The effect of diathermy therapy on isolated lumbar extension (ILEX) training

Study Type:	Other Clinical Trial according to ClinO, Chapter 4
Risk Categorisation:	Risk category A according to ClinO, Art. 61
Study Registration:	1. Swiss National Clinical Trial Portal 2. NCT06852872
Sponsor:	Thim van der Laan jr Thim van der Laan AG Weststrasse 8 7302 Landquart +41 81 300 01 70
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Investigated Intervention:	6 weeks of training on an isolated back extensor (ILEX) training machine combined with a prior diathermy treatment.
Protocol ID	Req-2023-02308
Version and Date:	Version 04 (dated 19/03/2024)

PROTOCOL SIGNATURE FORM

Study Title	The effect of diathermy therapy on isolated lumbar extension (ILEX) training
Study ID	Req-2023-02308

The Sponsor has approved the protocol version 04 (dated 09/03/2024) and confirm hereby to conduct the study according to the protocol, current version of the World Medical Association Declaration of Helsinki, and ICH-GCP guidelines as well as the local legally applicable requirements.

Sponsor:

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Date: _____ Signature: _____

Principal Investigator:

Name: *Dr. Ron Clijsen*

Date: _____ Signature: _____

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GLOSSARY OF ABBREVATIONS

AE	*Adverse Event*
ASR	*Annual Safety Repot*
BASEC	*Business Administration System for Ethical Committees*
BL	*Baseline*
CR-10	*Category-Ratio-Scale*
CRF	*Case Report Form*
CTCAE	*Common Terminology Criteria for Adverse Events*
FADP	*Federal Act on Data Protection (in German: DSG, in French: LPD, in Italian: LPD)*
eCRF	*electronic Case Report Form*
FOPH	*Federal Office of Public Health*
F/U1	*Follow-up 1*
F/U2	*Follow-up 2*
GCP	*Good Clinical Practice*
HSPs	*Heat shock proteins*
HRA	*Human Research Act (in German: HFG, in French: LRH, in Italian: LRUm)*
ICH	*International Conference on Harmonisation*
ILEX	*Isolated lumbar extension*
LBP	*Low back pain*
MF	*Momentary failure*
ClinO	*Ordinance on Clinical Trials in Human Research (in German: KlinV, in French: OClin, in Italian: OSRUm)*
RCT	*Randomized controlled trial*
RESLab	*Rehabilitation and Exercise Science Laboratory*
RPE-D	*Rating of perceived discomfort*
RPE-E	*Rating of perceived effort*
ROM	*Range of motion*
SAE	*Serious Adverse Event*
YLD	*Years lived with disability*

1 STUDY SYNOPSIS

Sponsor / Sponsor-Investigator	Name(s) and contact details of Sponsor / Sponsor-Investigator
Study Title	Full protocol title
Short Title / Study ID	Abbreviated protocol title or, if applicable, study ID, e.g. study number
Protocol Version and Date	Version x (dated DD/MM/YYYY)
Study Registration	Name of study registry, registration number (if not yet registered, name the intended registry)
Study Category and Rationale	Risk category and rationale
Background and Rationale	Background of the study and rationale
Risk / Benefit Assessment	Risk / benefit assessment
Objective(s)	Primary objective(s) and, if applicable, secondary including safety objective(s)
Endpoint(s)	Primary endpoint(s) and, if applicable, secondary including safety endpoint(s)
Study Design	Design attributes (e.g. confirmatory, non-randomised / randomised, open / single-blinded / one-arm / two-arm, cross-over/controlled)
Statistical Considerations	Description of the main elements of the statistical methodology to be used in the study including an explanation to sample size
Inclusion- / Exclusion Criteria	key inclusion and exclusion criteria and, if applicable, rationale for including vulnerable participants
Number of Participants with Rationale	Number of participants in the entire study, provide the total number as well as the number for each treatment group. Briefly explain the rationale for the number of participants.
Study Intervention	Description of the study intervention
Control Intervention	If applicable, description of the control group
Study procedures	Description of the overall study procedures
Study Duration and Schedule	Estimated duration for the main investigational plan, i.e. from start of screening of first participant to last participant last visit and finishing the study Planned MM/YYYY of First-Participant-In Planned MM/YYYY of Last-Participant-Out
Investigator(s)	Name(s) and contact details of Investigator(s)
Study Center(s)	Name(s) and address of Study Center(s) If multicenter study, number of centers to be involved If multinational study, countries to be involved
Data privacy	Explain how the privacy of data is guaranteed. Mention coding and confidentiality while handling data and if applicable biological material.
Ethical consideration	Explain the scientific value of the study, justify the methodology give a statement to the risks and the benefit. Explain if you include vulnerable populations.
GCP Statement	This study will be conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP, the HRA as well as other locally relevant legal and regulatory requirements. A clinical trial covered by ClinO Chapter 4 may be conducted in accordance with other rules than ICH-GCP guidelines, provided that such rules are recognised in the specialty in question and the protection of participants and data quality and security are guaranteed (ClinO Art. 5, Abs 2). If the clinical trial is not conducted according to ICH-GCP guidelines, the paragraph above must be adapted accordingly.

