

A Prospective Open Label pilot study investigating the impact of ThermaCare on flexibility, muscle relaxation & low back pain in two different populations.

## **A Prospective Open Label pilot study investigating the impact of ThermaCare on flexibility, muscle relaxation & low back pain in two different populations.**

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## PROTOCOL APPROVAL

**PROTOCOL TITLE:** A prospective Open Label pilot study investigating the impact of ThermaCare on flexibility, muscle relaxation & low back pain in two different populations.

**PROTOCOL NUMBER:** 2017THERMA

**UNIVERSAL TRIAL NUMBER:** U1111-1192-2140

**VERSION NUMBER:** Version 2. 2017May29

I have read and understand all sections of this protocol and confirm that it contains all the information necessary to conduct the study. The study will be carried out in conformity with this document.

Principal Investigator:

*ANDREW RONCHI*

Printed Name

*Andrew Ronchi*

Signature

*29.5.17*

Date

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## PROTOCOL SUMMARY

<b>Title:</b>	A Prospective Open Label pilot study investigating the impact of ThermaCare on flexibility, muscle relaxation & low back pain in two different populations.
<b>Device(s):</b>	The devices to be used for this study include: <ul style="list-style-type: none"> <li>• ThermaCare Lower Back HeatWraps, Pfizer Consumer Healthcare</li> <li>• ViMove wearable sensors, dorsaVi Ltd.</li> </ul>
<b>Study Objective:</b>	The objectives of this study are to evaluate the impact of ThermaCare HeatWraps as an intervention to: <ol style="list-style-type: none"> <li>1. Decrease pain during movement, improve muscle relaxation and increase flexibility in people with low back pain (Group 1).</li> <li>2. Improve muscle relaxation and increase flexibility in people who are actively involved in sport (Group 2).</li> </ol>
<b>Study Design:</b>	This research will utilize a prospective open-label investigator initiated study design. This allows the assessment of ThermaCare HeatWrap efficacy pre- and post- application, and may provide insight into the mechanisms of any observed pain relief. The nature of the ThermaCare intervention means that blinding is difficult, as there is no adequate placebo heat therapy.
<b>Enrolment Size:</b>	The enrolment size will be 40 total subjects from 2 discrete population groups. As we expect an attrition rate of 20%, we will initially recruit 50 subjects.
<b>Subject Population:</b>	As per the inclusion and exclusion criteria: <p>Group 1: 20 people with recent back pain</p> <p>Group 2: 20 people who regularly play sport</p>
<b>Timeframe:</b>	We expect 6-months will be required from first participant enrolment to the last participant visit. A further 3-months will be required for analysis and write-up.
<b>Primary Endpoints:</b>	<ol style="list-style-type: none"> <li>1. Collection of movement and erector spinae muscle activity data in all participants.</li> <li>2. A change over time in range of motion in any one plane of movement compared to pre-intervention range of motion.</li> <li>3. A change over time in Flexion-Relaxation response in those subjects where abnormal EMG activity in flexion during baseline assessment is detected.</li> <li>4. A change over time in maximum pain during movement score. (1-10 as recorded during the in-clinic ViMove assessment) for any one plane of movement.</li> </ol>
<b>Secondary Endpoints:</b>	<ol style="list-style-type: none"> <li>1. Capture changes in low back pain levels as assessed via a Numeric Rating Scale (NRS-Pain).</li> <li>2. Capture self-reported changes in functional status pre- and post-ThermaCare application as measured by the Oswestry Disability Index (ODI) and Roland Morris Disability Questionnaire (RMDQ) if subjects scored &gt;3 on the NRS.</li> <li>3. Capture impression of change from subjects post ThermaCare application using the Patient Global Impression of Change Scale (PGIC).</li> <li>4. Observe changes in activity levels as collected by ViMove monitoring.</li> <li>5. Correlation of Low Back Pain Classifier (LBPC) Score to ViMove Scores for flexion and extension.</li> </ol>

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<p><b>Inclusion Criteria:</b></p>	<p><u>Inclusion criteria for recent low back pain patients:</u></p> <ol style="list-style-type: none"> <li>1. Adults between the age of 21-54 inclusive, male and female.</li> <li>2. Low back pain is the primary source of pain over the last 3 weeks.</li> <li>3. Have experienced and/or received treatment for muscle related low back pain with an average score of at least 3/10 on a 10-point Numeric Rating scale over the past 3 weeks.</li> <li>4. Must be able to communicate fluently in English.</li> <li>5. Must provide written informed consent.</li> <li>6. Must agree to confidentiality.</li> </ol> <p><u>Inclusion criteria for people who are active in sports:</u></p> <ol style="list-style-type: none"> <li>1. Adults between the age of 21-54 inclusive, male and female.</li> <li>2. Participate in 30 min of moderate to high intensity exercise 3 times per week, as defined by the Borg Rating of Perceived Exertion scale.</li> <li>3. Must be able to communicate fluently in English.</li> <li>4. Must provide written informed consent.</li> <li>5. Must agree to confidentiality.</li> </ol>				
<p><b>Exclusion Criteria:</b></p>	<ol style="list-style-type: none"> <li>1. The subject is pregnant.</li> <li>2. The subject has a severe hearing impairment or an inability to follow verbal instructions in English.</li> <li>3. The subject is cognitively impaired.</li> <li>4. Known allergic skin reaction to tapes and plasters.</li> <li>5. Co-morbidities of neoplasm, infection, fracture, inflammatory or metabolic disorder that has potential to affect the lumbo-pelvic region.</li> <li>6. Preceding chronic myelopathy, specific neurological disease or neurological changes.</li> <li>7. Person who is currently enrolled in another investigational drug or device study.</li> <li>8. Any past or current heart or blood-circulation related disorders.</li> <li>9. The subject is contraindicated for this study for any other reason.</li> </ol>				
<p><b>Investigators:</b></p>	<p><u>Principal Investigator</u>          Dr. Andrew Ronchi,          dorsaVi Ltd          Level 1, 120 Jolimont Rd,          East Melbourne, Victoria, 3002          Ph: (03) 9652 2192</p> <p><u>Co-Investigators</u></p> <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; vertical-align: top;">                 Ms. Meagan Blackburn                  dorsaVi Ltd.                  Level 1, 120 Jolimont Rd,                  East Melbourne, Victoria, 3002                  Ph: (03) 9652 2198             </td> <td style="width: 50%; vertical-align: top;">                 Mr. Jayce Gilbert                  Peak MSK Physiotherapy                  Suite 4/544 Hampton St,                  Hampton, Victoria, 3188                  Ph: (03) 9533 5305             </td> </tr> <tr> <td style="vertical-align: top;">                 Dr. Sallie Cowan                  Clifton Hill Physiotherapy                  111 Queens Parade,                  Clifton Hill, Victoria, 3068                  Ph: (03) 9486 1918             </td> <td style="vertical-align: top;">                 Mr. Michael Tricarico                  Hoppers Crossing Physiotherapy                  171 Heaths Rd,                  Hoppers Crossing, Victoria, 3029                  Ph: (03) 9749 5110             </td> </tr> </table>	Ms. Meagan Blackburn dorsaVi Ltd. Level 1, 120 Jolimont Rd, East Melbourne, Victoria, 3002 Ph: (03) 9652 2198	Mr. Jayce Gilbert Peak MSK Physiotherapy Suite 4/544 Hampton St, Hampton, Victoria, 3188 Ph: (03) 9533 5305	Dr. Sallie Cowan Clifton Hill Physiotherapy 111 Queens Parade, Clifton Hill, Victoria, 3068 Ph: (03) 9486 1918	Mr. Michael Tricarico Hoppers Crossing Physiotherapy 171 Heaths Rd, Hoppers Crossing, Victoria, 3029 Ph: (03) 9749 5110
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## **STUDY TITLE**

