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Clinical Feasibility of Personalized Articulating Knee Joint Distraction

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Abstract

Introduction: Knee Joint Distraction (KJD) is a joint preserving procedure that can postpone arthroplasty in case of knee osteoarthritis. Distraction is applied with an external rigid fixation device for six weeks. To reduce the burden during treatment due to the absence of joint flexion, we developed a personalized articulating KJD-device. Its technical feasibility, joint-specific motion reproduction, was previously pre-clinically demonstrated. In this study, clinical feasibility of this new device was tested in three patients.

Materials and Methods: Patients received conventional KJD treatment with a rigid distraction device. After two to four weeks, the device was removed during a one-day hospital visit and the joint was flexed on a Continuous Passive Motion (CPM) device until 30 degrees of flexion was reached, or motion became too painful. Subsequently, the articulating frame was assembled and personalized with custom hinge parts based on a non-invasive joint motion measurement. Weight-bearing and non-weight-bearing radiographs were intended to be taken at 0, 15, and 30 degrees of flexion for joint space width measurements. Finally, the articulating device was replaced by the rigid distractor and conventional treatment was continued.

Results: For none of the patients, the articulating distractor could be personalized adequately. Insufficient joint motion was achieved during CPM due to intolerable pain at the pin sites.

Conclusions: Despite confirmation of joint-specific articulating distraction on cadaveric legs, clinical feasibility could not be demonstrated, mainly due to painful motion of soft tissues along the bone pins. Safe and solid anatomical location of pins is considered to hamper articulating distraction.

Keywords: Knee osteoarthritis; Joint distraction; Articulation; Joint-specific; Personalized

Introduction

Osteoarthritis (OA) patients encounter progressive pain and functional disabilities, including joint stiffness, due to degeneration of the joint tissues. OA is highly prevalent in the knee joint, which causes a significant contribution to the current general healthcare burden [1-5]. Moreover, the incidence of OA, and with that healthcare burden of this disease, is anticipated to increase when considering the occurrence of obesity and aging [6-8].

The available treatment strategies for knee OA are limited and focus primarily on minimizing the functional disability, inflammation, and pain in a conservative manner since still no unambiguously proven effective disease modifying approaches are available [8]. Progress in the development of joint sparing procedures however, has demonstrated the regenerative capacity of the osteoarthritic knee and with that the delay for conventional last resort therapy such as Total Knee Arthroplasty (TKA) [9-11].

The choice for TKA needs to be carefully considered specifically in case of younger patients. A high failure rate and limited patient satisfaction [12-15], is often followed by complex and costly revision surgery, especially for the physically active patients below the age of around 65 years [14,16-18].

Different joint saving surgical approaches can be applied dependent on the amount of joint degeneration. For focal cartilage defects, as precursors for OA, several options are available [19]. Unilateral tibiofemoral knee OA in case of mechanical axis deviation can be treated with osteotomy [20,21]. Alternatively, unilateral partial unloading, and with that pain relief, is aimed for by implanting a subcutaneous unloading device (KineSpring [22]). Although relieving pain, this technique has not demonstrated tissue structure repair. Also, uni-compartmental knee arthroplasty may be considered partially joint saving, by saving the other compartment from arthroplasty [23-26].

For predominant medial or more generalized tibio-femoral knee OA, Knee Joint Distraction (KJD) has been introduced and preservation of the joint has been demonstrated. The procedure can postpone the first TKA to a suitable moment later on in life, serving patients with a better chance of successful TKA treatment, and preventing revision surgery [12,13,18].

Most interestingly, KJD results in progressive and prolonged, clinically relevant, structural tissue regeneration (cartilage thickness

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and volume on weight bearing radiographs and quantitative MRI, as well as biochemical markers analyses for collagen type-II) [9,27,28]. Randomized controlled trials comparing KJD to HTO and TKA demonstrated similar efficacy, although follow-ups are still short [29-31]. Health technology assessment suggests, although based on the still limited data, KJD to have the potential of being very cost-effective specifically for younger (<65 years of age) patients [10]. As such, KJD is introduced as a disease modifying therapy delaying the need for TKA. Importantly, KJD leaves open the option for save follow-up treatment with conventional strategies, such as a TKA [32].

