University of Applied Sciences and Arts of Southern Switzerland
Department of Business Economics, Health and Social Care

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Clinical trial study to investigate the effectiveness of the Patellos device

Clinical Study Protocol

Lemma: Effectiveness study Patello

Study Type:	Clinical trial with a medical device of risk group C
Study Categorisation:	Clinical trial with a category C medical device in accordance with the Swiss Ordinance on Clinical Trials in Human Research (ClinO: Art. 20)
Study Registration:	-
Study Identifier:	-
Sponsor:	**Thim van der Laan AG** **Thim van der Laan jr.** Weststrasse 8, 7302 Landquart +41 81 300 01 70
Investigator:	***Contact / Director of Studies*** **Dr. Clijsen Ron**, PhD University of Applied Sciences and Arts Southern Switzerland, SUPSI Physiotherapy Graubünden Weststrasse 8, 7302 Landquart Phone: +41 81 300 01 75 ron.clijsen@supsi.ch
Investigational Product:	Patello (Patella Mobility, Srm-Projects GmbH, Chur)
Protocol Version and Date:	Study protocol – Version 01 – 05.04.2018

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Study Synopsis

Sponsor/ Sponsor-Investigator	**Sponsor** **Thim van der Laan AG Thim** **van der Laan jr.** Weststrasse 8 / CH-7302 Landquart **Investigator** **Dr. Clijsen Ron**, PhD University of Applied Sciences and Arts Southern Switzerland (SUPSI) Department of Business Economics, Health and Social Care Physiotherapy Graubünden Weststrasse 8 / CH-7302 Landquart
Study Title:	Clinical trial study to investigate the effectiveness of the patello
Short Title / Study ID:	Effectiveness study Patello
Protocol Version and Date:	Version 01 from 05.04.2018
Trial registration:	Cantonal Ethics Committee Zurich
Study category and Rationale	Clinical trial with a medical device of risk category C according to ClinV (Art. 20) The device under investigation, Patello, is an innovative product for passive, continuous mobilization of the patella. It consists of CE certified Individual components. As a complete device, the Patello is not yet CE certified.
Clinical Phase:	The Patello device will be tested for its effectiveness in this clinical trial before the clinical phase begins.

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Background and Rationale:	Restricted movement of the knee joint hinders the everyday life of the affected person. They can be caused by osteoarthritis or after surgical procedures on the knee joint. The therapy of choice for limited knee mobility is the active and passive mobilization of the knee joint (Art. Genu, Art. Patellofemorale, Art. Tibiofibulare) with involvement of the soft tissue mantle (muscles, connective tissue). Active mobilization is carried out by the patient independently through a specific exercise program. Passive mobilisation is part of physiotherapeutic treatment. The aim of mobilisation is to activate the formation of synovial fluid, to regulate the tone of the muscles and to influence the fibre alignment of the collagen tissue. The Patello device was built to perform passive, continuous mobilization of the patella as part of rehabilitation with limited knee mobility. The area of application and indication is based on the widely used "Kinetec" knee and hip mobilisation splint. What is innovative about the Patello is that only the Art. patellofemoral is mobilized; the patella is moved on its plain bearing in the cranial and caudal directions.
Objective(s):	The aim of this clinical trial is to prove the effectiveness of the patello.
Outcome(s):	Primary outcome: Objectification of the displacement of the patella to cranial and caudal measurement with an imaging ultrasound device (esaote MyLabClassicC, Genoa, Italy, www.esaote.com). Secondary outcome: Subjective well-being of the subject measured by a visual analogue scale (VAS scale 0 - 10). The knee to be tested is determined by lot (randomized) per test person. The outcomes are recorded after 1, after 10, after 20, after 30 and after 50 mobilizations in the caudal deposition position. The entire measurement procedure is carried out 2x in a week per test subject with a 2-day break in between.
Study design:	Clinical effectiveness study

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Inclusion/ Exclusion criteria:	**Inclusion Criteria:** - Adults aged 18 to 30 years - No surgical interventions and/or current complaints (pain at rest or during exertion) on the musculoskeletal apparatus in the area of the lower extremities - closed, intact skin conditions in the knee and thigh area - Don't be afraid of the intervention **Exclusion criteria:** - Adolescents and adults over 30 years of age - Surgical interventions and/or current complaints (pain at rest or during exertion) on the musculoskeletal apparatus in the area of the lower extremities - No closed, intact skin conditions in the knee and thigh area - Fear of intervention
Preparation	Subject recruitment The study is being advertised internally at the University of Applied Sciences and Arts Southern Switzerland SUPSI. Interested parties report to the study director in the research laboratory, who gives them the written subject information and the declaration of consent to read at home. The principal investigator verbally explains the objective, procedure and conditions of the study. If the interested party wants to participate in the study, he or she brings the signed declaration of consent to the research manager, who also signs it. If there is any ambiguity on the part of the interested party, questions can be asked at any time. A copy is given to the future test subject. The health questionnaire is then filled out. This clarifies the inclusion and exclusion criteria. If all inclusion criteria are met, the test subject draws a lot to determine the side to be tested. Afterwards, 2 appointments are arranged, which guarantee a 2-day break between the measurements. Subject preparation The test subject wears shorts and is barefoot. He sits down on the treatment table. The backrest is raised so that an upright sitting position can be assumed. The leg to be tested is placed on the patello and fixed according to the product description (Chapter 8). The foot is placed underneath so that the leg can lie relaxed. In a first phase, the contact pressure of the device is calculated based on the well-being of the test subjects. The setting is noted.

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Measurements and procedures:	Measurement procedure This is followed by the **1st measurement** (pre-mobilisation). Afterwards, the mobilization pressure is built up individually up to the tolerance limit of the test subject so that a displacement of the patella caudally takes place (**2nd measurement**). The maximum deflection of the patella to the reference point is determined and the device settings are noted. As described above, further measurements are carried out according to the following scheme: after 10 mobilisations (**3rd measurement**), after 20 mobilisations (**4th measurement**), after 30 mobilisations (**5th measurement**), after 50 mobilisations (**6th measurement**). The device settings are kept the same for all measurements per subject. *Objective Displacement* The displacement of the patella due to mobilization is objectified by means of an imaging ultrasound device. In a second step, the distance of the patellar displacement is evaluated using the ultrasound images using special software (OsiriX, www.Osirix-viewer.com). *Subjective information on general well-being* After each measurement interval, the subjects report their subjective well-being using a visual analogue scale (VAS). The scale is from "0" (maximum well-being) to "10" (maximum discomfort) in cm-steps. **Further processing of the data** Microsoft Excel from Windows is used for data pooling and the graphical representation of the end data.
Study Product / Intervention:	For this study, we use a device (Patello, Srm-Projects GmbH, Chur) that mobilizes the patella by apparatus, passively and continuously.
Control Intervention (if applicable):	There is no control intervention.
Number of Participants with Rationale:	We limit the number of subjects to n = 30. According to the g*power calculation, this gives us an effect size of 0.68 with a power of 0.95.

Study Duration:	June 2018 - December 2018
Study Schedule:	June 2018: planned start of measurements December 2018: planned end of measurements

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Investigator(s):	Examiner - Dr. Ron Clijsen1,2 - Erich Hohenauer, Drs.1,2 - Rahel Stoop, MSc[1] - Dr. Matthias Fenzl3 [1] *University of Applied Sciences and Arts Southern Switzerland SUPSI, Department of Business Economics, Health and Social Care, Physiotherapy Graubünden, Weststrasse 8, 7302 Landquart* [2] *THIM University of Applied Sciences in Physiotherapy, Weststrasse 8, 7302 Landquart* [3] *Medical Center Bad Ragaz, Hans Albrecht-Strasse, 7310 Bad Ragaz* ***Contact / Director of Studies*** **Dr. Clijsen Ron**, PhD University of Applied Sciences and Arts Southern Switzerland (SUPSI) Department of Business Economics, Health and Social Care Physiotherapy Graubünden Weststrasse 8, 7302 Landquart Phone: +41 81 300 01 75 ron.clijsen@supsi.ch
Study Centre(s):	Single Centre Study: Rehabilitation Research Laboratory University of Applied Sciences and Arts Southern Switzerland SUPSI Department of Business Economics, Health and Social Care Physiotherapy Graubünden Weststrasse 8 7302 Landquart
Statistical Considerations:	Patellar displacement during mobilization application by the patello. Repeated measures analysis of variance (MANOVA) A 2-factor analysis is carried out. Factor 1: Intervention Patello Factor 2: Time intervention: Start (pre-intervention, 1st measurement), after a single mobilization (2nd measurement), after 10 (3rd measurement), after 20 (4th measurement), after 30 (5th measurement), after 50 mobilizations (6th measurement). The significance level is set at $P < 0.05$, and distatistical data analysis is carried out using the Statistical Package for Social Sciences (SPSS V. 24) from IBM, New York, USA.

