Controls won't work -
The unit may be on LOCK, in which case the display will read "LOCK". Hold down the Lock button on the side for three seconds. If "LOCK" is not showing on the display, remove and replace the batteries.

No sensation / No leads alarm -
If you feel no sensation when you use itouch sure, first try increasing the strength level according to instructions. If that does not work, dampen your hand with water and a little table salt. Holding

the Probe in your hand, increase the strength gradually. If you don't feel anything, the unit may need to be replaced.

NOTE: If you are able to feel the sensation in your hand but not in your vagina, you may have nerve damage. Stop using itouch sure and call your physician

PRODUCT SPECIFICATIONS

Maximum Intensity	50V zero to peak.
Setting	0·100 in steps of 0.5
OC cutout	below 160 Ohm.
Constant current	160-470 Ohm 470-2000 Ohm constant voltage.
Channels	Single
Waveform	Asymmetrical rectangular
Max Pulse energy	*Total output limited to 25uC per pulse
Power	2 xAA Alkaline
Battery life	At least 15 hours at 5omA 3oouS 50Hz
Adjustable Timer	10, 20, 30 45, 60, 90 min defaults to 20 min
Pause button	"Clock" key when running
Output plug	Fully shielded: touch-proof mini USB
Weight	90 gms without batteries
Dimensions	102 x 53 x 30 mm
Safety Classification Type BF	Internal power source. Designed for continuous use. No special moisture protection.
Environmental Operating:	Humidity: 20% - 65% RH
Storage Humidity:	10 to 90% RH Temperature range: 0℃ to 55℃
Temperature range	0℃ to 35℃

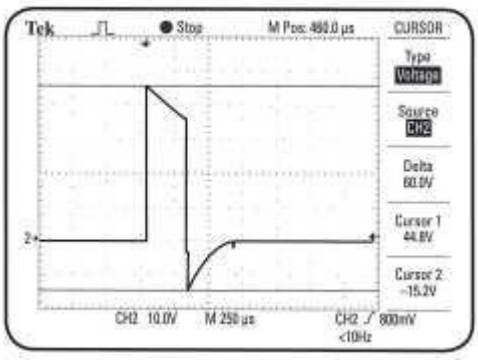
The electrical specifications are nominal and subject to variation from the listed values due to normal production tolerances.

PROGRAM SETTINGS

Program	Hz	Pulse Width (µS)	Ramp Up & Down (Sec)	Plateau (Sec)	Off (Sec)	Default Program Duration (Min)
STRESS	50	300	1	5	10	20
URGE	10	200	1	5	10	20
MIXED	20	250	2	5	10	20
TONE	35	250	2	3	6	20

Device Output Parameters and Waveform

The waveform below illustrates a typical output waveform from the itouch sure device:



Max Pulse Energy: 23 µC

Use special precautions regarding EMC according to the information provided below.

Other portable and mobile RF communications equipment can affect performance.
Do not use when adjacent to or stacked with other electrical equipment.

Assistance

If you have any problems with your device please contact your study doctor whose contact details are on the Informed Consent form you received at the beginning of the study. For further assistance you may contact

Expedite Research, LLC 15 Kerry Lane
Phoenixville, PA 19460-2771
Office 610 933 1529

These instructions for use were created specifically for study BMR 13 1001 by:

Bio-Medical Research Ltd. Parkmore Business Park West Galway, Ireland