The procedure of knee joint distraction

In KJD, the bony ends of the tibiofemoral joint are set at a distance of approximately 5 mm with an external fixator attached to the femur and tibia, e.g. as shown in (Figure 1), thereby distracting the joint in a bilateral (lateral and medial) manner, for a minimal period of six weeks [33]. Pin insertion sites are carefully chosen to provide sufficient stability during distraction and to prevent neuro-vascular and joint damage, as well as to allow safe TKA later in life (uncompromised arthroplasty area) [27,40]. This procedure is performed in several clinics in the Netherlands and Belgium, in regular practice now. Although patients are very satisfied with the results, the treatment is a six weeks burden, with a high risk of pin-tract infections as major complication. These pin-tract infections can be treated effectively with oral antibiotics. Joint motion is limited to a small axial motion from built-in springs when the joint is loaded and unloaded during walking with the frame. From this motion, intermittent hydrostatic pressure changes result, which are considered essential for the continuation of cartilage nourishment and stimulation of the affected tissues to reset to a regenerating state during and after treatment [9,27,34,35]. The actual absence of joint flexion, remains a six weeks burden.

Study Rationale

During conventional knee distraction, joint motion is restricted and in time, the joint stiffens and muscle strength and mass is affected. The absence of flexion poses a significant discomfort for patients during the period of distraction, despite the good and prolonged clinical benefit. Moreover, rehabilitation is required for restoring the muscular condition [9].

Motivated to solve the burden of stiff conventional knee distraction, and inspired by the reported benefits of articulating distraction in case of ankle OA [36,37], as well as the clinical efficacy of hinged knee joint distraction in Japanese case series, an articulating knee joint distractor was developed [38]. For this purpose, the same anatomical pin insertion sides for external fixation and equal distraction characteristics (5 mm distraction with 3 mm axial deflection from built-in springs; proven clinical benefit), was aimed for. Because of the complexity of the knee joint motion, a personalized approach was chosen for. The personalized approach allows for accurate reproduction of the complex kinematics that varies between patients while no intra-articular alignment tool (e.g. Kirschner wire) or 3D image-based treatment planning software is required [39,40]. This is in contrast to the Japanese approach, which uses an intra-articular technique with an imposed (generalized) motion path [38]. Moreover, the joint-specific approach allowed for a sufficiently large anatomical envelop for choosing optimal bone pin positions for each individual, which eases the procedure, possibly reduces surgery time, and enabling it for every individual [40]. This approach may lead to improvement of the comfort for the patient, keeping costs for the procedure in mind.

In short: to achieve joint-specific knee distraction, the physiological joint motion is determined for every patient using a non-invasive joint motion measurement device, followed by 'on site' fabrication of joint-specific frame components, one at each joint side, that provide accurate reproduction of the patient specific motion [39,40]. This accurate motion reproduction is considered important for preventing the possibility of damaging compressive loads on the cartilage due to incongruence of the articulating surfaces, which may occur when generalized knee motion is dictated to a joint. The process of measuring joint motion and subsequent production of joint-specific parts is automated and can be completed within an hour after surgery (pin placement), allowing for application during a one-day visit of the patient to the clinic.

The joint-specific distractor was pre-clinically tested in a technical feasibility study, which demonstrated that the mechanical characteristics of the articulating device were of equal proportions when compared to the conventional distraction frame [40]. Furthermore, the procedure of measuring, fabricating and assembling was tested on cadaver knees. From that it was concluded that the new articulating knee distractor was technically feasible. The goal of the present study is to test the clinical feasibility of the joint-specific knee distractor.