A Prospective Open Label pilot study investigating the impact of ThermaCare on flexibility, muscle relaxation & symptoms of low back pain in two different populations.

## **STUDY INVESTIGATOR(S)**

Principal Investigator: Dr. Andrew Ronchi

Co-Investigators: Ms. Meagan Blackburn, Dr. Sallie Cowan, Mr. Michael Tricarico, Mr. Jayce Gilbert.

## **1: INTRODUCTION**

Low back pain commonly occurs in the general population, making it an important target for intervention. ThermaCare HeatWraps may prevent and relieve pain in regions such as the low back through continuous, low-level, direct heat therapy. The objective of this Investigator Initiated study is to evaluate the effectiveness of ThermaCare HeatWraps in improving flexibility and low back muscle relaxation, and in participants experiencing pain, reducing pain during movement. This study is an intervention trial on two discrete subject samples; (1) people with recent back pain, and (2) people who regularly play sport. ViMove wearable sensors provide precise objective measurements of low back muscle activity and movement in real time and can capture a patient's reporting of pain during movement. Outcomes will be assessed through standard ViMove protocols in conjunction with multiple validated measures of pain, perception of change, and function.

## **2: BACKGROUND**

Low Back Pain (LBP) is common in the general population with a 12-month point prevalence of 12% and 1-month prevalence of 23% [1]. Nonspecific LBP, the most common presentation, is defined as pain of unclear pathology below the costal margin and above the inferior gluteal folds [2-5]. Although the prognosis for LBP appears to be favorable, rates of chronicity are high [6] with previous LBP being a strong risk factor for ongoing complaint or relapse [7]. This makes LBP one of the leading causes of years lived with disability in developed countries [8], resulting in direct and indirect costs of \$84.1 to \$624.8 billion in the United States [9]. As such, addressing LBP effectively is necessary to minimize the associated physical and financial burden [10].

There are numerous proposed methods to treat LBP. Effective interventions include spinal manipulation, and medications such as painkillers [11, 12]. However, these interventions can be invasive and are associated with extensive time requirements, high costs, and adverse side effects [13, 14]. Thus, non-invasive and easy-to-administer treatments such as heat therapy may be preferred, although their effectiveness is not as consistent [12, 15]. One such heat therapy is in the use of ThermaCare HeatWraps (Pfizer Consumer Healthcare, Richmond, VA). ThermaCare is a brand of non-invasive disposable heat wraps which provide the wearer with continuous low-level direct heat therapy for approximately 8 hours. ThermaCare HeatWraps are customized for specific parts of the body, including the low back. Clinical trials have demonstrated the efficacy of this intervention in the early treatment and prevention of Delayed Onset Muscle Soreness (DOMS) [5, 16]. Moreover, ThermaCare has been shown to be effective in the prevention of post-exercise pain and muscle soreness [16, 17]. Compared with the pain relievers ibuprofen and acetaminophen, ThermaCare provided more effective pain relief, and significantly improved flexibility and disability [18].

However, these studies are limited in their assessment of pain and disability. Pain was often measured using Likert-scale questionnaires, as pain is an inherently subjective experience despite being physiologically determined [19]. Disability was assessed using more comprehensive questionnaires, but was not compared with objective measures [20]. This is despite objective measures of movement being correlated with disability scores [21]. A Cochrane review assessing the efficacy of heat therapies such as ThermaCare, indicated that there is only moderate support from current research, as effects

are transient and relatively small [22]. However, these reviewed studies may be limited due to their qualitative and subjective measurement of pain and disability [23]. A systematic review and meta-analysis further indicated that current heat therapy research is of “very-poor-quality” [24]. As such, validated, objective and quantitative data into muscle activity and movement is required, to provide insight into subjectively reported changes in pain and disability.

Objective assessment of the association between pain and movement, and capturing a detailed view of the person’s movement, postures and activity levels is now possible due to the development of portable biofeedback sensors such as ViMove (dorsaVi Ltd). ViMove is wearable sensor technology, designed to precisely measure range of movement and static postures [25-27]. The device also measures low back muscle activity in real time through additional electromyography sensors. ViMove assessment of low back range of movement and posture has been shown to be highly correlated with 3D kinematic measurement [26]. Normative low back range of movement values have also been determined and are available for the adult population (normative data has FDA clearance, available upon request). The device also demonstrates high intra- and inter-rater reliability as a low back measurement tool [27]. Objective information and feedback is provided to the practitioner as a report evaluating a patient’s movement and function/activity pre- and post- low back pain intervention. The wearable and portable nature of the device allows monitoring in non-clinical environments for up to 24 hours (i.e. during normal daily activities). ViMove devices have TGA approval and FDA 510K clearance for use in Australia and the USA respectively.