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GCP Statement:	This study will be conducted in compliance with the protocol presented here, the current version of the Declaration of Helsinki, the ICH-GCP, ISO EN 14155 (where applicable), and the Swiss Human Research Ordinance HFV.

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Overview of the study

Knee joint mobility can be limited by arthritic or post-operative functional or structural changes. Reduced knee joint mobility can interfere with the affected person's everyday activities. Active movement of the knee promotes the formation of synovial fluid, which is essential for the supply of cartilage tissue. Passive mobilization techniques as part of a physiotherapeutic treatment release structural blockages and favor the fiber alignment of the collagen tissue.

In order to provide a further passive mobilisation option of the knee joint, specifically Art. Patellofemoral device, independent of therapists, the Patello device was developed. It performs apparatus, passively and continuously mobilization of the patella in the caudal and cranial directions. The movement deflections are determined by the patient independently based on the current tolerability.

Aim of the study

The aim of this study is to determine the effectiveness of the Patello device. We want to prove that the Patello device moves the patella on the patellofemoral bearing.

The primary outcome is the objectification of the displacement of the patella measured with an imaging ultrasound device (esaote MyLabClassicC, Genoa, Italy, www.esaote.com).

As a secondary outcome, the subjective well-being of the subject is recorded, measured using a visual analogue scale (VAS scale 0 - 10).

In order to record a possible positive effect of repetitive mobilization, the measurements are carried out several times: after the positioning of the device (1st measurement, pre-mobilization), after 1 mobilization, after 10 mobilizations, after 20 mobilizations, after 30 mobilizations and after 50 mobilizations (2nd to 6th measurement). The measurements are carried out on 2 days, with a 2-day break in between.

Abbreviations

CEC	Competent Ethics Committee
GCP	Good Clinical Practice
KlinV	Ordinance on Clinical Trials in Human Research Study Schedule

The completion of the measurement series is planned for December 2018, and the completion of the entire project for December 2019.

Table 1: Schedule

June, 2018	July-December, 2018	January-May, 2019	June-December, 2019
Subject Information, Screening, Planning	Data collection and Statistics	Writing the article	Publishing the article

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1 STUDY ADMINISTRATION

1.1 Sponsor

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Other examiners

Rahel Stoop, MSc[1] *(GCP Module I-III & GCP Basic Course)*
Selection of subjects, obtaining consent to study participation, study administration, implementation of the Measurements – collecting the data, analyzing the data, interpreting the data, writing the report Erich Hohenauer, Drs, MSc[1,2] *(GCP Module I-III & GCP Basic Course)*
Selection of test subjects, obtaining consent to participate in the study, study administration, carrying out measurements – collecting data, data analysis, interpreting the data, writing the report

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Dr. Matthias Fenzl3 (*PhD, GCP Module I-III)*
Data analysis, interpretation of the results, writing of the report

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1.6 Monitoring of the study

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1.7 Privacy

All data obtained from study participants will be coded and not passed on to other people. Personal data and personal details are stored in paper form in a locked filing cabinet. The head of the research laboratory and at the same time the head of the study has access here, and the administration of the documents also falls within his area of responsibility.

All digital data is encrypted and encoded. No conclusions can be drawn about individuals. The digital data is stored on internal computers, archived and not released to outsiders.

Employees involved in data processing have no insight into the personal data and the coding of it.

1.8 Other committees or institutes involved

The study is being conducted in the research laboratory at the University of Applied Sciences and Arts Southern Switzerland SUPSI, Department of Business Economics, Health and Social Care Physiotherapy Graubünden, Weststrasse 8, 7302 Landquart, Switzerland.

The measuring equipment is all located in this room, so all measurements can be carried out at the same location. The room offers enough space.

At present, no further studies with this arrangement are taking place in this experimental laboratory. Another study is currently taking place at our institute (NCT 03016221). However, the measurements of these studies do not take place at the same time and do not hinder or influence each other. Thus, the utilization of the infrastructure is not excessive and therefore justifiable.

No other institutes and committees are involved in this study or in the approval or monitoring of the study.

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2 ETHICAL AND REGULATORY ASPECTS

2.1 Study Registration

The conduct of the present study is the responsibility of the Cantonal Ethics Committee Zurich and Swissmedic, as it is a category C medical device (pre-market). An application for admission is submitted to both institutions. Any further conditions imposed by the responsible ethics committee and/or Swissmedic must be implemented in the study protocol.

When the study protocol is submitted to the Cantonal Ethics Committee in Zurich, the study is also registered with the Swiss Coordination Office for Research on Human Subjects.

2.2 Categorization of the study

The study is categorized as a clinical trial with a medical device of risk category C (ClinO, Art. 20). The test subjects are not administered medication or tissue samples are taken. No invasive methods are used.

2.3 Competent Ethics Committee (CEC)

Human research in the Canton of Graubünden falls under the remit of the Cantonal Ethics Commission Zurich. Changes to the study protocol are not permitted without the prior consent of the CEC, except for the immediate elimination of obvious hazards to the participants. According to chap. 2.10 to the CEC.

An early termination or interruption of the study must be reported to the CEC within 15 days, and the regular end within 90 days. The final report must be submitted within one year of the end of the programme. Corrections are to be reported in accordance with Chapter 2.10.

2.4 Competent Authorities (CA)

The present study falls under the remit of the Cantonal Ethics Committee Zurich. Obligations and deadlines can be found in the previous point.

2.5 Ethical Leadership of the Study

The study will be conducted in accordance with this protocol and the current version of the Helsinki Declaration, the ICH-GCP, the European Medical Device Directive 93/42/EEC and the ISO standard 14155 and ISO 14971 (where applicable), as well as the Swiss Human Research Ordinance and thus Swiss law.

The CEC receives an annual report and is informed about the course of studies.

2.6 Conflict

There is no financial conflict of interest on the part of the sponsor/investigator, nor is there a corresponding relationship of dependency.

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2.7 Patient information and informed consent

The examiners will explain to each participant individually the nature of the study, its content, intent and objective. This includes the protocol flow, approximate time duration, possible risks and benefits. The participant is informed that participation is voluntary and can be withdrawn from the study at any time, without personal consequences of any kind. The participant will be informed about data protection, the handling of personal data and their access.

Each participant receives written subject information and the declaration of consent with the detailed study description and all necessary information to be able to decide whether to participate in the study. The participant will also be given sufficient time to read this written information and to ask questions to the responsible examiners.

The subject information and the informed consent form are submitted to the CEC, where they must be reviewed and approved.

The signed declaration of consent must be submitted before the start of the study process. The participant should read them before signing and check their contents. The responsible examiner then also signs the declaration of consent. Finally, the participant receives a copy of the declaration of consent. The signed declaration of consent is kept in the original as a study document in a locked filing cabinet.

2.8 Confidentiality & Privacy

The examiners ensure that the privacy of the participants is maintained. In particular, data protection and confidentiality are guaranteed, and no personal data is presented or published. The signed declaration of consent, as well as the completed questionnaire with the other personal details, are kept in the original as a study document in a locked filing cabinet.

The digital data is encrypted and treated confidentially, and access to the personal data is denied to third parties. The digital data collected is stored solely on the institute's own computers and is not passed on to any external persons or transferred to other computers.

Direct access to the personal data is allowed only to the head of the research laboratory (study leader), as well as authorized persons of the CEC.

2.9 Early termination of the study

The sponsor or principal investigator may discontinue the study early if/if

- ethical concerns
- insufficient number of subjects
- the safety of the participants cannot be guaranteed
- Findings from clinical practice make it pointless to continue the study
- early evidence or harm of the experimental intervention has been proven

2.10 Protocol Adjustments

Adjustments and changes to the current study are only permissible after review by the CEC and Swissmedic. Short-term changes to the protocol before a review by the CEC and Swissmedic can be made to ensure the rights and safety of the participants. However, such adjustments must be documented and reported to the CEC and Swissmedic as soon as possible.