2 BACKGROUND AND RATIONALE

Low back pain (LBP) constitutes a global public health concern, affecting an estimated 619 million individuals across all age groups (Collaborators, 2023; Hartvigsen et al., 2018; Hoy et al., 2012). Projections, based on trends in population growth and aging, suggest that by the year 2050, there will be a further increase of 36.4%, resulting in a total of 843 million individuals worldwide affected by LBP (Collaborators, 2023). In 2020, low back pain accounted for a 7.7% of all years lived with disability (YLD) globally, establishing it as the primary cause of the world's disability burden, accompanied with substantial associated costs of care (Collaborators, 2023). Approximately one third of individuals experience a recurrence of low back pain within one year after recovering from a prior episode (da Silva et al., 2017). For most individuals presenting with low back pain, to pinpointing a specific cause proves challenging. Consequently, these individuals are classified as having non-specific low back pain (Maher et al., 2017). While there are numerous potential causes of LBP, it has been suggested that these often relate to weakness of the muscles responsible for extending the lumbar spine (lumbar erector spinae and multifidus) (Steele et al., 2014).

Isolated lumbar extension (ILEX) training utilizing resistance machines has demonstrated superior effectiveness in strengthening the lumbar extensors compared to alternative methods such as bench and roman chair trunks extensions, free weight exercises, or floor and stability ball exercises (Steele et al., 2015b). Furthermore, ILEX resistance training has shown efficacy in reducing pain and improving disability associated with LBP (Steele et al., 2015a). What sets ILEX resistance machines apart is their unique ability to isolate the lumbar muscles to be primarily responsible for the work performed by stabilizing the pelvis through specially designed restraints. Previous studies have documented the necessity of pelvic stabilization in order to optimal increases in low back strength by eliminating the contribution of gluteal and hamstring muscles (Graves et al., 1994; Smith et al., 2011). Moreover, it has been established that a semi-sitting position is the most effective to reduce the activation of the hip extensor muscle (da Silva et al., 2009).

Exercise training is a powerful stimulus for physiological adaptations and a crucial aspect of maintaining good health (Egan & Zierath, 2013). Resistance exercises are particularly effective in enhancing skeletal muscle development, growth, and function (Egan & Zierath, 2013). However, factors such as limited physical capabilities and poor health status can prevent individuals from meeting the recommended level of exercise (Fennel et al., 2022). Recently, there has been an increasing interest in the potential of heat as adaptive aid to promote hypertrophy in resistance training. There is some evidence that heat stress alone (Ihsan et al., 2020; Rodrigues et al., 2020) and in combination with resistance exercise (Goto et al., 2007; Nakamura et al., 2019; Yoon et al., 2017) can increase hypertrophy and associated muscle strength. Heat shock proteins (HSPs), expressed in response to stimuli including heat stress and exercise, play a critical role in protecting from muscular atrophy or confer hypertrophic benefits (Fennel et al., 2022). The exact mechanisms by which HSPs might associate with or influence relevant signalling responses in skeletal muscle are not fully elucidated (Fennel et al., 2022). It has been known that expression of HSPs in skeletal muscle increases when the muscle temperature is increased over 40°C (Oishi et al. 2002 (Oishi et al., 2002; Selsby & Dodd, 2005). To date, four studies have investigated the impact of repeated heat stress in direct combination with resistance training over a period of several weeks (Goto et al., 2007; Nakamura et al., 2019; Stadnyk et al., 2018; Yoon et al., 2017). Three studies found a beneficial effect (Goto et al., 2007; Nakamura et al., 2019; Yoon et al., 2017), whilst one study reported no evident advantages (Stadnyk et al., 2018). Training protocols, involved muscle groups, as well as type and duration of heat applications varied in the four studies. Nakamura and colleagues concluded that incorporating heat stress prior to resistance training, rather than afterwards, may be crucial for enhancing muscle mass and increasing strength (Nakamura et al., 2019). To the best of our knowledge, no studies have been published to investigate the effect of heat stress and resistance training on the back extensor muscle.

Different methods can be used to heat the whole body or specific body areas. Shortwave or microwave electromagnetic diathermy is a heating modality that uses a radiofrequency electromagnetic field to increase the temperature in deeper structures, such as muscles, without an excessive increase of skin temperature to uncomfortable levels (Guy et al., 1974). Microwave diathermy has shown to increase muscle temperature by ~3-7°C depending on the time of application and power of the instrument (Castellani et al., 2016; Draper et al., 1999; Nosaka et al., 2007; Nosaka et al., 2004).

The aim of this study is to investigate strength gains of the back extensor after 6 weeks of resistance training on an ILEX machine in combination with microwave diathermy.

3 STUDY OBJECTIVES AND DESIGN

3.1 Hypothesis and primary objective

The main aim of this study is to investigate the effect of back extensor strength after 6 weeks of ILEX training and diathermy therapy.

- H_0: 6 weeks of resistance training on the ILEX machine does not improve lumbar extensor muscle strength.
- H_1: 6 weeks of resistance training on the ILEX machine improves the strength of the lumbar extensor muscle.
- H_0: There is no difference in the improvement in lumbar extensor muscle strength between those who receive a microwave diathermy treatment before each resistance training session and those in the sham group.
- H_1: Individuals who receive a microwave diathermy treatment prior to each resistance training session improve their lumbar extensor muscle strength more than those in the sham group.

Secondary objectives are to examine the development of M. erector spinae thickness, isometric back extension endurance, and lumbar extensor flexibility after 6 weeks of resistance training and diathermy therapy.

- H_0: 6 weeks of resistance training on the ILEX machine does not enhance the thickness of the M. erector spinae.
- H_1: 6 weeks of resistance training on the ILEX machine enhances the thickness of the M. erector spinae.
- H_0: There is no difference in the increase of the thickness of the M. erector spinae between those who receive a microwave diathermy treatment before each resistance training session and those in the sham group.
- H_1: Individuals who receive a microwave diathermy treatment prior to each resistance training session enhance the thickness of the M. erector spinae more than those in the sham group.
- H_0: 6 weeks of resistance training on the ILEX machine does not improve isometric back extension strength endurance.