Materials and Methods

Study design

The choice for external fixation with equal bone pins at the same anatomical sites as used in conventional knee distraction [40], was based on the limited anatomical options for save (prevention of neuro-vascular damage and extra-articular placement) and mechanically functional bone pin placement. The positions were proven safe and effective. Moreover, for the present study, it allowed for testing the device in patients that were treated in clinical practice with conventional stiff distraction therapy, with testing of the clinical feasibility of the new device during a single study day for each patient. Since patients were not withheld of regular distraction treatment, the clinical test was ethically acceptable.

Testing of the device in patients that are treated with conventional distraction made this a non-interventional, observational, clinical feasibility study. Nonetheless, for evaluation of the distractor performance, radiographs (eight additional radiographs compared to standard care) were needed. No follow-up of the patients was done. Medical ethical approval was obtained from the University Medical Center of Utrecht (NL48424.041.14) according to the principles of the Declaration of Helsinki.

Distraction method and device

At both the medial and the lateral joint side, a femoral part of the articulating device was aligned in the sagittal plane of motion with the condyles, and a tibial part was axially aligned with the tibia, followed by fixation of those parts to the bone pins within the bone pin clamps. Next, a modular measurement device was coupled to the femoral and tibial parts and the joint-specific motion was recorded. Subsequently, the motion data was automatically processed by an in-

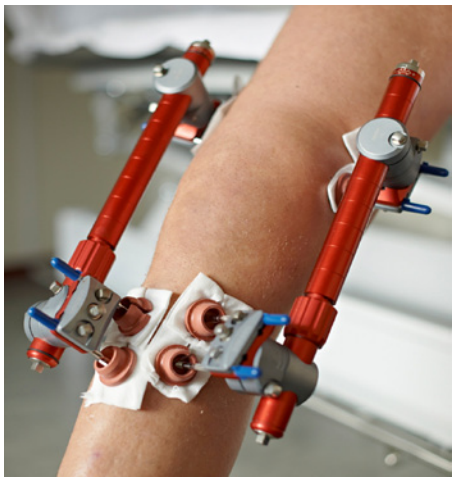

Figure 1: Knee joint distraction as conventionally applied in clinical practice for treatment of severe tibiofemoral osteoarthritis.

house developed software package for computer numerical controlled manufacturing of parts that mimic the joint-specific motion when assembled [40].

In full extension, the joint was distracted (5 mm) and the quality of motion was subsequently evaluated by an orthopedic surgeon for abnormalities (crepitus) before the functional testing was performed and radiographs to be taken.

Patient selection

Patients that were considered for treatment with conventional knee joint distraction in general practice at the orthopedics department in the University Medical Center Utrecht in case of severe tibiofemoral osteoarthritis, were screened and included when inclusion and exclusion criteria were met.

Study procedure

The steps in the study, including the personalization, are represented in (Figure 2) and comprise:

- The patients were treated with conventional knee distraction and received 5 mm distraction (2 mm per operatively and increased with additional 3 mm in the next three days) for a total period of six weeks according to standard protocol.

- After two to four weeks conventional distraction, patients visited the clinic for one day in which the study activities were conducted.

- A standardized weight-bearing radiograph was made to establish the extend of distraction, and the conventional distraction frame was removed, while bone pins remained *in vivo*.

- On a Continuous Passive Motion (CPM) device, controlled in speed and in the amount of flexion by the patient, the joint was flexed to overcome joint stiffness until at least 30 degrees of flexion was reached. (This approach was based on a previously performed study where the distraction device was two weekly removed for CPM training to prevent contractures during prolonged distraction [27]).

- Subsequently, the articulating frame was assembled to the bone pins, using the same bone pin clamps for fixation. The measurement device was modularly attached to the articulating frame components, followed by measurement of the joint-specific motion (Figure 3).

- From the obtained motion data, joint-specific parts were automatically generated by the dedicated software for direct Computerized Numerically Controlled (CNC) manufacturing within the department of Medical Technology & Clinical Physics within our medical center.