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Significant changes are only permissible after an examination by the CEC and Swissmedic. Any other changes must be notified to the CEC and Swissmedic as soon as possible and listed in the annual report.

3 BACKGROUND AND RATIONALE

3.1 Background and justification

3.1.1 Physiology – Elastoplastic tissue properties (tissue treatment area of the knee)

Painful restriction of mobility is nothing unusual after surgical interventions on the knee joint. Collagen resynthesis plays a decisive role in the healing process. It is characterized by tissue remodeling. It is not uncommon for the recovery phase to be delayed, which has a negative effect on knee mobility. Permanently restricted knee mobility leads to structurally shortened periarticular tissues. In about 10% of patients, the periarticular tissue remains permanently altered, limiting joint mobility. Early signs of structurally induced hypomobility are often adhesions of connective tissue, excessive connective tissue formation or the formation of pathological crosslinks (collagenous cross-connections).

Knowledge of the indicators and the recognition of delayed healing processes is important in order to exert targeted structural and form-forming stimuli on the collagen tissue at an early stage. The standardised procedures include intensive passive and active mobilisation.

In this study, the collagen soft tissue sheath of the kneecap is to be mobilized in a targeted manner, which is why the further explanations of the repair process refer to the anterior knee joint compartment.

From a biophysical point of view, the collagen fibrils of ligaments and tendons are stretched and stretched during mobilization. The change in length of the tendinous tissue is attributed to elastic, plastic and viscous properties. Elasticity refers to the strain-stress curve on tensile load. Plasticity is equated with mold elongation and viscosity with shape change due to flow properties. While the muscle can be stretched to 160% of its resting length with over 70% wet mass (water, sarcoplasm), the elasticity of the tendon with 30% wet mass is only between 4% and 10% of its initial length *(Hüter-Becker, 1997*).

Tendon tissue has only a low elasticity, but a high resistance (stiffness). As tensile stress increases on the tendon tissue, more and more fibers counteract the tension. The high resistance of tendon tissue is based on the arrangement of collagen fibers in bundles, and the cross-linking of proteoglycans in the collagen matrix *(Jakob, 1990).*

In the experimental situation in the laboratory, tendons were lengthened by exposing them to a constant tensile load in order to investigate the viscoelastic properties of tendinous tissue. This process is called "creep" and can be observed even when the forces acting on it are low. The physiological stretching loads did not lead to permanent deformities or damage to the tendons if the tendon was given enough time to stretch *(Wilcke, 2004).* The creep phenomenon observed in laboratory situations is also observed in cyclic long-term stimulus loads such as in endurance disciplines, whereby the tendons and ligaments recover after cyclic conditioning and return to their initial length *(Van den Berg, 1999).*

The high plasticity and viscosity of tendon tissue is used in surgical practice for the preparation of tendon tissue. For use as an autologous graft, the tendons are subjected to a defined deformity. The tendons are stretched for 5 minutes under a defined tensile force in order to expand the collagen fibers in a targeted manner and align them parallel. Cyclic preconditioning or pre-tensioning of the quadriceps, patellar and semitendinosus tendons has proven to be useful in order to maintain the graft its intended length after installation. Even more than the quadriceps tendon, the patellar tendon benefits from conditioning in terms of tear resistance *(Schatzmann, 1998).*

These examples show that a targeted tensile force in the grain course on tendons is essential to achieve a functional parallel fiber arrangement and resistivity. Obviously, repeated stimulation can restore the normal length ratio and also increase tissue tolerance.

Efficacy studies have shown that static and dynamic tension-specific stimuli change the biomechanical properties of the tendinous system.

According to *Salter* (1989), the alignment of collagen fibers in tendons and ligaments changes as a result of the regular load following the mechanical force. Under tensile and compressive stress of connective tissue structures, the crosslinks unfold in a physiological mass and thus contribute to the stabilization of filamentary structures. Induced by the mechanical stress stimulus, fibroblasts synthesize more procollagen, which serve as the basic building block of collagen fibers. In fibril synthesis, the collagen arrangement is aligned with the effective lines of force of the practicing stimulus.

At the tissue physiological level, the connective tissue is metabolically active in targeted, longer-lasting stretching stimuli. As a result of the increased collagen turnover and its beneficial influence on collagen metabolism, the tissue can adapt to the load in the long term *(Cook, 2002).*

3.1.2 Indications for instrumental kneecap mobilization

3.1.2.1 Arthrofibrosis (AF) of the knee joint

AF is one of the most feared complications after surgical procedures on the knee joint and is caused by excessive tissue formation. Pathologically, AF is an increase in connective tissue cells (fibrocytes) that leads to intra-articular adhesions and scarring. The anterior knee joint is most commonly affected, accompanied by restricted movement of the anterior joint compartment (*Robertson, 2008).* Pathophysiologically, primary AF must be distinguished from the secondary form:
AF accumulate intra-articular molecules of the extracellular matrix in the context of impaired wound healing *(Faust, 2015).* In the secondary form, there is mechanical irritation, and in some cases there are symptoms of entrapment. The majority of AF is more common than anterior and less common than generalized *(Paulos, 1995).* Anterior AF is accompanied by extensor inhibition due to adipose body and retinaculum fibrosis (infrapatellar contraction syndrome, patella entrapment), while generalized AF often leads to hypomobility of the entire knee joint due to fibrosclerosing scarring.

Following the guidelines in the treatment of secondary arthrofibrosis, the periarticular collagen structures should be treated in a targeted manner by intermittent mobilization. Intermittent tensile loads release collagenases in proliferative fibrous hyperplasia. They are able to break up collagen adhesions and pathological crosslinks. Tissue collagenases cleave collagen molecules. The resulting fragments are degraded by non-specific proteases down to the individual amino acids *(Gelse, 2003).*

In the rather rare cases of primary AF with dysfunction of reparative processes and the biology of fibroblasts, the dysregulated sympathetic nervous system is held responsible. The risk of sympathetic reflex dystrophy is particularly high after knee joint replacement (total endoprosthesis, TEP) and after replacement of the anterior cruciate ligament. The enzymes responsible for the excessive formation of connective tissue must not be exacerbated by mechanical stimuli and pain. In these cases, specific mobilisation is dispensed with. The
Intervention is limited to reflex therapy measures to dampen fibroblast activity and sympathetic tone: slight movement within the pain-free range is indicated, additional drug treatment with low-dose prednisolone and propanolol *(Traut, 2012).* For the desired treatment success, the ligamentary and capsular structures of the anterior knee must be addressed in a differentiated manner in the case of anterior AF or stiffening.

3.1.2.2 Knee endoprosthesis

The indication for the use of a bicondylar sled prosthesis or knee TEP is specified by the surgical side, a surgical intervention or joint replacement is carried out in the case of preoperative osteoarthritis from a severity grade III according to WHO criteria.

A not uncommon complication after knee replacement is persistent restriction of mobility. From a clinical point of view, mobility is limited with an extensor or flexion deficit of more than 10° or 15° to the opposite

side *(Nwachukwu, 2011; Kim, 2004),* although the definition is inconsistent and often oriented towards function.