- H_1: 6 weeks of resistance training on the ILEX machine improves isometric back extension strength endurance.

- H_0: There is no difference in the improvement of the isometric back extension strength endurance between those who receive a microwave diathermy treatment before each resistance training session and those in the sham group.

- H_1: Individuals who receive a microwave diathermy treatment prior to each resistance training session improve the isometric back extension strength endurance more than those in the sham group.

- H_0: 6 weeks of resistance training on the ILEX machine does not increase lumbar ROM.

- H_1: 6 weeks of resistance training on the ILEX machine increases lumbar ROM.

- H_0: There is no difference in the increase of the lumbar ROM between those who receive a microwave diathermy treatment before each resistance training session and those in the sham group.

- H_1: Individuals who receive a microwave diathermy treatment prior to each resistance training session increase of the lumbar ROM more than those in the sham group.

3.2 Primary and secondary endpoints

Primary endpoint

Maximal isometric force of the back extensor

The maximum voluntary isometric contraction (in Newtons) of the back extensor is measured with the CE-certified ILEX machine Myosom (Heftec GmbH, Oberurnen, Switzerland) before, after 6 sessions and after 12 sessions of resistance training and diathermy therapy to examine strength growth. ILEX resistance machines are designed to primarily train the lumbar muscles by stabilizing the pelvis through specially designed restraints (Steele et al., 2015b). Participants are seated in the machine in a semi-sitting position with the feet placed on a footrest and the thoracal back leaned against a squared restrained. The movement arm is locked causing a slight flexion in the lumbar back and restrain belts are secured around the pelvis and shoulders. The participants are advised to extend their back slowly and continuously against the upper-back pad for 2 to 3 seconds. Peak torque is registered electronically.

Secondary endpoints

Isometric back extension strength endurance

Isometric back extension endurance (in seconds) is assessed using the Biering-Sørensen test before, after 6 sessions and after 12 sessions of resistance training and diathermy therapy to confirm the strength growth in the back extensor. The Biering-Sørensen test is the most widely used test in published studies evaluating the isometric endurance of trunk extensor muscles. It is a rapid, simple, and reproducible test (Demoulin et al., 2006). The participant is lying prone on an examination table with the upper border of the iliac crests in line with the edge of the table. The lower body is secured to the table by three straps around the pelvis, knees, and ankles. With the arms folded across the chest, the participant is asked to hold the upper body isometrically in a horizontal position. It is measured how many seconds the participant can keep the unsupported upper body touching a horizontal object (Biering-Sørensen, 1984).

Thickness of M. erector spinae

The thickness of the M. erector spinae (in millimeter) is measured using the ultrasound system Mylab2 (Esaote, Maastricht, Netherlands) in B-mode and the software Horos™ (Horos Project,

Annapolis, MD, USA) before, after 6 sessions and 12 sessions of resistance training to confirm the strength growth in the back extensor. Muscle strength is associated with the cross-sectional area of the muscles (Jones et al., 2008) and measuring the thickness of the M. erectors spinae with ultrasound has been shown to be a safe and easy method for estimating back muscle strength (Fujiwara et al., 2017). The participant is lying prone on the examination table. The probe head is coated with coupling gel and applied perpendicular to the muscle on the right side without pressure to not compress the dermal surface. The thickness of the longissimus is defined as the distance between the midpoints of fascia posterior and the outermost point of transversus process of the L3 vertebra (Fujiwara et al., 2017).

Lumbar flexibility

There is evidence that strength training is effective in improving the ROM (Afonso et al., 2021). Moreover, a diminished ROM is associated with muscle weakness. The lumbar flexibility is assessed with the help of a goniometer built into the ILEX machine and the sit-and-reach test before, after 6 sessions and 12 sessions of resistance training to control its association with the muscle strength growth. Participants are seated in the ILEX machine in a semi-sitting position with the feet placed on a footrest and the thoracal back leaned against a squared restrained. Restrain belts are secured around the pelvis and shoulders. The movement arm is deblocked and the participants are advised to move dynamically backwards and forwards as far as possible. Three repetitions are done, and peak flexion and extension are registered electronically. Additionally, the combined flexibility of the M. erector spinae and hamstrings is measured using the sit-and-reach test. The sit-and-reach test is probably the most widely used lineal measure of flexibility and it is a simple, easy to administer test with requiring minimal skills. The participant is seated in front of the test box, keeping the knees fully extended and the feet dorsiflexed against the foot-support. The participant is moving actively, slowly forward, bringing the body to the pain-free limit. The participant's hands move the block along the scale until the movement is terminated because the participant can go no farther. The final position is held with an isometric contraction for 2 seconds, and the distance is read on the scale. The test is repeated twice and an average score is taken for further analysis (Holt et al., 1999).

Skin temperature

Radiofrequency-based therapy at 448kHz in the capacity mode increases skin temperature by around 3°C (Kumaran & Watson, 2015). Skin temperature in the area of the M. erector spinae is measured twice, immediately after the first and last diathermy therapy, using infrared thermal imaging (FLIR A615 series, Emitec Industrial, Rotkreuz, Switzerland) and data analysis software (FLIR ResearchIR Max). Participants are placed on an examination table to receive the diathermy treatment. The camera is installed on top of the examination table to take a picture of the right side of the erector spinae immediately after the treatment without the participant moving.