By utilizing ViMove, this study will objectively assess muscle activity and movement, prior to, during, and following the use of ThermaCare HeatWraps. This study will include 2 discrete population samples; (1) people with recent back pain, and (2) people who regularly play sport. As such, it will evaluate the efficacy of ThermaCare in these respective samples. Previous research has primarily assessed ThermaCare as an intervention in the USA, with the efficacy of ThermaCare not being examined in Australian samples. However, epidemiological studies indicate comparable prevalence of low back pain between the two countries [28, 29].



### **3: AIMS, HYPOTHESES, AND OBJECTIVES**

#### **3.1 Aims**

The aims of this study are to evaluate the efficacy of ThermaCare HeatWraps:

1. As an intervention for people with low back pain.
2. As an intervention for people who are actively involved in sport.

#### **3.2 Hypotheses**

The Hypotheses for each aim are as follows:

1. ThermaCare HeatWraps are an effective intervention for people with low back pain as it:
  - a. Decreases pain during movement.
  - b. Improves muscle relaxation.
  - c. Increases flexibility (range of movement).
2. ThermaCare HeatWraps are an effective intervention for people actively involved in sport as it:
  - a. Improves muscle relaxation.
  - b. Increases flexibility.
  - c. Delays or reduces the incidence of pain as defined by an increase in existing pain or the occurrence of new pain.

#### **3.3 Objectives**

The objectives of this study are to determine if ThermaCare HeatWraps:

1. Affect muscle relaxation, perceived pain, and flexibility in people with low back pain.
2. Affect muscle relaxation, perceived pain, and flexibility in people who are actively involved in sport.
3. Result in changes in subjective measures of pain and disability following 8-hours of usage.
4. Induce changes in movement and surface muscle activity, by collecting and assessing objective movement and EMG data pre- and post- intervention.

### **4: STUDY DESIGN**

This investigator-initiated study will utilize a prospective open-label study design. This allows the assessment of ThermaCare HeatWrap efficacy pre- and post- intervention, and may provide insight into the mechanisms of any observed pain relief. The nature of the ThermaCare intervention means that blinding is difficult, as there is no adequate placebo heat therapy.

#### **1. In clinic assessments:**

- a. Obtainment of demographic data and brief medical history.
- b. ViMove Assessment comprised of:
  - i. Assessment of Range of Movement (ROM) – Flexion, Extension, Lateral Flexion, and rotation, standing and sitting positions, walking (40m speed test), sit-to-stand test (number of repetitions in 30 seconds and movement pattern, lift and carry task and squatting task).
  - ii. Simultaneous collection of muscle activity data using ViMove EMG sensors.
- c. Questionnaires:
  - i. Oswestry Disability Index (ODI)
  - ii. Roland Morris Disability Questionnaire
  - iii. Low Back Pain Classifier
  - iv. Numeric Scale for Pain (NRS-Pain)
  - v. Patient's Global Impression of Change Scale (PGIC)

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## **2. Out of clinic assessments:**

- a. ViMove Monitoring- All day (out of clinic) monitoring assessment of:
  - i. Peak angle ROM
  - ii. Total ROM score
  - iii. Total dynamic time over the monitoring period
  - iv. Body orientation summary over monitoring session (% time spent sitting, standing, horizontal, dynamic)

## **5: STUDY SETTING/LOCATIONS**

Both groups of participants will be recruited and assessed at the following clinics:

1. Clifton Hill Physiotherapy. 111 Queens Parade, Clifton Hill, Victoria, 3068.
2. Peak MSK Physiotherapy. Suite 4/544 Hampton St, Hampton, Victoria, 3188.
3. Hoppers Crossing Physiotherapy. 171 Heaths Rd, Hoppers Crossing, Victoria, 3029.

## **6: STUDY POPULATION**

20 participants will be recruited from each arm of the study, resulting in a total of 40 valid subjects. Although we will initially recruit 50 subjects, we expect an attrition rate of 20%.

## **7: ELIGIBILITY CRITERIA**

### **7.1 Inclusion Criteria**

There are two respective sets of inclusion criteria which subjects from each study arm must meet to be eligible for the study:

#### **7.1.1 Inclusion Criteria for Low Back Pain Patients:**

1. Males and Females between the age of 21-54 inclusive.
2. Low back pain is the primary source of pain over the last 3 weeks.
3. Have experienced and received treatment for muscle related low back pain over the past 3 weeks with an average score of at least 3/10 on a 10-point Numeric Rating Scale.
4. Must be able to communicate fluently in English.
5. Must provide written informed consent.
6. Must agree to confidentiality.

#### **7.1.2 Inclusion Criteria for Active in Sport:**

1. Adults between the age of 21-54 inclusive, male and female.
2. Participate in 30 min of moderate to high intensity exercise 3 times per week.  
- Intensity is assessed using the Borg Rating of Perceived Exertion (RPE)
3. Must be able to communicate fluently in English.
4. Must provide written informed consent.
5. Must agree to confidentiality.

## 7.2 Exclusion Criteria

Potential subjects who meet any of the following criteria will not be eligible for participation in this study:

1. The subject is pregnant.
2. The subject has a severe hearing impairment or an inability to follow verbal instructions in English.
3. The subject is cognitively impaired.
4. Known allergic skin reaction to tapes and plasters.
5. Co-morbidities of neoplasm, infection, fracture, inflammatory or metabolic disorder that has potential to affect the lumbo-pelvic region.
6. Preceding chronic myelopathy, specific neurological disease or neurological changes.
7. Person who is currently enrolled in another investigational drug or device study.
8. Any past or current heart or blood-circulation related disorders.
9. The subject is contraindicated for this study for any other reason.