In reviews and large cohort studies, the incidence of knee hypomobility after knee replacement is reported to be 1.3% to 5.3% *(Kim, 2004; Yercan, 2006; Gandhi, 2006).*

The reasons for a movement deficit are multifactorial, and the etiology and pathogenesis are sometimes insufficiently understood *(Manrique, 2015).* Most often, the femorotibial joint is affected. In only 12% of complex cases, the extensor apparatus or the patellofemoral joint is involved *(Nam, 2004).* The problems, also referred to as the extensor mechanism, are based on various causes in the differential diagnosis: patellar maltracking, rupture of the extensor mechanism (patellar fracture, patellar and quadricle tendon rupture), patellar joint surface problems (lateral facet impingement with undersized patellar posterior replacement, unreplaced patellar posterior replacement, posterior surface replacement that is too thick, arthrofibrosis (AF), patella alta and baja *(Mandalia, 2008).*

In most cases, persistent hypomobility of the knee joint is surgically arthrolytically addressed *(Schairer, 2014).* The indication for mobilization under anesthesia or arthroscopic arthrolysis is usually 3 months postoperatively *(Manrique, 2015)* with an extension/flexion deficit of 20°, retrospectively 40° *(Tröger, 2014).* The number of cases with AF is reported in various studies with strongly fluctuating figures of 1.2 to 17% *(Schiavone, 2009*). AF is one of the most common reasons for revision surgery *(Schiavone, 2009).* In two recent large multicenter cohort studies *(Schroer 2013; Lombardi, 2014)* and in a retrospective survey (*Huang, 2015),* incidence rates of 6.9% to 10% were reported. There are many reasons for revision surgery, often due to mechanical causes such as adhesions and scar tissue, and primary AF (also known as dystrophy or vegetative dysregulation) is rarely seen *(Tröger, 2014).*

The analysis shows that, according to current data, there is a high risk of the persistence or occurrence of movement restrictions. The anterior knee joint is less frequently affected after implantation of a knee TEP. For a targeted treatment of the femoropatellar compartment, the cause must first be clarified by differential diagnosis. The kneecap mobilization must therefore be addressed to persistent mobility restrictions of the femoropatellar plain bearing.

After knee TP with patellar replacement, the occurrence of femoropatellar problems is far more common. *Barrack (1997)* and *Campbell (2006)* estimate complications with a prevalence of up to 50%. The causes are a greater contact pressure load due to a small contact surface *(Stukenborg, 2003)* and higher shear forces *(Singerman, 1999)* due to dysfunctional guidance of the medial and lateral patellomensicealia ligaments, which finely control the movement of the patella. In this respect, retropatellar replacement is controversially discussed.

3.1.2.3 Fractures near the joint and tibial head realignments

Adhesion of the synovial membranes is particularly often seen after osteosynthetic treatment after fractures of the tibial head or kneecap *(expert opinion: personal communication from orthopaedic surgeons at the Gut Clinic, St. Moritz).* The soft tissue sheath is then less easy to move and it is not uncommon for a patella baja (deepening of the patella) to develop. This also explains why a restricted caudal-cranial movement component is most commonly seen.

3.1.2.4 Replacement of the anterior cruciate ligament (ACL)

Soft tissue-related movement restrictions of the knee joint are often found after surgical interventions. Many of these fibrosed knee joints affect the Hoffa's fat body or retinacula, which leads to limited mobility of the entire knee joint due to scarring *(Mayr, 2008; Mayr 2014).* From the abundance of studies on suitable replacement plastics, it has been shown that the Lig. patellae is suitable for marcoscopic reasons (ultrastructure, remodeling) *(Jakob, 1990).* The unfavorable findings of the extensor apparatus are to be commented on. In general, good stabilization performance was achieved, but new problems were

created in the anterior knee joint (scarring in the donor area, especially in the area of Hoffmann's fat body). Rosenberg *(1990)* pointed this out early on. A review of the recent literature shows that today the quadriceps or semitendinosus tendon are preferred as transplants and that the symptoms of femoropatellar pain syndrome are therefore seen less frequently.

3.1.3 Repetitive Strain Stresses

3.1.3.1. Motorized Motion Rails (CPM)

Motorized motion splints are of great importance in the postoperative early rehabilitation phase with limited joint mobility. Intermittent dynamic mobilizations provide specific chronic stretching stimuli and trigger structural adjustments of the plastic tissue. Motorized motion splints for continuous movements are therefore firmly anchored in the guidelines of medical professional associations for the follow-up treatment of fractures close to the joint, for tibial head realignments, after ACL replacement and other indications.

The use of motion splints is considered useful and indispensable due to the state of knowledge in joint hypomobility and in the early stages of the postoperative healing process such as bleeding, granulation tissue, oedema and generally in soft tissue-related movement restrictions (fibrosis) (*Milne, 2003; Haller, 2015*). However, the therapeutic benefit of motorized motion splints (CPM) is also controversially discussed with regard to the long-term healing process *(Lenssen, 2008; Harvey, 2014; Herbold, 2014).* In more recent studies, the developmental trajectories of movement deficits initially progress faster with CPM application, but the effect levels out over longer observation periods.

3.1.3.2. Manual therapy Treatment Connective tissue Structures of anterior knee joint

Manual techniques, such as those used in physiotherapy, improve the displacement of ligamentous components (Figs. 1 – 3). A finely balanced ligamentary system controls the sliding and displacement movements of the patella in the trochlea *(Kyung, 2008).* Both longitudinal tensile forces of the quadriceps and patellar tendon, as well as tensile forces of the lateral retinacula, which act in the transverse direction, have a load-balancing function. By directing the patella in the femoral groove, they compensate for the incongruities of the cartilage surfaces and distribute the forces over a large cross-section.

It should be added that after a knee TEP, the medial or lateral
Kneecap mobilization has no effect on knee function *(Ota, 2010).*

In the case of structural movement restrictions, only slightly - especially in the case of pathological adhesion of the capsular fold - should be entered into the tissue resistance *(Hüter-Becker, 2009),* without provoking pain, so as not to trigger a sympathetic reflex dystrophy *(Faust, 2015).* The movement sector is continuously adjusted to the current pain threshold in order to achieve a maximum range (amplitude).

Fig. 1: Joint technique for femoropatellar stress pain with increasing knee flexion due to reduced sliding of the patella and translational movement in the tibiofemoral joint.

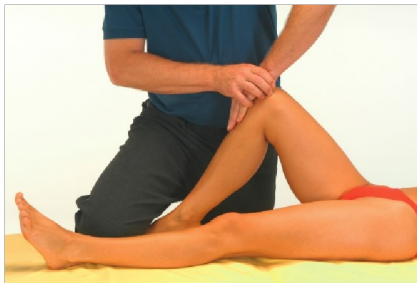

Fig. 2: The knee is bent while the examiner exerts light pressure on the patella with one hand.

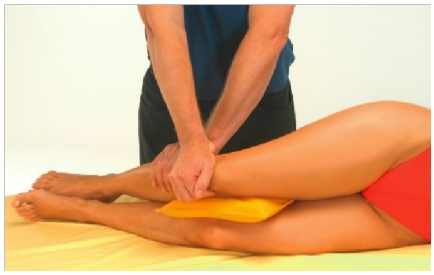

Fig. 3: The knee is extended and the examiner moves the patella alternately from proximal to distal or lateral and medial under light pressure (low retropatellar compression) with limited sliding function *(Winkel, 1985).*

Aim of the study

The aim of this study is to determine the effectiveness of the Patello device. We would like to provide evidence of a displacement of the patella in the caudal / cranial direction by the Patello device.

The primary outcome is the objectification of the displacement of the patella measured with an imaging ultrasound device (esaote MyLabClassicC, Genoa, Italy, www.esaote.com).

As a secondary outcome, the subjective well-being of the subject is recorded, measured using a visual analogue scale (VAS scale 0 - 10).

In order to record a possible positive effect of repetitive mobilization, the measurements are carried out several times: after the positioning of the device (1st measurement, pre-mobilization), after 1 mobilization, after 10 mobilizations, after 20 mobilizations, after 30 mobilizations and after 50 mobilizations (2nd to 6th measurement). The measurements are carried out on 2 days, with a 2-day break in between. The settings are redefined per measurement day, but are maintained during measurements 1-6 to guarantee comparability.