Rating of perceived effort (RPE-E)

Training to momentary failure (MF) is considered to be optimal for improving strength. In submaximal efforts, the dose-response relationship for adaptations is not fully clear yet (Steele et al., 2016). The rating of perceived effort (RPE-E) provides a valid and easily accessible measure of exercise intensity in resistance training (Lea et al., 2022). We use the Borg's Category-Ratio-Scale (CR-10) for strength training (Buckley & Borg, 2011) which is based on the original 15-grade Borg's scale for ratings of perceived exertion (Borg, 1982). Immediately after completion of every single of the 12 training sessions on the back extensor machine, the examiner asks the participant "How hard do you think you're working?". The participant reports her/his perceived effort verbally with a number from 0 (no exertion at all) to 10 (maximal effort) orientating on a scale visually.

Rating of perceived discomfort (RPE-D)

Particularly in resistance training it is important to differentiate between the perception of effort (RPE-E) and discomfort (RPE-D) (Steele et al., 2016). Discomfort is the physiological and

unpleasant sensations associated with exercise. Increasing number of repetitions and longer time under muscular tension leads to higher discomfort. Therefore, higher discomfort is experienced in low load than in high load training (Fisher et al., 2018). We use a Category-Ratio-Scale (CR-10) for the RPE-D (Steele et al., 2016). Immediately after the completion of each of the 12 training sessions on the ILEX machine, the participant is asked to report her/his perceived discomfort verbally with a number from 0 (no discomfort) to 10 (maximal discomfort) orientating on a scale visually.

Rating of thermal sensation
Immediately after each of the 12 diathermy treatments, the participant is asked to rate the thermal sensation in the area of the back extensor according to the ISO 10551. The participant rates thermal sensation ("How does this feel like?") using a 9-point Likert scale from 4 (very hot) to -4 (very cold) (Fabbri, 2015).

Rating of perceived comfort
After completion of the rating of thermal sensation, participants are asked to rate the comfort felt during the diathermy treatment on a 5-point scale ranging from 0 "angenehm" to 4 "äusserst unangenehm" (1 "etwas unangenehm", 2"unangenehm", 3 "sehr unangenehm") (Zhang et al., 2004).

3.3 Study design

This is a monocentric clinical trial with minimal risks and burden of the risk class A (KlinV, Art. 20). A block randomization with covariates (i.e. sex) is used. The preheating is done as a single blinded randomized controlled trial (RCT) with the sham group receiving a 10-minute diathermy treatment with the Tecar device turned off and not sending radiofrequency before each exercise session. The intervention group undergoes a 10-minute treatment with the Tecar device to induce 448kHz capacitive monopolar radiofrequency and facilitate warming up of deep tissues. In order to be able to carry out a single-blind situation as far as possible, the test subjects are not told that the therapy causes heat of the deep tissue and that this is the factor being investigated. Instead, we speak of high-frequency Tecar therapy and its known use to promote tissue healing processes.

3.4. Study intervention

We recruit a cohort of 14 healthy persons, both men and women, who have not trained their back extensors in isolation in the last 12 months. During a 6-week program consisting of a total of 12 sessions, the participants receive a diathermy treatment with the CE-certified device Tecar (T-Plus, Wintecare SA, Chiasso, Switzerland) and carry out a back extensor resistance training on the CE-certified ILEX machine Myosom (Heftec GmbH, Oberurnen, Switzerland).

Participants are randomly assigned to either the sham group, which receive a 10-minute treatment with the diathermy device turned off and not sending radiofrequency before each exercise session, or the intervention group, which undergo a 10-minute diathermy treatment to induce 448kHz capacitive monopolar radiofrequency and facilitate warming up of deep tissues. After all treatments participants are asked to rate their thermal sensation and comfort.

After the 10-minute diathermy treatment, the participants are seated in the ILEX machine in a semi-seated position with the feet placed on a footrest. The lumbar back is leaning against a round restraint that is free to rotate on its axis, the thoracal back against a squared restraint, hosting the load cells measuring torques produced by the left and right side separately. The machine incorporates a counterweighting procedure to counterbalance the effect of gravity acting on the upper body. Restraining belts are secured around the pelvis and around both shoulders. Over the anterior part of the upper thigh a restraint pad is positioned. All restraints

are tightened until a pressure but not pain occurs. These restraints prevent unwanted vertical movement of the pelvis or thighs.

Training will take place twice a week, beginning with a dynamic warm-up of the lumbar extensor for 120s, followed by three sets of resistance training lasting 120s, 120s, and 150s respectively, and concluding with a final set of dynamic recovery lasting 60s. 30-second recovery will be provided between every set. A low load will be used for the warm-up and recovery. The initial load is based on the maximum isometric force and subsequently increased until volitional fatigue. Repetitions will be executed by taking three seconds from complete flexion to complete extension, ensuring standardization at 20 repetitions per minute. A metronome with 40 beats per minute will provide audible feedback. The ILEX machine emits an audible signal upon completion of each phase of the repetition to guarantee a complete range of motion (ROM) is achieved. Subsequent to every training session, participants will be requested to provide their effort (RPE-E) and discomfort (RPE-D) values.