## 7.3 Withdrawal Criteria

The following are a list of reasons for participants to be discontinued from the trial by the Investigator:

1. Withdrawal of Participant's consent.
2. Failure to maintain an adequate level of compliance with wearing sensors.
3. Failure to co-operate adequately with the Principal Investigator or staff during clinical visits.
4. Failure to adequately adhere to protocol requirements within or outside the clinical environment.
5. Participant experiences a serious adverse event (see section 10)
6. Participant no longer meets the inclusion criteria (see section 7.1)
7. Pregnancy.

# 8: STUDY PROCEDURES

## 8.1 Recruitment of Subjects

Two discrete groups of people will participate in this study.

1. The first group will be comprised of patients who have experienced and/or received treatment for low back pain within the past 3 weeks. This group will be recruited from private physiotherapy clinics.
2. The second group will be comprised of people who participate in 30-minutes of moderate-to-high intensity exercise 3-times per week. This group will also be recruited from private physiotherapy clinics.

## 8.2 Randomization

This study has been designed as an initial feasibility study providing insights that would guide an RCT. As such, this is a non-randomized partially blinded study, as the investigator and participants will be blinded to ViMove results, but not the test condition. Groups will not be randomized, and will be based on recruitment.

## 8.3 Study Protocols

### 8.3.1 Guidelines for Scheduling Subjects' Clinic Visits

Following enrolment into the study, an appointment is made for the subject within 3 weeks at their preferred clinic to begin the assessment.

### 8.3.2 Study Personnel Training

All personnel performing the ViMove fitting and assessment will undergo a training program in the use of the devices.

## 8.4 Methodology

The following tasks will be conducted on the recruitment day (Day 0) for all subjects, and will be recorded in each subject's respective source documents and case report forms (CRFs):

1. Assessment of eligibility against inclusion and exclusion criteria
2. An explanation of study procedures.
3. Provision and obtainment of written informed consent.
4. Obtainment of demographic information and medical history.
5. Booking of Day 1 and Day 2 (based on convenience).

The main study will be conducted over 2 consecutive days for each subject.

Participants will be asked to complete each of the following - 30 minutes prior to their appointment on Day 1; the Oswestry Disability Index (ODI), a Numeric Rating Scale for Pain (NRS Pain), the Roland Morris Disability Questionnaire, and a Low Back Pain Classifier.

Both subject groups will then have a "start interview" on their allocated baseline assessment day (Day 1). This will include fitting of the ViMove movement and EMG sensors, as well as a ViMove live "pain on movement" assessment. This session will take approximately 20-30 minutes. Whilst wearing the ViMove sensors, subjects will then leave the clinic and conduct normal daily activities for a pre-determined monitoring period. No ThermaCare HeatWraps are worn on Day 1. This allows a baseline assessment and allows any placebo effects from the sensors to be discounted. At the end of the monitoring session, subjects will return to the clinic to have an "end-of-day" interview. Participants will complete a Patient Global Impression of Change scale (PGIC), a repeat NRS, and will have another live ViMove assessment. Movement sensors will then be removed, and the subject will be reimbursed for that day.

The intervention day (Day 2) will have the same procedure as Day 1 (baseline), with the only difference being the additional application of ThermaCare HeatWraps during the "start interview". ThermaCare will only be applied after the live assessment, so will not be worn at the same time as the EMG sensors. Subjects will continue to wear the HeatWrap and ViMove sensors during the 8-hour daily activity monitoring period, with the wrap and sensors being removed during the end-of-day interview, prior to the end-of-day live assessment. The subject will then be reimbursed for Day 2. A schedule of events can be seen in Table 1, and a summary of the procedure can be seen in Figure 1.

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**Table 1. Schedule of Events**

	Visit 1* (Day 0) Enrol- ment	Visit 2* <u>Baseline</u> Start Interview (within 3 weeks of Visit 1)	Visit 3 <u>Baseline</u> End of Day Interview	Visit 4 <u>Intervention</u> Start Interview	Visit 5 <u>Intervention</u> End of Day Interview
Eligibility	x				
Informed consent	x				
Demographics & Medical History	x				
Enrolment and scheduling	x				
Questionnaires		x		x	x
ViMove application		x		x	
ViMove in clinic assessment		x	x	x	x
ViMove monitoring assessment		x		x	
ViMove removal			x		x
ThermaCare application				x	
ThermaCare removal					x
Adverse Events		x	x	x	x
Changes in medications		x		x	
Study Termination					x