3.2 Medical product and indication

The Patello is a device for "Continuous Passive Motion" (CPM) of the patella. It grips the kneecap and mobilizes it in the caudal / cranial direction. Among other things, the system supports rehabilitation in the event of limited mobility of the knee joint, such as knee surgery (see Chapter 3).
The most important components of the Patello are highlighted in the following image:

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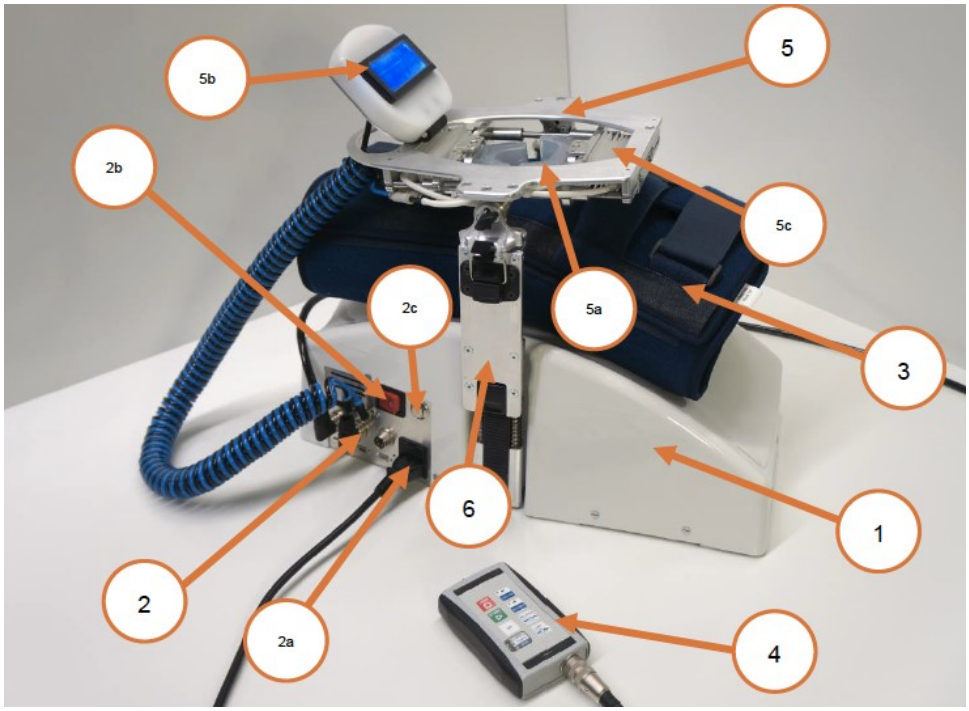

Fig. 4: Patello

1. Knee brace
2. Switch panel
    a. Slot for power plug
    b. On/Off Switch
    c. Reset button
3. Knee brace
4. Handheld control unit with emergency stop switch
5. Essay
    a. Patellar Gripper
    b. Display
    c. Air cushion
6. Lifting columns

Handling Patello

1. To turn on the Patello:

Press the red on/off switch on the switch panel. The device will start initializing. After initialization is complete, the device switches to teaching mode (visible on the display).

2. Moving the grippers:

Press the "Grip" button on the hand control unit. The grippers move together until they grasp the patella from caudal and cranial.

Fig. 5: Handheld control unit

3. Operate and release the emergency stop: Switch the emergency stop toggle switch on the handheld control unit to "O". The grippers relax and the display shows the emergency stop mode. Switch the emergency stop toggle switch back to "I". Press the reset button on the switch panel.


Fig. 6: Emergency stop toggle switch

3.3 Preclinical evidence

See Chapter 3.1 above.

3.4 Current clinical evidence

To the knowledge of the authors, there are currently no studies that have investigated apparatus-based, passive continuous mobilization in the caudal / cranial direction of the patella. The majority of existing studies are limited to the effect of manual therapy interventions (see 3.1 Background and Rationale below).

3.5 Medical product: method of application in the study

As part of this clinical study, the displacement of the patella in the caudal / cranial direction by the Patello device will be recorded and quantified. This is to prove the effectiveness of this device. For more detailed specifications, see Chapter 3.2 Medical Device and Indication.

3.6 Intervention Patello

In order to record a possible positive effect of repetitive mobilization, the measurements are carried out several times: after the positioning of the device (1st measurement, pre-mobilization), after 1 mobilization, after 10 mobilizations, after 20 mobilizations, after 30 mobilizations and after 50 mobilizations (2nd to 6th measurement). The measurements are carried out on 2 days, with a 2-day

break in between. The settings are redefined per measurement day, but are maintained during measurements 1-6 to guarantee comparability.

The exact procedure for the measurements can be seen in Chapter 9.2.

Randomization

The allocation of the application page will be randomly assigned by lot.

3.7 Risk / Benefits

The possible occurrence of risks from the use of the Patello is to be assessed as small: short-term skin irritations and/or paraesthesia could occur.

The subjects do not benefit from participating in the study. The study serves to prove the effectiveness of the Patello device. If this is the case, the device can be used in the rehabilitation process of patients with the above-mentioned knee joint problems.

Justification of the choice of population

This series of studies will be conducted with healthy adults to assess the extent of the
Quantify displacement of the kneecap by means of the patello.

Table 1: Overview of inclusion and exclusion criteria

Inclusion Criteria	**Exclusion criteria**
- Adults aged 18 to 30 Years - No surgical interventions and/or current complaints (pain at rest or during exertion) on the musculoskeletal apparatus in the area of the lower extremities - closed, intact skin conditions in the knee and thigh area - Don't be afraid of the intervention	- Adolescents and adults over 30 years of age - Surgical interventions and/or current complaints (pain at rest or during exertion) on the musculoskeletal Apparatus in the area of the lower extremities - no closed, intact Skin conditions in the knee and thigh area - Fear of intervention

The test subjects are comprehensively informed about the course of the study and possible risks before they are accepted to participate in the study. You will also receive the information in written form and have the opportunity to ask questions if anything is unclear. The declaration of consent explains to them what their rights and obligations are when participating. In addition, they are informed that they may withdraw from participation at any time without giving reasons, without incurring any disadvantages as a result.

4 STUDY OBJECTIVES

4.1 General objectives

The aim of this study is to measure the effectiveness of the Patello device. It is designed to move the patella on its plain bearing in the caudal / cranial direction, passively and continuously. However, it is still unclear whether and to what extent the displacement of the patella is effective.

4.2 Primary objectives

A primary and secondary outcome was defined as the primary goal. The primary outcome, the displacement of the patella, detected by an imaging ultrasound device (esaote MyLabClassicC, Genoa, Italy, www.esaote.com) and evaluated by a dedicated software (OsiriX, www.osirix-viewer.com), is represented in mm and is considered an objective parameter.

The secondary outcome, the recording of the subjective well-being of the test person, is determined using a visual analogue scale (VAS scale 0-10) and reflected in the number of cm. It is considered a subjective parameter.

4.3 Secondary Objectives

Multiple measurements will be performed to detect a possible sustained and/or cumulative effect of patellar mobilization. The measurements are repeated 2x per week in the same week, with a break of at least 2 days, as described in chapter 4.2.

4.4 Other safety aspects (long-term)

No short-term risks are to be expected from this study other than those discussed so far (see 3.7 Risks / Benefits).

5 STUDY OUTCOMES

5.1 Primary outcomes

A primary and secondary outcome was defined as the primary goal. The primary outcome, the displacement of the patella, detected by an imaging ultrasound device (esaote MyLabClassicC, Genoa, Italy, www.esaote.com) and evaluated by a dedicated software (OsiriX, www.osirix-viewer.com), is represented in mm and is considered an objective parameter.

5.2 Secondary outcomes

Subjective information on general well-being

The secondary outcome, the recording of the subjective well-being of the test person, is determined using a visual analogue scale (VAS scale 0 - 10) and reflected in the number of cm. The value "0" describes "maximum feeling of well-being", the value "10" a "maximum feeling of discomfort". The value is considered a subjective parameter.

Security considerations

No further results are recorded that would serve safety.

Discontinuation of the experiment is the responsibility of the examiner with regard to the subject's subjective feelings and expressions.

If a test subject does not feel comfortable during the intervention according to his or her subjective assessments, he or she can discontinue the experiment and withdraw participation in the study without any disadvantages.

6 STUDY DESIGN

Study design and justification

This clinical effectiveness study investigates the effect of apparatus-based, passive mobilization of the patella. The group size is n = 30.

Table 2: Study design

Time	Preparation	Pre	1 Mob.	10 Mob.	20 Mob.	30 Mob.	50 Mob.
Time (min)		5	10	20	30	40	50
Measurement		1.	2.	3.	4.	5.	6.
Subject information	X						
Consent	X						
Demographics	X						
Intervention			X	X	X	X	X
Ultrasound image		X	X	X	X	X	X
Subj. Well-being		X	X	X	X	X	X

6.1 Method for minimizing influencing factors

6.1.1 Randomization

Randomization is used to randomly determine the application side, left or right knee.

6.1.2 Blinding

Blinding the test persons and/or the examiners is not possible with regard to the intervention.
The implementation of the intervention and the measurements of the primary and secondary outcome parameters are not carried out by the same examiner.