Baseline (BL) measurements are conducted before the initiation of training, and two follow-up measurements (F/U 1 and F/U 2) carried out after the sixth and twelfth session, with a minimum break of 48 hours after the last training session to ensure proper recovery and to prevent inaccuracies in muscle thickness measurement arising due to acute edema. At BL, participants need to give written informed consent and be familiarized with the ILEX machine and Category-Ratio-Scale (CR10) for the assessment of perceived effort and discomfort as well as a 9-point Likert scale for thermal sensation and 5-point scale for comfort. BL assessment include epidemiological data such as age, sex, height, and weight. Physical activity is assessed using the self-administered short German version of the International Physical Activity Questionnaire (IPAQ) with a “last 7 d recall” (IPAQ Research Committee, 2005) at BL, F/U1 and F/U2. At all three measurements (BL, F/U 1, F/U 2), the lumbar extensor musculature thickness (M. erector spinae), the maximum ROM, the maximum voluntary isometric contraction, the lower back flexibility, and the isometric back extension endurance are measured. Skin temperature is measured using an infrared thermal imaging (FLIR A615 series, Emitec Industrial, Rotkreuz, Switzerland) after the first and final diathermy treatment.

4 STUDY POPULATION AND STUDY PROCEDURES

4.1 Inclusion and exclusion criteria, justification of study population

Power analysis was conducted with G*power to determine participants numbers (n) calculating a treatment effect size of 0.46 from previous research with the comparable MedX ILEX device in healthy volunteers (Fisher et al., 2018). The priori sample size was calculated (α = 0.05; effect size = 0.46; test family = F test, and statistical test = analysis of variance (ANOVA) repeated measures, within-between interaction; number of groups = 2; number of measurements = 3; power = 0.8) and revealed n = 10 participants. 14 healthy volunteers will be recruited according to the following criteria:

Study inclusion criteria:

- Healthy (no acute musculoskeletal injuries or illness),
- Pain free,
- Sufficient understanding of the German language,
- Able to give informed consent as documented by signature,
- Between 18 and 50 years old

Study exclusion criteria:

- Pregnant (urine pregnancy test is given to participating woman) or lactating women,
- Medication,
- Previous surgery in the lumbar spine,
- Knee or hip disorders contraindicating the use of ILEX device,
- Currently experiencing LBP,
- History of LBP or lumbar spine pathologies or known deformities,
- Psychological or neuromuscular disorders, spinal pathologies or any other injuries or illness that would restrict normal movement,
- Previous (last 12 months) or current isolated training of the lumbar extensor.

This study will be conducted in healthy people. The risk of injury will be low in this population group.

4.2 Recruitment, screening and informed consent procedure

Participants will be recruited on the websites of the physiotherapy schools Thim van der Laan (www.physioschule.ch) and University of Applied Sciences of Southern Switzerland SUPSI (www.supsi-landquart.ch). An electronic advertisement will be activated on the screens in the building of the Thim van der Laan AG in Landquart. The advertisement texts are in line with the guidelines published by the Zurich Cantonal Ethics Committee.

During the initial contact, potential participants are informed about the procedure and risks of the study, as well as the conditions and the amount of compensation. A checklist is used as the basis for telephone contact. During the first telephone contact, a questionnaire will be completed by the investigator to assess suitability for participation in the study.

The investigators will explain to each participant the nature of the study, its purpose, the procedures involved, the expected duration, the potential risks and benefits and any discomfort it may entail. Each participant will be informed that the participation in the study is voluntary and that he or she may withdraw from the study at any time and that withdrawal of consent will not affect his or her subsequent medical assistance and treatment.

The participant will be informed that his or her medical records may be examined by authorised individuals other than their treating physician.

All participants for the study will be provided a participant information sheet and a consent form describing the study and providing sufficient information for participant to make an informed decision about their participation in the study. Enough time will be given to the participant to read the written informed consent at home, ask questions to the responsible examiner and decide whether to participate or not.

The formal consent of a participant, using the approved consent form, will be obtained before the participant is submitted to any study procedure.

The consent form will be signed and dated by the investigator or his designee at the same time as the participant sign. A copy of the signed informed consent will be given to the study participant. The consent form will be retained as part of the study records. The original signed informed consent form will be stored as a study document in a locked filing cabinet.

Upon successful completion of the training sessions and the 3 test days, the participants are receiving a remuneration of 200 Swiss Francs.

The advertisements, questionnaire, and checklist for the first contact can be found in the enclosure.

4.3 Study procedures

A table listing all study visits, relevant procedures, as well as all timelines, can be found in

appendix 1.

12 sessions of back extensor resistance training on the ILEX machine take place over a 6-week period (twice a week). Before each exercise, a diathermy treatment is taking place. Before, after 6 sessions and after completion of the 12 sessions, tests are conducted on separate days.

On intervention days, the participants enter the RES laboratory in Landquart wearing sports clothing. First, they lay on an examination table in a prone position receiving a treatment with the diathermy device for 10 minutes from a trained examiner. The intervention group is treated with the diathermy device inducing 448kHz capacitive monopolar radiofrequency, warming up the deep tissues. The sham group receives a massage with the diathermy device without radiofrequency. Directly after the first and last diathermy treatment, a picture will be taken with an infrared camera (FLIR A600 series, Emitec Industrial, Rotkreuz, Switzerland). Then, participants translocate to the ILEX machine and are seated according to their individual settings. The training session lasts 12 minutes. Participants begin the training session with a dynamic warm-up of the lumbar extensor for 120s, followed by three sets of resistance training lasting 120s, 120s, and 150s respectively, and concluding with a final set of dynamic recovery lasting 60s. Between each set, a 30-second recovery is provided. Repetitions will be executed by taking three seconds from complete flexion to complete extension, ensuring standardization at 20 repetitions per minute. A metronome with 40 beats per minute will provide audible feedback. The ILEX machine emits an audible signal upon completion of each phase of the repetition to guarantee a complete ROM is achieved. A low load is used for the warm-up and recovery. For the three training sets, the initial load is based on the maximal isometric force and subsequently increased until volitional fatigue. Immediately subsequent to each training session, participants will be requested to provide their effort (RPE-E) and discomfort (RPE-D) values. Immediately after the first and final diathermy treatment before dislocating to the ILEX machine, participants skin temperature is measured while laying prone on the examination table making an imaging with the FLIR camera.