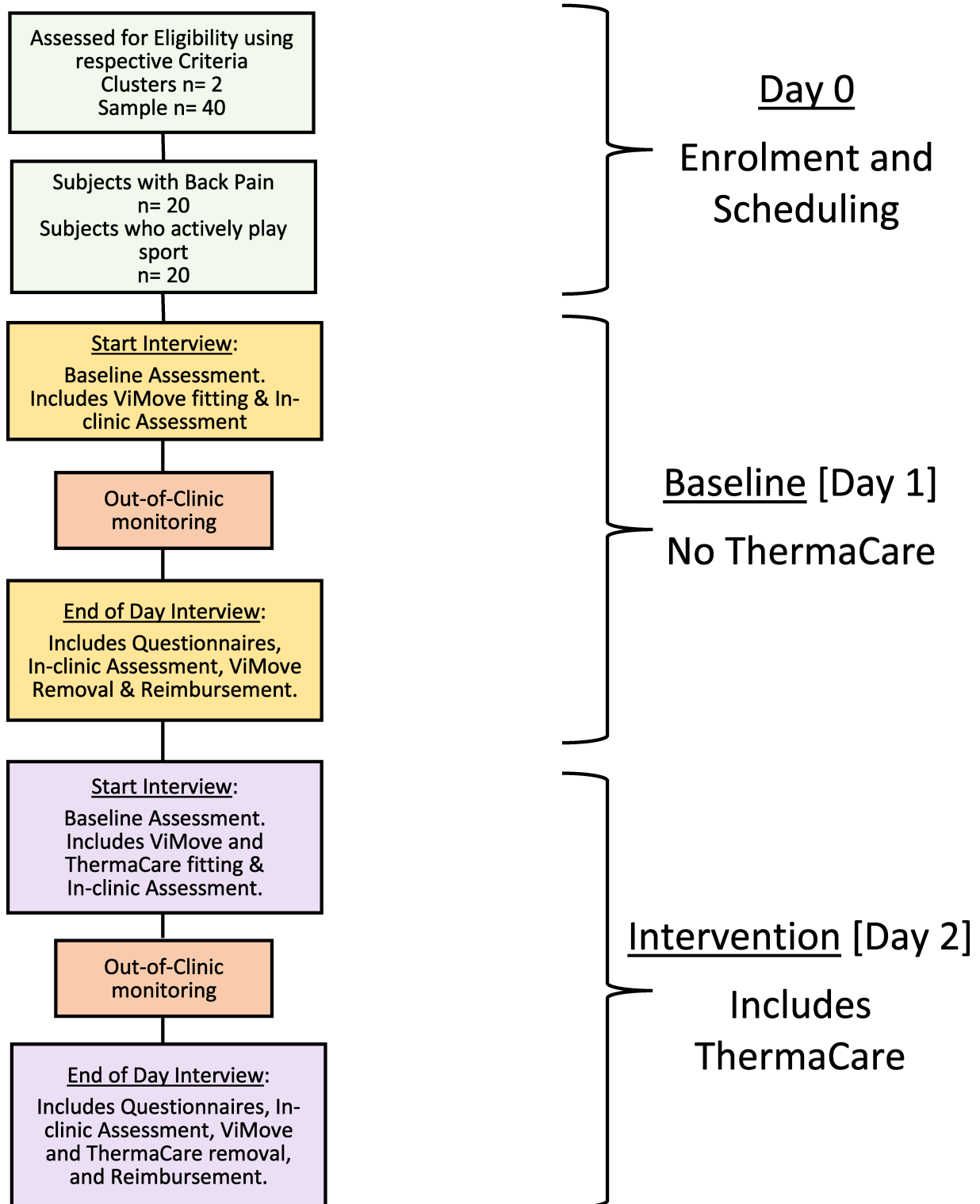
\*Baseline may occur on the same day as Visit 1 (i.e. enrolment).

Subjects who withdraw from the study after providing informed consent are referred to as “drop-outs” or premature withdrawals. The drop-out rate will be summarized. If the patient has provided a whole set of Day 1 data, this will be included in the study.

We expect 6-months will be required from first participant enrolment to the last participant visit. A further 3-months will be required for analysis and write-up.

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Figure 1. Summarized Procedure



## 8.5 Measurement Tools Used

### 8.5.1 ViMove Live – Range of Movement and Surface Muscle Activity

ViMove is a validated and reliable tool used for measuring movement and muscle activity of the low back. The ViMove devices will be fitted during the “start interview”. This requires the attachment of the sensors to skin over the lumbar region with adhesive pads using the standardized protocol. ViMove will be used to provide the primary outcome measures relating to movement data, surface muscle activity and recording pain on movement.

### 8.5.2 ViMove – Pain on movement

Pain on movement compares subjective responses of pain, with objective movement data from ViMove sensors. Assessment requires subjects to move within a maximum tolerable range. A numeric pain rating scale (see below) will be used during each movement, to obtain a value for the level of pain that each subject experiences. Consistent and standardized instructions are used, with the pain scores being recorded in the ViMove system. If no pain on movement is reported, a score of 0 will be documented.

(No Pain) 0    1    2    3    4    5    6    7    8    9    10 (Worst Pain)

### 8.5.3 ViMove – Monitoring (Out-of-clinic Assessment)

The monitoring period, in which subjects wear the ViMove devices during normal daily activity, aims to obtain or assess:

1. Total time spent in a dynamic vs. static state.
2. Sitting data; number and duration of sitting and walking events.
3. Timed walking test.
4. Postures and movement data throughout the day.

### 8.5.4 Questionnaires

The following questionnaires will be completed by subjects on a tablet onsite at their respective timepoints.

#### **Oswestry Disability Index (ODI)**

The ODI is a validated self-report questionnaire which quantifies the extent to which a person’s functional status is restricted by low back pain, and assesses the associated detriment [23]. It measures disability in the context of pain, rather than considering pain as the impairment. Ten 6-point scales assess the intensity (1) and effect (2) of pain on: personal care, lifting, walking, standing, sleep quality, sexual function, social life, and the ability to travel.

#### **Numeric Rating Scale for Pain (NRSP)**

The NRSP is a measure of pain intensity. It consists of a horizontal line anchored by 11 descriptions of pain (no pain vs. worst possible pain). Subjects are asked to circle a value along the line. The scale can be seen below:

(No Pain) 0    1    2    3    4    5    6    7    8    9    10 (Worst Pain)

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### **Roland Morris Disability Questionnaire**

The Roland-Morris Questionnaire (RMDQ) is a self-administered disability measure in which greater levels of disability are reflected by higher numbers on a 24-point scale. The RMDQ has been shown to yield reliable measurements, which are valid for inferring the level of disability, and to be sensitive to change over time for groups of patients with LBP.

### **Patient's Global Impression of Change Scale (PGIC)**

The PGIC assesses a subject's perceived efficacy of a treatment [30]. In the context of this study, it will assess the subject's beliefs around any changes in their low back pain following the use of ViMove only (Baseline [Day 1]), and following the wearing of ViMove + ThermaCare (Intervention [Day 2]) during the respective periods of daily activity/monitoring. This assessment will utilize a 7-point scale as follows:

- |                        |                     |
|------------------------|---------------------|
| (1) Very much improved | (5) Minimally worse |
| (2) Much improved      | (6) Much worse      |
| (3) Minimally improved | (7) Very much worse |
| (4) No change          |                     |

### **Low Back Pain Classifier (LBPC)**

The Low Back Pain Classifier (LBPC) is a questionnaire which is available as part of the ViMove software. It can be completed electronically by patients or clinicians. The results are delivered as part of a Low Back Live Assessment Report.