- Within one hour after measuring, the joint-specific parts were assembled to the articulating frame, distraction was reinstalled, and motion was evaluated by the orthopedic surgeon (RC) (Figure 4). If no irregularities were present, weight bearing and non-weight bearing radiographs were intended to be made at 0, 15, and 30 degrees joint flexion.

- Finally, the articulating frame was removed, the conventional frame was reinstalled, and distraction was applied. After radiographic control of the extend of joint distraction, patients were discharged and they continued conventional treatment.

Outcome parameters

As primary outcome, the Joint Space Width (JSW) was intended to be measured on standardized radiographs by Knee Image Digital Analyses (KIDA [41]), incorporating the minimum and the mean JSW medially and laterally, and the overall mean JSW. Analyses of non-weight bearing and weight bearing (half body weight) at 0, 15 and 30 degrees was intended. For every evaluated angle, a difference in JSW of 2 mm was expected between non-weight bearing and weight bearing conditions (3 mm resilience within 5 mm distraction).

Secondary, the articulating distraction was described on pain, comfort, and quality of motion, arbitrary based on patients' satisfaction and the orthopedic surgeon's judgment.

Statistical analysis

For all outcome measures of the JSW, mean values and standard error of the mean were intended to be given. Comparison with pre-operative data had to be performed by 2-sided paired t tests. No statistical analysis on the secondary measures was intended.