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The blinding of the statistician can be guaranteed, who has no access to the personal data of the test persons and is not present during the data collection.

6.1.3 Other Methods

No other methods are used.

6.2 Procedure for unblinding (code break)

There is no provision for the statistician to be blinded.

6.3 Procedure for unblinding (code break)

Blinding is only permitted if an unforeseen incident or medical problems occur in a subject during or after completion of study participation, which may be attributable to participation in the study.

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7 POPULATION STUDIES

7.1 Inclusion Criteria

Table 3: Overview of inclusion and exclusion criteria

Inclusion Criteria	Exclusion criteria
- Adults aged 18 to 30 Years - No surgical interventions and/or current complaints (pain at rest or during exertion) on the musculoskeletal apparatus in the area of the lower extremities - closed, intact skin conditions in the knee and thigh area - Don't be afraid of the intervention	- Adolescents and adults over 30 years of age - Surgical interventions and/or current complaints (pain at rest or during exertion) on the musculoskeletal Apparatus in the area of the lower extremities - no closed, intact Skin conditions in the knee and thigh area - Fear of intervention

7.2 Recruitment and Screening

Recruitment

The study is being advertised internally at the University of Applied Sciences and Arts Southern Switzerland SUPSI. The exact texts have been prepared according to the checklist of the Cantonal Ethics Commission Zurich.

As advertisements (text visible):

- Facebook page of the SUPSI Physiotherapy Training https://www.facebook.com/supsi.physiotherapie/notifications/

Screening

Interested parties should contact the director of studies at the research office of the University of Applied Sciences and Arts Southern Switzerland (SUPSI) for an initial consultation. Interested parties will be informed about the conditions of participation, the content and procedure of the study, as well as the amount of compensation. If you are still interested, the written study information and the confirmation of consent will be handed out. Interested parties can read the written documents at their leisure and ask any questions. If you agree to the terms of the study and wish to participate in the study, bring the signed documents to the principal investigator. A copy of the signed declaration of consent (by the interested party and the study director) will be handed over to the interested party. The health questionnaire is then filled out, which clarifies the suitability of the interested party to participate in the study. If the inclusion criteria are met, the interested party has passed the screening and is admitted to participate in the study.

7.3 Group assignment

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There will be no group assignment.

7.4 Discontinuation of study participation

If a participant withdraws from the study before the measurements have begun, the allocation lot is returned to the pot in a new envelope and a new participant is sought.

If a participant is eliminated during the measurements, all data collected up to that point will be evaluated as far as possible and included in the data analysis (in accordance with Art. 9 ClinO). In this case, no new participant will be recruited to collect the missing records.

The data will be stored encrypted with a code during the study period and evaluation of the data.

The conditions for the termination of the experiment were described in chap. 5.4.

Participants are not disadvantaged by discontinuing their participation in the study.

8 STUDY INTERVENTION

8.1 Medical Device ID

8.1.1 Intervention product

The Patello is a device for "Continuous Passive Motion" (CPM) of the patella. It grips the kneecap and mobilizes it in the caudal / cranial direction. Among other things, the system supports rehabilitation in the event of limited mobility of the knee joint, such as knee surgery (see Chapter 3).
The most important components of the Patello are highlighted in the following image:

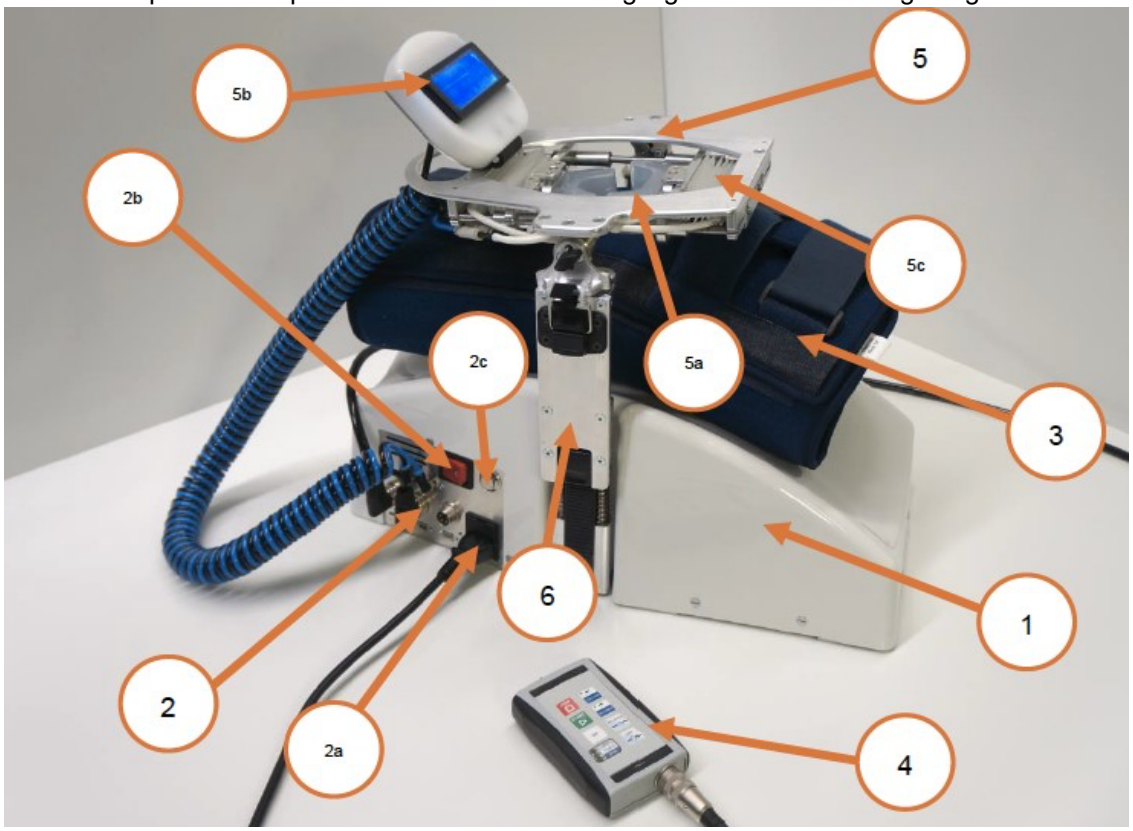

Fig . 7: Patello

1. Knee brace
2. Switch panel
    a. Slot for power plug
    b. On/Off Switch
    c. Reset button
3. Knee brace
4. Handheld control unit with emergency stop switch
5. Essay
    a. Patellar Gripper
    b. Display
    c. Air cushion

6. Lifting columns

Handling Patello

1. To turn on the Patello:

Press the red on/off switch on the switch panel. The device will start initializing. After initialization is complete, the device switches to teaching mode (visible on the display).

2. Moving the grippers:

Press the "Grip" button on the hand control unit. The grippers move together until they grasp the patella from caudal and cranial.

Fig. 8: Handheld control unit

3. Operate and release the emergency stop: Switch the emergency stop toggle switch on the handheld control unit to "O". The grippers relax and the display shows the emergency stop mode. Switch the emergency stop toggle switch back to "I". Press the reset button on the switch panel.

Fig. 9: Emergency stop toggle switch

Securing the test subjects

Through the screening process (filling out the health questionnaire with examination of the inclusion and exclusion criteria), only subjects who are suitable for participation in the study are recruited. In this way, at-risk test subjects are identified at an early stage and are not recruited/included in the study.

8.1.2 Control intervention

No control intervention is carried out.

8.1.3 Packaging, labeling and use

n/a

8.1.4 Storage

When the patello is not in use, it is stored in a lockable cabinet.

8.2 Administration of the experiment

Since no drugs or invasive methods are used, the experiment is not discussed further in chapter 8.2-8.4 and only chapter 9 is referred to.

8.2.1 Experimental intervention

The experimental intervention (repetitive passive mobilization of the patella in the caudal / cranial direction by the patello) will be carried out on the right or left leg according to randomization.

8.2.2 Control intervention

There is no control intervention.

8.3 Dosage, application modification

In a first phase, the device settings (contact and mobilization pressure of the patello) are adjusted based on the well-being of the test subject. The mobilization pressure is built up individually to the tolerance limit so that a displacement of the patella takes place. The selected intensities are noted and maintained during all measurements per subject.