On the examination days (BL, F/U1 and F/U2), the participants enter the RES laboratory in Landquart wearing sports clothing. At baseline, participants are asked to sign an informed consent form and are screened for inclusion and exclusion criteria. Participants are then asked for their age and sex, height is measured using a stadiometer (GPM Stadiometer, Zurich, Switzerland), and weight and lower body fat percentage are measured using a scale (TANITA-TBF 611 scale, Tokyo, Japan). At all three measurements (BL, F/U1 and F/U2) participants are asked to complete the IPAQ to assess physical activity. Next participants are placed on the examination table in a prone position for an ultrasound scan to measure the thickness of the M. erector spinae on the right side. The probe head is coated with coupling gel and applied perpendicular to the muscle on the right side without pressure to not compress the dermal surface. The images are saved, and the distance is measured later. Participants are then familiarised with the ILEX machine and positioned for individual adjustments. After a warmup for 120s with a low load and a short break, participants are asked to move dynamically into full flexion and full extension over the full ROM for three times. The test is repeated a second time. After a 2-minutes break, participants are asked to slowly move backwards to maximal tension and repeat the isometric force test after 2-minutes break. Next, the participant is seated in front of the sit-and-reach test box keeping the knees fully extended and the feet dorsiflexed against the foot-support. The participant is moving actively, slowly forward, bringing the body to the pain-free limit. The participant's hands move along the scale on the block until the movement is terminated because the participant can go no farther. The final position is held with an isometric contraction for 2 seconds, and the distance is read on the scale. After a 2-minutes break, the test is repeated. The rating scales for perceived effort, discomfort and thermal sensation are then presented for familiarization. Finally, the isometric back extension endurance is measured through the Biering-Sørrensen test. The participant is lying prone on an examination table with the upper border of the iliac crests in line with the edge of the table. The lower body is secured to the table by three straps around the pelvis, knees, and ankles. With the arms folded across the chest, the participant is asked to hold the upper body isometrically in a horizontal position. A stopwatch is used to measure the time the participant can keep the unsupported upper body in contact with a horizontal object. The examination takes about 1 hour.

Withdrawal and discontinuation

Participants can withdraw from the study at any time without giving a reason. Previous research has shown that training the back extensor muscles with ILEX machines once a week is as effective as training two or three times a week for increasing isometric lumbar extension strength (Carpenter et al., 1991; Graves et al., 1990). Missed training sessions are analysed on a case-by-case basis to decide whether to withdraw from the study. Participants will be withdrawn from the study if an impending injury or illness contraindicates the use of the ILEX device. For scientific and economic reasons, data already collected are included in the analyses as far as possible.

5 STATISTICS AND METHODOLOGY

5.1. Statistical analysis plan and sample size calculation

A priori sample size calculation was performed using G*power (Version 3.1, Franz Faul, Germany) to determine participants numbers (n) ($\alpha = 0.05$; effect size = 0.46; test family = F test, and statistical test = analysis of variance (ANOVA) repeated measures, within-between interaction; number of groups = 2; number of measurements = 3; power = 0.8) and revealed n = 10 participants. The effect size was estimated based on previous research with a comparable ILEX device in healthy volunteers (Fisher et al., 2018).

Assumption of normality will be verified using the Shapiro-Wilk test. Mauchly's test will indicate the violation of the assumption of sphericity. Normally distributed data will be analysed applying ANOVA repeated measures with within-between interactions to compare the means of each variable over the three repeated observations (within) and between the intervention and sham group (between). Not normally distributed data will be examined using non-parametric statistics (Friedman's two-way ANOVA). Post hoc Bonferroni test correction will be applied. Probability values $p < 0.05$ will be considered statistically significant.

Men and women are included in this study and will be part of the randomization process. The planned sample size of this study does not allow for gender-specific analysis. A gender difference analysis will have to be part of a future study.

Analyses will be performed using RStudio Team (2023) (RStudio: Integrated Development Environment for R. Boston, MA) and IBM SPSS Statistics (Version 27, IBM Corp., Armonk, NY, USA).

5.2. Handling of missing data and drop-outs

Missing data, missed training sessions or discontinuation are recorded on the CRF. Data from patients who drop out are achieved and stored. Drop-outs are not replaced by recruitment of new participant. If consent is withdrawn, the data already collected are included in the analysis for scientific and safety reasons. These are only anonymised after the analysis (Art. 9 ClinO).

6 REGULATORY ASPECTS AND SAFETY

6.1 Local regulations / Declaration of Helsinki

This study is conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP, the HRA as well as other locally relevant legal and regulatory requirements.

6.2 (Serious) Adverse Events and notification of safety and protective measures

An Adverse Event (AE) is any untoward medical occurrence in a patient or a clinical investigation subject which does not necessarily have a causal relationship with the trial procedure. An AE can

therefore be any unfavourable or unintended finding, symptom, or disease temporally associated with a trial procedure, whether or not related to it.