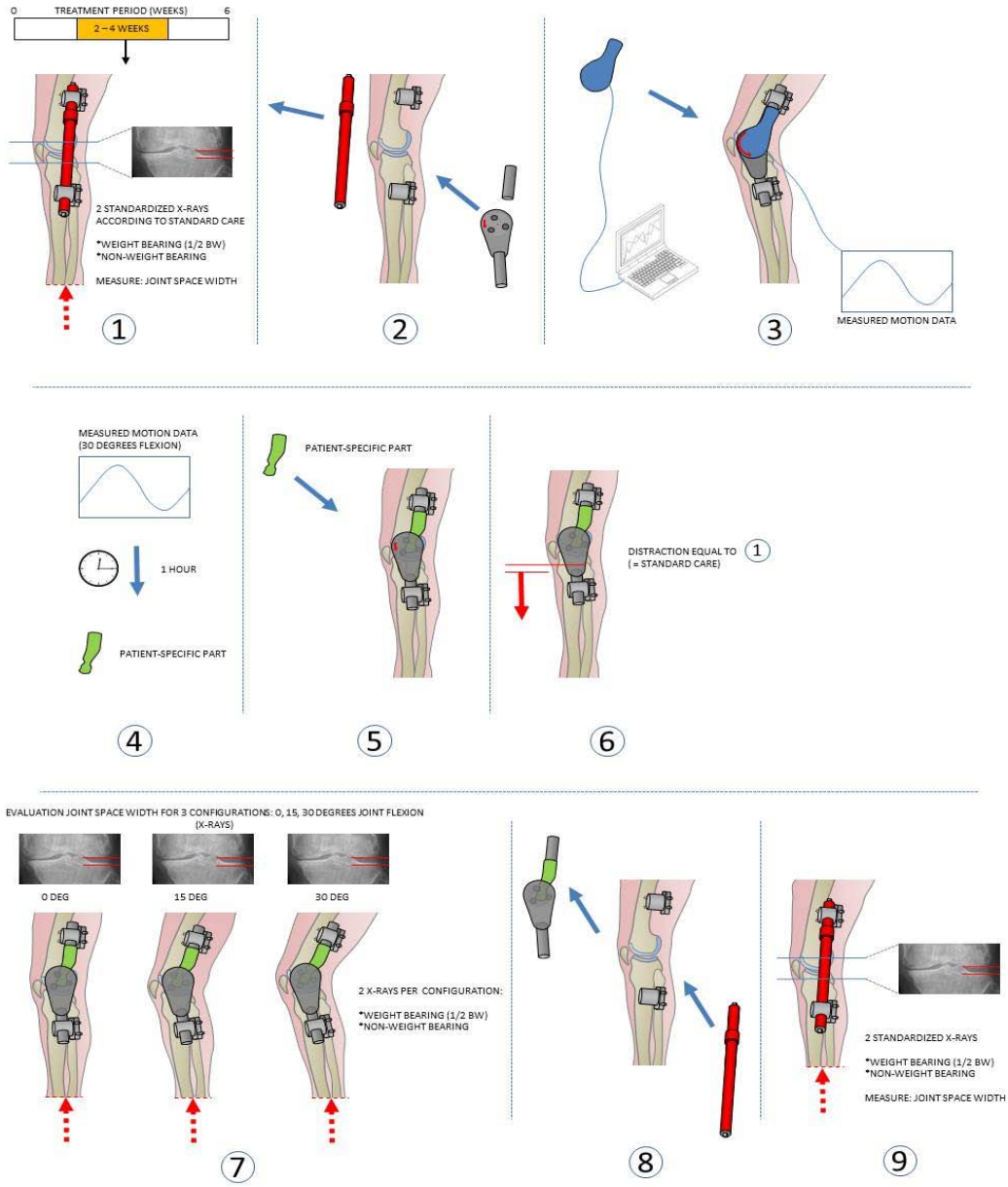

Figure 2: Schematic representation of the study procedure.
1) Patient with conventional knee distraction frame visits clinic and a radiograph is made as control. 2) The conventional frame is removed and femoral and tibial parts of the articulating frame are assembled. 3) Joint-specific motion is measured with modularly coupled measurement device. 4) Motion data is processed and joint-specific distractor parts are manufactured. 5) Personalized hinge parts are assembled. 6) Distraction is applied. 7) Radiographs are taken at 0, 15, 30 degrees non-weight bearing and weight bearing (half body weight). 8) The articulating frame is removed, the conventional frame is assembled, and distraction is restored. 9) Distraction is evaluated on radiograph and the patient is discharged.

Results

Based on ethical considerations, three out of four patients that signed informed consent, were actually included for testing of the articulating device. The fourth patient was excluded due to a pin tract infection during the planned study period. Based on the clinical results of the first three patients, no further inclusion was performed and the study was halted. The technical performance of the articulating knee joint distraction device was unaffected and had no part in that consideration.

Range of motion

In order to measure joint-specific motion for reproduction, the knee of every patient was passively flexed in a CPM device for release of joint stiffness. While 30 degrees joint flexion was aimed for in order to have a proper reproduction of motion, patients reached 15, 8 and 15 degrees joint flexion, respectively. It appeared that joint motion was restricted by intolerable painful motion of the soft tissues along the bone pins at the pin tracts, which mainly occurred in the upper leg. Although the range of motion was below the required range, the protocol of motion reproduction was continued and measurement of

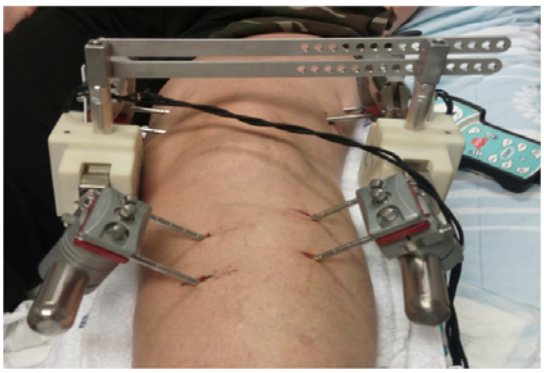

Figure 3: The measurement device is attached to the distractor for capturing the joint-specific motion.