8.4 Adherence to the study intervention

The test subjects are not unnecessarily distracted by the examiners or the study director with conversations. Communication is kept to a minimum, only study-related discussions are held in order not to influence the results and to ensure homogeneity.

8.5 Follow-up treatment of eliminated participants

Data already collected from eliminated participants will be evaluated as far as possible and will be included in the data analysis of the study.

There is no disadvantage for the participants if they discontinue their participation in the study and no further interventions are necessary for follow-up treatment.

If study participation was discontinued due to an excessive reaction/injury occurring during study participation, this will be recorded and reported to the sponsor investigator (head of the research laboratory), who is also the study leader, and the supervisor of the study. If medical care is necessary, the report is forwarded to the business liability insurance of Thim van der Laan AG (Basler Versicherung) in order to ensure the appropriate follow-up treatment.

8.6 Preventive measurements

The questionnaire determines the eligibility to participate in the study by recording the inclusion and exclusion criteria.

8.7 Accompaniments

No further side effects are expected from study participation.

8.8 Liability

The measurements take place exclusively in the research laboratory of the University of Applied Sciences and Arts Southern Switzerland SUPSI in Landquart. Thus, there is no transport of the apparatus used or the test subjects. Liability for transport is therefore not necessary.

8.9 Return of the medical device

The Patello device is returned to the manufacturer at the end of the measurement period.

9 STUDY STRUCTURE & EVALUATION

9.1 Schedule Study Protocol

Table 4: Overview of the measurement process

Time	Preparation	Pre	1 Mob.	10 Mob.	20 Mob.	30 Mob.	50 Mob.
Time (min)		5	10	20	30	40	50
Measurement		1.	2.	3.	4.	5.	6.
Subject information	X						
Consent	X						
Demographics	X						
Intervention			X	X	X	X	X
Ultrasound image		X	X	X	X	X	X
Subj. Well-being		X	X	X	X	X	X

9.1.1 Measurement of primary and secondary outcomes

The primary outcome, the displacement of the patella, detected by an imaging ultrasound device (esaote MyLabClassicC, Genoa, Italy, www.esaote.com) and evaluated by a dedicated software (OsiriX, www.osirix-viewer.com), is represented in mm and is considered an objective parameter.

The secondary outcome, the recording of the subjective well-being of the test person, is determined using a visual analogue scale (VAS scale 0 - 10) and reflected in the number of cm. The value "0" describes "maximum feeling of well-being", the value "10" a "maximum feeling of discomfort". The value is considered a subjective parameter.

9.1.2 Measurement of primary outcomes

The ultrasound probe is used to record one reference point on the patella and one on the thigh (lateral epicondyle femoris) and store it as an image. After caudal mobilization, the same reference points are recorded and again stored as an image. This process is performed before the first and after each mobilization interval (1st-6th measurement). With the OsiriX software, the DICOM images obtained can be analyzed and evaluated. The distance of the displacement of the patella is shown in mm and transferred to the data sheet.

9.1.3 Measurement of secondary outcomes

Using a visual analogue scale, which goes from 0 – 10, subjective well-being is asked directly after the mobilisation intervals. The value "0" stands for "maximum well-being" and the value "10" for "maximum discomfort". The values are transferred to the data sheet.

9.1.4 Collection of further results

No further results will be collected.

9.1.5 Collection of safety parameters

No safety parameters are collected except for the health questionnaire.

9.1.5.1 Unfavorable Events

-

9.1.5.2 Laboratory Parameters

-

9.1.5.3 Vital signs

-

9.1.6 Collection of data in case of early termination of studies

For the participants, there is no disadvantage in the event of an (arbitrary) discontinuation of study participation and no further interventions are necessary for follow-up treatment. The data collected to date will be evaluated as far as possible and included in the data analysis (in accordance with Art. 9 ClinO).

If study participation was discontinued due to an excessive reaction/injury occurring during study participation, this will be recorded and reported to the sponsor investigator (head of the research laboratory), who is also the study leader, and the supervisor of the study. In the event of necessary medical treatment, the report is sent to the business liability insurance of Thim van der Laan AG (Basler Versicherung).

The following are recorded:

- Date and time of the incident
- Course of the incident
- Persons involved & witnesses
- Study ID (specified by the CEC)
- Personal data of the person concerned (if not previously recorded)

9.2 Procedure at each visit of the test subjects

9.2.1 Subject recruitment – screening and randomization

The study is being advertised internally at the University of Applied Sciences and Arts Southern Switzerland SUPSI. Interested parties should contact the director of studies at the research office of the University of Applied Sciences and Arts Southern Switzerland (SUPSI) for an initial consultation. Interested parties will be informed about the conditions of participation, the content and procedure of the study, as well as the amount of compensation. If you are still interested, the written study information and the confirmation of consent will be handed out. Interested parties can read the written documents at their leisure and ask any questions. If you agree to the terms of the study and wish to participate in the study, bring the signed documents to the principal investigator. A copy of the consent form signed by both parties will be given to the interested party. The health questionnaire is then filled out, which clarifies the suitability of the interested party to participate in the study. If the inclusion criteria are met, the interested party has passed the screening and is admitted to participate in the study. This is followed by the randomization of the application page by drawing lots and making an appointment for the 2 measurement days, in the same week with at least 2 days break between the measurements.

9.2.2 Preparation of test subjects

The test subject wears shorts and is barefoot. He sits down on the treatment table. The backrest is raised so that an upright sitting position can be assumed. The leg of the application side is placed on the patello and fixed according to the product description (Chapter 8). The foot is placed underneath so that the leg can lie relaxed. In a first phase, the contact pressure of the device is adjusted based on the well-being of the test subject. The setting is noted.

9.2.3 Sequence of the measurements

After determining the contact pressure, the pre-mobilization measurement is carried out (**1st measurement**). The ultrasound probe is used to visualize a reference point on the patella and at the same time the lateral femoral epicondyle on the thigh and save it as an image. Afterwards, the mobilization pressure is built up individually up to the tolerance limit of the test subject so that a displacement of the patella caudally takes place. The maximum deflection of the patella to the reference point on the thigh is determined, the device settings are noted and transferred to the data sheet (**2nd measurement**).

As described above, further measurements are carried out according to the following scheme: after 10 mobilisations (**3rd measurement**), after 20 mobilisations (**4th measurement**), after 30 mobilisations (**5th measurement**) and after 50 mobilisations (**6th measurement**).

Table 5: Overview of the course of studies

Time	Preparation	Pre	1 Mob.	10 Mob.	20 Mob.	30 Mob.	50 Mob.
Time (min)		5	10	20	30	40	50
Measurement		1.	2.	3.	4.	5.	6.
Subject information	X						
Consent	X						
Demographics	X						
Intervention			X	X	X	X	X
Ultrasound image		X	X	X	X	X	X
Subj. Well-being		X	X	X	X	X	X

9.2.4 Multiple visits

The procedure described above is carried out over 2 days. We know from practice that patients are usually treated by a physiotherapist 1-2 times a week. Thus, the subjects are measured 2x within the same week in order to be able to make a practical statement about possible lasting and/or cumulative effects.

At the end of both measurement days, he/she will receive the amount due to him/her according to the advertisement.

The lump sum is CHF 50.

9.3 Drug study

-

9.3.1 Definition and assessment of (serious) adverse events and other safety related events

-

9.3.2 Reporting of serious adverse events (SAE) and other safety related events

-

9.3.3 Follow up of (Serious) Adverse Events

-

9.4 Medical Device Category C studies

The Patello device is an innovative product that does not yet have CE certification. All individual components of the device are CE certified.

In this experimental study for the effectiveness study, 30 test subjects are to be tested. The study focuses on basic findings. It serves as proof of effectiveness. The monitoring for quality assurance is carried out by Prof. Dr. Peter Clarys.

9.4.1 Definition and Assessment of (Serious) Adverse Events and other safety related events

An adverse event (ADVERSE EVENT) AE) is any unfortunate medical occurrence in a study subject who is exposed to the intervention (as listed in Chapter 8.1.1) that is not necessarily causally related to the study process. An AE can therefore be any adverse and unintended sign, symptom, or temporal illness with the use of an intervention product (according to Chapter 8.1.1), either or in relation to the medical intervention product (according to Chapter 8.1.1).