A Serious Adverse Event (SAE) (ClinO, Art. 63) is any untoward medical occurrence that

- Results in death or is life-threatening,
- Requires in-patient hospitalisation or prolongation of existing hospitalisation,
- Results in persistent or significant disability or incapacity, or
- Causes a congenital anomaly or birth defect

Both Investigator and Sponsor-Investigator make a causality assessment of the event to the trial intervention, (see table below based on the terms given in ICH E2A guidelines). Any event assessed as possibly, probably or definitely related is classified as related to the trial intervention.

Relationship	**Description**
Definitely	Temporal relationship Improvement after dechallenge* Recurrence after rechallenge (or other proof of drug cause)
Probably	Temporal relationship Improvement after dechallenge No other cause evident
Possibly	Temporal relationship Other cause possible
Unlikely	Any assessable reaction that does not fulfil the above conditions
Not related	Causal relationship can be ruled out
*Improvement after dechallenge only taken into consideration, if applicable to reaction	

Both Investigator and Sponsor-Investigator make a severity assessment of the event as mild, moderate or severe. Mild means the complication is tolerable, moderate means it interferes with daily activities and severe means it renders daily activities impossible.

No (serious) Adverse Events are expected.

Reporting of SAEs (see ClinO, Art. 63)

All SAEs are documented and reported immediately (within a maximum of 24 hours) to the Sponsor-Investigator of the study.

If it cannot be excluded that the SAE occurring in Switzerland is attributable to the intervention under investigation, the Investigator reports it to the Ethics Committee via BASEC within 15 days.

Follow up of (Serious) Adverse Events

Not applicable, no SAE are expected in this study design.

Notification of safety and protective measures (see ClinO, Art 62, b)

If immediate safety and protective measures have to be taken during the conduct of the study, the investigator notifies the Ethics committee of these measures, and of the circumstances necessitating them, within 7 days.

6.3 (Periodic) safety reporting

An annual safety report (ASR) is submitted once a year to the local Ethics Committee by the Investigator (ClinO, Art. 43 Abs 1).

6.4 Radiation

The radiofrequency electromagnetic field caused by the diathermy device induces 448kHz capacitive monopolar radiation. This electromagnetic energy generates heat by oscillation and friction of charged molecules (Guy et al., 1974). Ultrasound is using high-frequency sound waves and not ionizing radiation to capture images like X-ray imaging. Therefore, no hazardous radiation is used in this study.

6.5 Pregnancy

Pregnant or breastfeeding woman are excluded from participating in the study. A urine pregnancy test is given to the women together with the participant information. The negative test result must be presented on the first examination day. In the event of a positive test, women will be asked to report this by telephone and will not be included in the study.
No risks regarding contraception of any kind are to be expected; to date, no such risks are known for this procedure. Participants who become pregnant during the study must inform their investigator immediately and may not continue to participate in the study.

6.6 Amendments

Substantial changes to the study setup, organization, protocol and related study documents will be submitted to the Ethics Committee for approval prior to implementation.

Under emergency circumstances, deviations from the protocol to protect the rights, safety and well-being of human subjects will be documented and reported to the Ethics Committee as soon as possible.

6.7 Notification and reporting upon completion, discontinuation or interruption of the study

Upon regular study completion, the Ethics Committee is notified via BASEC within 90 days (ClinO, Art. 38).

The Sponsor-Investigator may terminate the study prematurely according to certain circumstances, e.g.

- Ethical concerns,
- Insufficient participant recruitment,
- When the safety of the participants is doubtful or at risk (e.g. when the benefit-risk assessment is no longer positive),
- Alterations in accepted clinical practice that make the continuation of the study unwise, or
- Early evidence of harm or benefit of the experimental intervention

Upon premature study termination or study interruption, the Ethics Committee is notified via BASEC within 15 days (ClinO, Art. 38).

A final report is submitted to the Ethics Committee via BASEC within a year after completion or discontinuation of the study, unless a longer period is specified in the protocol (ClinO, Art. 38).

6.8 Insurance

In the event of study-related damage or injuries, the liability of the institution Thim van der Laan AG provides compensation, except for claims that arise from misconduct or gross negligence.

7 FURTHER ASPECTS

7.1 Overall ethical considerations

The study is being carried out on healthy volunteers. However, ILEX machines are also designed to provide a safe way for people with back problems to exercise. Therefore, training experience with ILEX machines will help not only healthy people, but also patients with back problems. In addition, heat therapy has the potential to support hypertrophy in resistance training. The results from the diathermy therapy will provide guidance for patients who are unable to examine resistance training to voluntary fatigue. Future studies in patients are planned to investigate the effect of training and preheating in relation to back problems.

7.2 Risk-benefit assessment

There are no health risks associated with participating in this study. The ILEX machine is CE-certified and based on equipment that has already been tested. The product is used in accordance with the instructions for use. The training sessions take place at low load and with a slow increase in load, which means that there is a negligible risk of injury. It is possible that fatigue of the back muscles or slight muscle soreness limited to the back may occur as a result of the training.

The use of diathermy therapies has been common practice for two decades. Treatment with the diathermy device is safe and most people find it very pleasant. Very sensitive skin may experience temporary redness and/or tingling. The tecar device is CE-certified and is used in accordance with the instructions for use.

Participation in the study does not result in any direct benefits for the test person. Ideally, the test participants improve the strength of the back extension muscles. The results of the study will help future people with back pain to receive effective treatment.