The LBPC was originally developed by Dr. Andrew Ronchi and extended/modified by Rob Laird. It was developed to assist clinicians gain a better understanding of the type of movement dysfunction affecting their patients. The questions direct clinicians towards lumbar flexion or extension biased aggravating activities. Questions 1-3 are about flexion aggravating activities and questions 4-6 relate to extension easing activities. Questions 7-9 are about extension aggravating activities whilst the final 3 questions (10-12) are about flexion easing activities. There are now additional questions quantifying walking versus sitting aggravation. These questions serve two purposes: (i) measure walking and sitting with much greater precision than a RMDQ or ODI and (ii) to flag if an extension activity (walking) is better or worse than a flexion (maybe flexion but could be extension or loading problem in an upright sitting posture) activity.

The questionnaire has not been formally validated.

## **9: ANTICIPATED BENEFITS AND RISKS**

### **9.1 Potential Benefits**

We cannot guarantee that there will be any benefits from this research. However, possible benefits may include:

#### **1. Personal benefit:**

The ViMove in-clinic and monitoring (out-of-clinic) assessment data will be provided to the treating clinician after the baseline and follow-up sessions. Practitioners will receive a report detailing the participant's movements during the assessment periods, and highlighting any abnormal movement patterns. The clinician may use this information to help educate the participant on healthier movement patterns and postures.



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ThermaCare HeatWraps may be beneficial due to it being a heat therapy, and the normally associated effects of such therapies.

2. Assisting in the understanding of assessment data:

This study will add to our knowledge of movement and activity in people with low back pain, and specifically how different factors related to back pain are influenced by each other.

3. This study will further our understanding of the roles of both of self-reported functional questionnaires, ViMove data, and ThermaCare in the management and prevention of Low Back Pain.

## 9.2 Potential Risks

Possible risks, side effects, and discomforts include:

Risk	Likelihood	Consequences
ViMove not registering body movements	Low	Device will warn the health care professional (HCP) and subject that it can no longer provide assessment. If this occurs during a monitoring session you need to inform your HCP immediately.
Possible irritation of the skin from wearing ViMove	Low	Low Skin Itching and/or discomfort for up to 8 hours.
ThermaCare related issues	Low	Skin reactions to ThermaCare. This may include itching. Subjects may also be sensitive to heat.

ViMove has undergone rigorous verification, validation, user acceptance and post market testing and is not expected to malfunction. However, anyone participating in this study who has concerns about the safety or other functioning of ViMove should report them immediately to the investigative team.

### 9.2.1 Risk Minimization

Ensuring the safety of participants is of upmost importance. As such, numerous protocols and procedures will be in place to minimize the risk of harm.

- Strict adherence to the eligibility criteria is the foremost step in mitigating any potential harm.
- Participants are also permitted to withdraw consent for any reason at any point in the trial.
- Protocol for recording, reporting and follow-up of any adverse effects.
- Selection of qualified investigators and site personnel.
- Stringent training of investigative staff, regarding the use of questionnaires and devices.
  - This includes training of ViMove fitment and assessment.
- ThermaCare usage has a risk of prolonged skin redness or burns for some people. Products will be applied and used as directed.

## 10: SAFETY CONSIDERATIONS

An Adverse Event (AE) is any undesirable clinical occurrence in a Subject whether or not it is related to ThermaCare or ViMove. This includes a clinical sign, symptom, condition, and/or an observation of an unintended therapeutic effect.

An Adverse Device Event is a clinical sign, symptom or condition that is caused by the presence of the device or the performance of the device system.

A Serious Adverse Event (SAE) is an occurrence of: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, or a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions.

### 10.1 Documentation and Reporting of Adverse Events

All participants will be evaluated and monitored for AEs from recruitment. Once onset of an AE has been determined, evaluation will continue until its resolution is observed, or until the investigator determines that the subject's condition is stable. The investigator will take appropriate and necessary therapeutic measures required for the resolution of the AD. Any medication necessary for the treatment of an adverse event must be recorded on the concomitant medication case report form.

All AEs, regardless of severity, will be recorded in the source documents and CRFs using standard medical terminology. Colloquialisms and/or abbreviations should not be used. Only one medical concept, preferably a diagnosis rather than individual symptoms, should be recorded as the AE.

If more than one distinct adverse event occurs, each event should be recorded separately. However, if a diagnosis (i.e., disease or syndrome) is known at the time of reporting, it should be recorded on the CRF rather than recording individual signs and symptoms (e.g. record congestive heart failure rather than dyspnea, rales and cyanosis). However, if a group of signs and/or symptoms cannot be medically characterized as a single diagnosis or syndrome at the time of reporting, each individual event should be recorded as a separate AE. A diagnosis that is subsequently established should be reported as follow-up information. However, signs and symptoms that are considered unrelated to an encountered syndrome or disease should be recorded as individual AEs (e.g. if congestive heart failure and severe headache are observed at the same time, each event should be recorded as an individual AE).

Conditions or diseases that are chronic but stable should not be recorded on AE pages of the CRF but should be recorded on the medical history. Changes in a chronic condition or disease that are consistent with natural disease progression do not need to be recorded as adverse events and should not be recorded on the AE pages of the CRF.

Adverse events occurring secondary to other events (e.g. sequelae) should be identified by the primary cause. A "primary" event, if clearly identifiable, should represent the most accurate clinical term to record as the AE event term. For example: Orthostatic hypotension, fainting and fall to floor, head trauma, neck pain. The primary event is orthostatic hypotension and the sequelae are head trauma and neck pain.

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AE grading and severity are as follows:

<b>Grade 1</b>	<b>MILD</b>	Transient discomfort; no medical intervention/therapy required and does not interfere with daily activities.
<b>Grade 2</b>	<b>MODERATE</b>	Low level of discomfort or concern with mild to moderate limitation in daily activities; some assistance may be needed; minimal or no medical intervention/therapy required.
<b>Grade 3</b>	<b>SEVERE</b>	<p>Extreme discomfort and limitation in daily activities; significant assistance required; significant medical intervention/therapy required.</p> <p>Note: There is a distinction between the severity and the seriousness of an adverse event.</p> <p>Severity is a measurement of intensity; thus, a severe reaction is not necessarily a serious adverse event (SAE). For example, a headache may be severe in intensity, but would not be serious unless it met one of the criteria for serious adverse events.</p>
<b>Grade 4</b>	<b>POTENTIALLY LIFE-THREATENING OR DISABLING</b>	AE that is potentially life-threatening or may lead to a permanent disability.
<b>Grade 5</b>	<b>FATAL</b>	AE that leads to death.