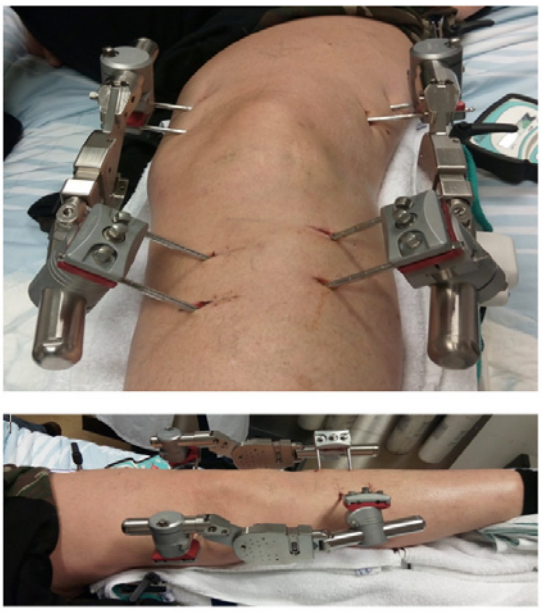

Figure 4: The articulating frame assembled to the same bone pins and bone pin clamps as used for rigid joint distraction in clinical practice, and previous to measurement of the joint-specific motion and customization of joint-specific hinge parts.

joint motion was performed for further evaluation of the personalized approach.

Positioning and assembling of the articulating distractor

During assembling of the articulation distractor, the sets of bone pins that were drilled for the conventional distraction treatment were used and the same bone pin clamps were used for fixation of the femoral and tibial parts of the articulating distractor. In the first patient, it appeared that the distance between the bone pin sets at the medial side was insufficient for positioning of all articulating frame components. Although it is likely that this can be overcome in a redesign of the articulating frame, the required area for correct placement might need reconsideration.

Nevertheless, no changes in the surgical protocol were made for the other patients and the components of the articulating distractor were there successfully installed for measurement of joint-specific motion.

Measurement of joint-specific motion

Within the limited range of motion, joint motion was recorded with the custom-built measurement device at the lateral joint side for the first patient, and bilaterally for the second and third patient.

Although measurements could be performed for the limited joint motion, the software did not succeed in automated generation of the joint-specific parts in either of the three patients. This was in the first patient (15 degrees) due to a unilateral measurement (only unilateral application of the device was established as a result of too close positioned bone pins medially), while bilateral data was required for the software to generate joint-specific hinge parts.

The dedicated software was furthermore programmed for generating output of joint-specific parts when a minimal motion of 15 degrees was reached, which was chosen as the least amount of flexion that was considered to improve conventional joint distraction. This flexion angle was not reached in the second patient (8 degrees), and therefore no output was generated. In the third patient (15 degrees), the patient was not able to bend the joint in a continuous manner due to pain at the pin tracts, which resulted in irregular and jerky motion data from which no continuous motion could be reproduced by the software.

In none of the cases a joint specific articulating hinge was manufactured and applied.

Discussion

Patient selection

For this study, patients with normal pre-treatment joint stability and range of motion despite the OA of the affected knee, including normal flexion and full extension, were included. In addition, the Varus/valgus deformity had to be less than five degrees, which was a functional requirement for the articulating device. Surprisingly, it appeared that only few patients in our clinic did meet the Varus/valgus deformity criteria, which firmly restricted the patient selection. This might be the result of predominance of medial compartmental tibio-femoral cartilage loss, which adds to Varus deformity by medial-lateral wedging of the joint. This fits also with inclusion characteristics of patients in the first open prospective KJD study, comprising an over-representation of dominant medial compartmental knee OA [27]. The fact that in clinical practice many patients of the knee OA population that currently receive conventional knee distraction could not be included for this study, might challenge the proposed personalized articulating distraction in clinical practice.

External fixation

The method for external fixation was chosen identical to the conventional distraction treatment which was primarily based on anatomically optimal (neuro-muscular safe, extra-articular, and mechanically stable) positions and for which efficacy has extensively been studied [10,27]. As such, the effects of the articulating device on the clinical outcome were anticipated to be minimal. However, the positions of the bone pins interfered with the soft tissues at the pin tracts when articulation of the joint was unrestricted by removing the distraction tubes, resulting in intolerable painful joint motion, especially in the upper leg.