According to swissethics.ch, a serious adverse event (SAE) is classified as any unfortunate medical occurrence that results in death, is life-threatening, requires or prolongs hospitalization of the subject, results in a persistent or significant disability/inability, or is a congenital anomaly/birth defect. In our study, an SAE is not to be expected.

If the intervention leads to a side effect, this is classified as a safety-relevant event by the study leader. For the affected study participant, the study is completed at this time, and the data already collected will be processed as described in chapters 7.4 and 9.1.6.

On the last page of the subject-specific demographic data collection sheet, the following are recorded:

- Date and time of the incident
- Course of the incident
- Persons involved & witnesses
- Study ID (specified by the CEC)
- Personal data of the person concerned (if not previously recorded)

9.4.2 Reporting of (Serious) Adverse Events and other safety related events

In accordance with Art. 37, Art. 42, Art. 43

9.4.3 Follow up of (Serious) Adverse Events

A safety-related event is logged and immediately reported to the sponsor investigator (head of the research laboratory), who is also the study leader, and the supervisor of the study.

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The CEC will be informed as soon as possible and appropriate changes will be made to the protocol of the study. Further explanations can be found in chapter 2.10. Safety and protective measures must be reported to the responsible CEC within two days.

The report continues to the business liability insurance (Basler Versicherung) of Thim van der Laan AG in Landquart.

9.5 Medical Device Category A studies

-

9.5.1 Definition and recording of safety-relevant events

-

9.5.2 Reporting of Safety related events

-

9.5.3 Notification of a security-relevant event

-

10 STATISTICAL METHODS

10.1 Hypotheses & Factors

Mobilization of the patella in the caudal / cranial direction by the patello – repetitive mobilizations versus one-time mobilization Objective displacement of the patella:

H0 The patella does not shift significantly more during repetitive mobilizations than during a single mobilization by the patello.

H1 The patella shifts significantly more during repetitive mobilizations than during a single mobilization by the patello.

Subjective well-being of the subject:

H0 Subjective well-being does not change significantly more with repetitive mobilizations than with a single mobilization by the patello.

H1 Subjective well-being changes significantly more with repetitive mobilizations than with a single mobilization by the patello.

A 2-factor analysis is carried out.

Factor 1: Intervention

Factor 2: Time intervention: Start (pre-intervention, 1st measurement), after a single mobilization (2nd measurement), after 10 (3rd measurement), after 20 (4th measurement), after 30 (5th measurement), after
50 mobilizations (6th measurement)

Sample size

The planned sample size is n = 30 subjects. This size is expedient, time-wise and financially feasible for the study.

10.2 Criteria for the statistical use of data in the case of incomplete data sets

A complete mobilization interval must be completed for the data to be included in the study. If a mobilisation interval (e.g. interval '20 mobilisations', but termination after 15 mobilisations) has to be interrupted, only the previously collected complete mobilisation interval data can be used. This ensures that all data remains homogeneous and comparable. No substitute is sought for the missing mobilization interval data.

10.3 Planned analyses

10.3.1 Datasets and Data Population

Only complete mobilization interval datasets will be included in the study and integrated into the analysis. No new test subject is being sought to replace the missing data.

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10.3.2 Primary Analysis

The statistical data analysis is carried out by the statistician after completion of the data collection of the entire project.

Repeated measures analysis of variance (MANOVA) A 2-factor analysis is performed.

Factor 1:	Intervention
Factor 2:	Time intervention: Start (pre-intervention, 1st measurement), after a single mobilization (2nd measurement), after 10 (3rd measurement), after 20 (4th measurement), after 30 (5th measurement), after 50 mobilizations (6th measurement)

The significance level is set at $P < 0.05$, and the statistical data analysis is carried out with SPSS V. 24.

10.3.3 Secondary Analysis Not

Available.

10.3.4 Interim analyses

The data is processed after the project ends. No additional interim analyses are planned.

10.3.5 Security Analyses

No security analyses are provided.

10.3.6 Discrepancies

Deviations from the planned statistical analysis are recorded and justified and reported to the CEC in the annual report.

10.4 Drop-outs and Missing Data

If a subject wishes to withdraw from the study before the end of all measurement days and interventions, or if he or she has to be excluded by the study leader due to an event, the complete mobilization interval data collected up to that point will be included in the data analysis.

No replacement of test persons is being sought for the missing data sets.

11 QUALITY ASSURANCE AND CONTROL

11.1 Data Archiving

11.1.1 Forms

Data protection and confidentiality are guaranteed and no personal data is presented or published. The signed declaration of consent, as well as the completed questionnaire with the other personal data and demographic and medical personal data are stored in the original as a study document in a locked filing cabinet. Only the head of the study (head of the research laboratory of the University of Applied Sciences and Arts Southern Switzerland SUPSI, Physiotherapy Graubünden) has access (key possession) to this

cabinet. The encryption of the identity of the test persons is not digitally recorded, i.e. surname, first name and date of birth are not digitally recorded in any way.

Direct access to the personal data will continue to be allowed only to authorized persons of the CEC.

11.1.2 Specification of Forms

The data collected in writing is recorded in the form listed in the enclosures and is marked as study data. They are therefore subject to data protection and are stored in accordance with the information described in chapter 12.1.1.

11.1.3 Archiving the Data

The data collected will be kept for 10 years. Data protection will continue to be guaranteed.

11.2 Data Management

11.2.1 Data Management System

The raw data of the ultrasound are processed with the OsiriX software and the results are transferred to the data sheet of the test subject (number of mm displacement of the patella). The subjective perceptual parameters are asked orally and the answers are handwritten on the data sheet. For further data analysis, Microsoft Excel is used by Windowsâ. Microsoft Excel from Windows is also used for data pooling and for the graphical representation of the end data.

11.2.2 Data Security and Backup

The digital data is encrypted and treated confidentially, access to the personal data is not allowed to third parties. The digital data collected is stored solely on the institute's own computers and is not passed on to any external persons or transferred to other computers. Access to the computers of the research laboratory is only granted to the principal investigator and the investigators (listed in Chapter 1), as well as persons authorized by the CEC.

11.2.3 Analysis and Archiving

After collection, the digital data is encrypted and stored on another external hard drive for further backup. This is stored in a locked filing cabinet to ensure data protection.

11.2.4 Validation of electronic data

Immediately after data collection, the quality of the data is checked and verified with the help of the visual representation.

11.3 Monitoring

The data collected can be viewed by authorised persons at any time (see Chapter 12.2.2)

The study is to be monitored by the following person:

Prof. Dr. Peter Clarys
Vrije Universiteit Brussels
Faculty of Physical Education and Physiotherapy
Pleinlaan 2, 1050 Brussels peter.clarys@vub.ac.be

11.4 Audits and inspections

A report on the current status of the study is given orally to the study supervisor (Prof. Dr. Peter Clarys) on a monthly basis. This also includes demonstrating and presenting results and statistical analyses.

An annual report on the course of the study will be submitted to the CEC. Authorized persons of the CEC can view the data forms as well as the digital data on the institute's own computers at any time.

Data protection is guaranteed at all times.

11.5 Confidentiality and data protection

The examiners ensure that the privacy of the participant is guaranteed. In particular, data protection and confidentiality are guaranteed and no personal data is presented or published. The signed declaration of consent, as well as the completed questionnaire with the other personal details, are kept in the original as a study document in a locked filing cabinet.

The digital data is encrypted and treated confidentially, access to the personal data is not allowed to third parties. The digital data collected is stored solely on the institute's own computers and is not passed on to any external persons or transferred to other computers.

Direct access to the personal data is only allowed to authorized persons of the CEC.

11.6 Retention of biological material and health-related data

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12 PUBLICATION AND DISCLOSURE OF DATA

The examiners ensure that the privacy of the participant is maintained. In particular, the data protection and confidentiality of the data are guaranteed and no personal data is presented or published nor passed on to outsiders and unauthorized persons.

14 FUNDING AND SUPPORT

14.1 Financing

The study is being conducted by the University of Applied Sciences and Arts Southern Switzerland SUPSI, Physiotherapy Graubünden with a
CTI support contribution. The auditors are employed by this institute and are remunerated for their work on this study in accordance with their employment contracts. No further support is needed.

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15 INSURANCE

There is a business liability insurance with Baloise Insurance for Thim van der Laan AG in Landquart.

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