The relationship of an AE following the use of the devices (ThermaCare or ViMove) is classified as follows:

<b>UNRELATED</b>	<p>Evidence indicates no plausible direct relationship to the devices such that:</p> <ul style="list-style-type: none"> <li>• A clinically plausible temporal sequence is inconsistent with the onset of the AE and device administration, and/or</li> <li>• A causal relationship is considered biologically implausible</li> <li>• The AE can be attributed to concurrent/underlying illness, other drugs or procedures.</li> </ul>
<b>POSSIBLY RELATED</b>	<p>Evidence indicates a possible relationship to the devices such that:</p> <ol style="list-style-type: none"> <li>1. The event occurs within a reasonable period of time relative to the treatment that makes a causal relationship possible, but plausible explanations may also be provided by other causes such as other drugs, products, chemicals, underlying disease, environment, etc.</li> <li>2. The event is possibly related to either of the devices.</li> </ol>

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<b>RELATED</b>	Evidence indicates a reasonable temporal sequence of the event with device administration exists or that the association of the event with device administration is unknown and the event is not reasonably supported by other conditions such that: <ol style="list-style-type: none"><li>1. There is a clinically plausible time sequence between onset of the AE and device administration, and/or</li><li>2. There is a biologically plausible mechanism for the device causing or contributing to the AE, and</li><li>3. The AE cannot be reasonably attributed to concurrent/underlying illness, other drugs or procedures.</li></ol>
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The outcome of the AE is classified as one of the following:

<b>RESOLVED</b>	All symptoms associated with the AE have subsided.
<b>ONGOING</b>	Subject continues to experience some or all of the symptoms associated with the AE.
<b>FATAL</b>	Subject died as a result of the AE.

## 10.2 Documentation and Reporting of Serious Adverse Events

SAEs will be documented and reported in accordance with ICH Good Clinical Practice (GCP) guidelines [32]. SAE reporting procedures for investigator initiated studies are as follows:

The Investigator must report all SAEs to the Human Research Ethics Committee Bellberry Ltd firstly by telephone and then via fax on an SAE form within 24 hours of learning of the event. Any serious event that occurs at any time over the duration of the study, regardless of whether or not the subject has undergone any study-related procedures must be reported to Bellberry Ltd.

Information on SAEs will be recorded on an SAE form. Blank copies are included in the study Investigator's File.

SAE forms should be directed to:

Bellberry Ltd  
129 Glen Osmond Road, Eastwood  
South Australia 5063  
Telephone: 08 8361 3222  
Fax: 08 8361 3322  
Email: bellberry@bellberry.com.au

The Investigator should follow up the event until resolution or stabilization of the condition. Follow-up reports (as many as required) should be completed and emailed following the same procedure above.

A final report is required in any case once the condition is resolved or stabilized and no more information about the event is expected. The final report should be completed and faxed following the same procedures above.

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For deaths that occur following a Subject's enrolment into the study a Record of Death CRF as well as an autopsy report (when/if available) must be submitted to Bellberry Ltd. The Investigator must keep a copy of all documentation related to the event in the site's study files.

By participating in this study the Investigator agrees to submit reports of serious adverse events according to the timeline and method outlined in the protocol. In addition, the Investigator agrees to submit annual reports to his/her IRB/IEC as appropriate. The Investigator also agrees to provide Bellberry Ltd with a summary report within 30 days and full report within 60 days of completion of the Investigator's participation in the study.

### **10.3 Device-Related Observations (DROs)**

A device-related observation (DRO) is defined as any malfunction, failure to operate as defined by the Instructions for Use, technical problems, or operator error associated with use of the device. For each DRO, Investigators are to report the following to Bellberry Ltd.:

- Date and time of DRO;
- Description of DRO;
- Serial number of the device with a complication;
- Clinical consequences, if any (to be reported on an AE form);
- Whether the device was replaced, and the serial number of the replacement;
- Whether or not the procedure could be completed.

## **11: STATISTICAL CONSIDERATIONS AND DATA ANALYSIS**

### **11.1 Sample Size and Statistical Power**

The purpose of this study is feasibility testing to provide insights to develop a RCT. As such, a sample size of N=40, with 20 participants in each of the 2 population samples has been chosen. As we expect an attrition rate of 20%, we will initially recruit 50 subjects.

### **11.2 Statistical Methods**

An initial descriptive analysis will be completed on the baseline measures of movement to determine mean scores, ranges and standard deviations of each sample group. This analysis will be repeated at later time points. Wilcoxon Signed Ranked Tests will be completed to determine if participant movement significantly changes following an intervention: One each for Baseline and Intervention. A repeated measures ANOVA will then be completed on all post trial data for the 2 separate groups to determine movement changes in the post-trial period.

Bivariate correlational analyses through the Pearson product-moment coefficient, will be undertaken to determine if there is a relationship between movement and "pain on movement" using data collected at each time point. This potential relationship will be mapped to assess any temporal influences.

Similarly, correlational analyses will be conducted to determine if there is a relationship between daily activity and ODI scores, using data collected at each of the four total time points. This potential relationship will also be mapped over time to determine if there are any temporal effects following initial treatment.

All findings with a p-value < 0.05 will be deemed significant.

## **12: ETHICS CONSIDERATIONS**

The Investigator agrees that the study will be conducted in full accordance with the protocol, the principles of the ICH Guideline on GCP [32], the current revised principles of the Declaration of Helsinki [33], the National Statement on Ethical Conduct in Human Research [34], and applicable local laws and regulations of the country in which the research is conducted which provide the greatest protection to the individual.

It is the Investigator's responsibility to obtain written informed consent in compliance with ICH GCP Guidelines (Guidelines for Good Clinical Research Practice) from each subject prior to the Subject's entrance into the study or the performance of any unusual, invasive, or non-routine procedure that involves risk to the Subject. The Investigator must also explain to the Subject that participation is voluntary and that they can withdraw from the study at any time without a reason and without having to fear any loss in his/her medical care.