8 QUALITY CONTROL AND DATA PROTECTION

8.1 Quality measures

For quality assurance the sponsor, the Ethics Committee or an independent trial monitor may visit the research sites. Direct access to the source data and all study related files is granted on such occasions. All involved parties keep the participant data strictly confidential.

8.2 Data recording and source data

For this study, all data will be reported in the paper CRF and translated into a Microsoft Excel file (Version 16.79 (2023), Microsoft Corporation, Redmond, Washington, USA). Maximum isometric force and ROM of the back extensor are both automatically saved in Microsoft Access (Version 6_4, Microsoft Corporation, Redmond, Washington, USA), translated to the CRF and exported to Microsoft Excel. The image of the M. erector spinae, generated through the ultrasound system Mylab2 (Esaote, Maastricht, Netherlands), is exported to the software Horos™ (Horos Project, Annapolis, MD, USA). The result of measuring the muscle thickness is reported on the CRF file and entered into Microsoft excel. Epidemiologic data, inclusion and exclusion criteria, measurements of the sit-and-reach test, Biering-Sørrensen test, ratings of perceived effort, discomfort, thermal sensation, and comfort, and details of each training session are recorded directly on the CRF and transferred to Microsoft Excel.

8.3 Confidentiality and coding

Trial and participant data will be handled with uttermost discretion and is only accessible to authorized personnel who require the data to fulfil their duties within the scope of the study. On

the CRFs and other study specific documents, participants are only identified by a unique participant number.

The generated data are coded by a unique participant number. The Excel file is stored in Microsoft Teams classic (version 1.6.00.29954, Microsoft Corporation, Redmond, Washington, USA), which is accessible by the team of the Rehabilitation and Exercise Science Laboratory RESlab in Landquart with a password. The participation identification list is stored separately in Microsoft Teams in a password-protected area accessible only to the principal investigator of the study. Printed documents (CRF) are stored in a separate lockable filing cabinet. Only the principal investigator has the key to this cabinet. An automatic back-up of the Microsoft team takes place every night.

8.4 Retention and destruction of study data and biological material

All study data are archived for 10 after study termination or premature termination of the study. The generated data are transferred to a password-protected archive in Microsoft teams accessible for the RESLab team. The participation identification list is stored separately in Microsoft Teams in a password-protected area accessible only to the principal investigator of the study. Printed documents are stored in a separate lockable filing cabinet, only accessible for the principal investigator.

9 MONITORING AND REGISTRATION

The monitoring will be done by Dr. Ursula Hohenauer Küng from the institution THIM – Die internationale Hochschule für Physiotherapie, Weststrasse 8, 73002 Landquart.
Dr. Küng will ensure that trial is conducted and documented properly by carrying out the following activities when relevant and necessary to the trial:

- Verifying that the investigator has adequate qualifications and resources and remain adequate throughout the trial period, that facilities, including laboratories, equipment and staff, are adequate to safety and properly conduct the trial and remain adequate throughout the trial period.
- Verifying for the study interventions:
    - That the intervention conditions are acceptable.
    - That the study interventions are supplied only to subjects who are eligible to receive it.
    - That subjects are provided with necessary instructions on the study interventions.
- Verifying that the investigator follows the approved protocol and all approved amendments, if any.
- Verifying that written informed consent was obtained before each subject participation in the trial.
- Ensuring that the investigator and the investigator's trial staff are adequately informed about the trial.
- Verifying that the investigator is enrolling only eligible subjects.
- Reporting the subject recruitment rate.
- Verifying that the investigator provides all the required reports, notifications, applications, and submissions, and that these documents are accurate, complete, timely, legible, dated, and identify the trial.
- Adverse events, concomitant medications and intercurrent illnesses are reported in accordance with the protocol on the CRFs
- Visits that the subjects fail to make, tests that are not conducted and examinations that are not performed are clearly reported as such on the CRFs.
- All withdrawals and dropouts of enrolled subjects from the trial are reported and explained on the CRFs.

This study will be registered on the Swiss National Clinical Trial Portal.

10. FUNDING / PUBLICATION / DECLARATION OF INTEREST

The Thim van der Laan AG, headed by Thim van der Laan Jr., is responsible for the management of a Bachelor's degree course in physiotherapy for the University of Applied Sciences of Southern Switzerland (SUPSI), which includes a scientific research laboratory. The study is financed by the University of Applied Sciences of Southern Switzerland SUPSI. The sponsor is Thim van der Laan AG.

The diathermy device is provided by Wintecare (Wintecare SA, Chiasso, Switzerland) and the ILEX machine by Heftec (Heftec GmbH, Oberurnen, Switzerland) for the duration of the study.

The examiners ensure that the participant's privacy is guaranteed. In particular, data protection and confidentiality are guaranteed, and no personal data is presented or published or passed on to outsiders or unauthorised persons. Gender effects are analysed and published.

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Appendix 1: Schedule of assessments

Visit	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
Week	1	1	2	2	3	3	4	6	6	6	7	7	8	8	10
Time (hour)	1	½	½	½	½	½	½	1	½	½	½	½	½	½	1
Therapy and training		✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	
Skin temperature		✓												✓	
Rating of perceived effort		✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	
Rating of perceived discomfort		✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	
Rating of thermal sensation		✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	
Rating of perceived comfort		✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	
Examination	✓							✓							✓
Maximal isometric force	✓							✓							✓
Maximal range of motion (ROM)	✓							✓							✓
Sit-And-Reach-Test	✓							✓							✓
Biering-Sørensen test	✓							✓							✓
Ultrasound	✓							✓							✓
Physical activity	✓							✓							✓