Prior to any study-related screening procedures being performed, the consent form will be reviewed and signed and dated by the Subject or legally authorized representatives and the person who administered the informed consent.

Subjects will have sufficient time and opportunity to clarify and resolve questions before the Subject starts the study. Furthermore, the Subject will be handed a Subject Information Sheet containing all the important information in writing. A copy of the consent form will be given to the Subject or legally authorized representatives and the original will be placed in the Investigator Study File. An entry must also be made in the Subject's source documents to confirm that informed consent was obtained prior to any study-related procedures and that the Subject received a signed copy.

The Investigator will submit the consent to the appropriate IRB/IEC for review and approval prior to the start of the study in this case Bellberry Ltd needs to approve the informed consent. If the consent form is revised during the course of the study, all active participating subjects must sign the revised form.

### **12.1 Quality Assurance**

According to the ICH guidelines on GCP, the Investigator is responsible for implementing and maintaining quality assurance (QA) and quality control systems with written Standard Operating Procedures (SOPs). This is to ensure that the trial is conducted and data is generated, recorded and reported in compliance with the protocol, GCP and the applicable regulatory requirements.

Data recorded on the Subject CRFs will be subjected to a quality control review according to the investigating site's SOPs. All source document reviews will be performed against entries on the CRF and quality assurance checks will be performed to ensure that the Investigator is complying with the protocol and regulations.

All data entered in the database will be verified and cleaned by the Data Management Team. Any discrepancies will be reviewed against the CRF hard copy and corrected. After completion of the entry process, computer logic checks will be run to check for such items as inconsistent study dates and outlying laboratory values. Any necessary corrections will be made to the database and documented via addenda or audit trails.

On one or more occasions the study site may be audited by a third party or regulatory agency on behalf of the investigating site.

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The Regulatory Authority or its designee, has the obligation to follow the study closely. The investigator may delegate or appoint a third party to monitor the study to ensure compliance with Good Clinical Practice (GCP). In doing so, the monitor will visit the Investigator and study facilities at periodic intervals, in addition to maintaining necessary telephone and written contact, as appropriate. The monitor will maintain a working knowledge of the study through observation, review of study records and source documentation, and discussion of the conduct of the study with the Investigator and staff.

All aspects of the study will be carefully monitored by its designee for adherence to the protocol and for compliance with applicable government regulations, current good clinical practice, and current standard operating procedures.

## **12.2 Confidentiality of Study Data**

The aims, contents, and results of this study are confidential and are not to be transmitted to any third party in any form or fashion without prior approval by the Principal Investigator and the study subject.

The Investigator should keep a separate log (Subject Master List) of the assigned Subject numbers and corresponding names, addresses, telephone number and site number (if applicable).

Permission for direct access to a Subject's data will be sought in writing by the Investigator and from the Subject as part of the informed consent procedure. This gives permission to examine, analyze, verify, and reproduce any records and reports that are important to the evaluation of the study. Any party (e.g. domestic and foreign regulatory authorities, monitors and auditors) with direct access must take all reasonable precautions within the constraints of the applicable regulatory requirements to maintain the confidentiality of the subjects' identities and the Hospital Authority's proprietary information.

It is the study monitor's responsibility to verify that each Subject has consented, in writing, to direct access to their information.

### **12.2.1 Case Report Forms**

CRFs are the sole property of the Investigator and should not be made available in any form to any third parties, except for approved representatives of appropriate health, regulatory, or auditing authorities.

As part of the responsibilities assumed by participating in the study, the Investigator agrees to maintain adequate case histories for the subjects treated under this protocol. The Investigator agrees to maintain accurate CRFs and source documentation as part of the case histories.

All CRFs should be completed legibly in black ink or typed. Case report forms should never be completed in pencil.

All requested information should be entered in the CRFs. If an item is not available or is not applicable, this fact should be so indicated. Blank spaces should not be present unless otherwise directed. A correction should be made by striking through the incorrect entry with a single line and by entering the correct information adjacent to it. The correction must be initialed and dated by the person making the correction.

The Investigator must review, sign, and date each completed CRF in a timely manner.

The Investigator will allow regulatory bodies to have direct access to the source documents to verify the data reported in the CRF.

### 12.2.2 Source Documents

Source documents are the originals of any documents used by the Investigator or institution that allow verification of the existence of the Subject and substantiate the integrity of the data collected during the trial. Source documents may include hospital records, clinical and office charts, laboratory data/information, evaluation checklists, pharmacy dispensing and other records, recorded data from automated instruments, microfiches, photographic negatives, microfilm or magnetic media and/or x-rays. Source documents should be available to support all the data recorded in the CRF.

## 13: STUDY OUTCOMES AND SIGNIFICANCE

### 13.1 Primary Endpoints

1. Collection of movement and erector spinae muscle activity data in all participants.
2. Change over time in range of motion (ROM) in any one plane of movement compared to pre-intervention ROM.
3. A change over time in Flexion-Relaxation response in those subjects where abnormal EMG activity in flexion during baseline assessment is detected.
4. A change over time in maximum pain during movement score (1-10 as recorded during the in-clinic ViMove assessment) for any one plane of movement.

### 13.2 Secondary Endpoints

1. Capture changes in low back pain levels as assessed via a Numeric Rating Scale (NRS-Pain).
2. Capture self-reported changes in functional status pre- and post- ThermaCare application as measured by the Oswestry Disability Index (ODI) and Roland Morris Disability Questionnaire (RMDQ) if subjects scored >3 on the NRS.
3. Capture impression of change from subjects post ThermaCare application using the Patient Global Impression of Change Scale (PGIC).
4. Observe changes in activity levels as collected by ViMove monitoring.
5. Correlation of Low Back Pain Classifier (LBPC) Score to ViMove Scores for flexion and extension.

### 13.3 Significance

This intervention study will provide information regarding changes in movement, flexibility, and pain following the use of ThermaCare HeatWraps in subjects who either suffer from low back pain, or are moderately or highly active. Moreover, it will assess any potential relationships between changes in pain, and responses to questionnaires as well as objectively measurable changes using ViMove systems.



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