Joint motion with a normal range of motion during knee joint distraction has been reported previously in a Japanese case series [42], where bone pins were drilled closer to the joint than in the surgical technique we prefer because of compromising the joint area for future TKA and the risk for articular penetration. Their applied articulating device dictates a generalized (one fits all) motion profile and requires a Kirschner wire through the condyles (intra-articular) for alignment during surgery. Although successful, the previously described method is more complex and poses higher risks of neuro-vascular damage. Furthermore, intra-articular positioned pins may increase the risk for complications during treatment, as well as the risk for latent infections that might prevent successful joint arthroplasty later in life.

Method for personalized articulation

During this study, problems were encountered in flexing the joint on a CPM device. In a previous explorative study on joint distraction, patients visited the clinic every two weeks, where the distraction frame was temporarily removed from the pins, and the joint was flexed within a CPM as we did in this study [27]. For those patients however, an average range of motion of 25 degrees (15-80 degrees) was reached after 3-4 hours. Although the CPM use was limited to 2 hours for our patients in order to fit the testing within one day, the maximal (still too limited) flexion for our study patients was reached well within the available time.

There is no documentation whether the previously obtained angles [27] were measured by the display of the CPM or measured by the actual knee angle. Most likely the measurement of this angle was obtained from the display of the CPM. However, due to the present bone pins, additional supporting pads were used for lifting the leg in the CPM device, which made that the flexion angle as displayed on the CPM was not representative for the flexion angle of the knee. This effect is supported by the measurement from the device for registration of the joint-specific motion that indicated a lesser angle compared to the CPM value.

In the pre-clinical tests of the method for joint-specific motion reproduction in fresh human cadaver knees, a continuous motion profile was observed. In this study the joint was passively flexed on the CPM during the measurement of the joint specific motion for designing the joint specific parts. No relevant unanticipated restrictions of muscles around the pins were observed in these cadaver tests. Although muscle tension lacked during the cadaver studies, complete legs attached to the pelvis were used, and similar motion profiles were expected in the present clinical set-up. It appeared however that the *in vivo* motion data, as far as could be obtained, contained more irregularities. Especially at the starting and ending points of the recorded motion, shifts were present. Those shifts can be explained by unintended active muscle contraction during CPM potentially resulting from pain during the passive motion.

Within the software package for processing the raw measurement data, filters were incorporated for smoothing the raw data, and the start and end points were cropped until a continuous motion profile was obtained [40]. The irregularities that were measured in our patients could nevertheless not be filtered out with preservation of the continuity of the motion.

As a solution to the limited knee flexion after three to four weeks of rigid distraction, it was considered to test the articulating knee distraction directly after pin placement or in the first week of treatment, since stiffening of the joint and fibrosis around the pins is likely to be less present shortly after bone pin placement. However, for evaluation of the articulating frame, loading of the treated leg is required for an adequate muscle controlled flexion during walking, which typically can be done only after a familiarization period of more than a week. Furthermore, the limited flexion on the CPM originates from pain at the pin sites during flexion, and no suitable options for different bone pin positioning are considered adequate (safe with respect to neuro-muscular damage and future TKA).

Overall, the articulation during knee distraction with the proposed method appears not to be clinically feasible and possibly also not beneficial for the patient. The therapy might however still need improvement on other aspects of comfort during wearing of the distraction device. Also, a reduction of pin tract infections, a common complication in knee joint distraction [10,27], would greatly improve the quality of the treatment. In this respect, it is not unlikely that the hinged distraction as aimed for, would have led to an increase in pin tract infections due to movement of the pins within the pin tract.

In the development of new medical devices, regulations demand that the risks that are associated with the introduction of new medical equipment, are decreased to a minimal, acceptable level. Certain risks can often pre-clinically be evaluated in representative settings. As such, cadaver tests can serve as a tool for evaluation of new surgical techniques. Also in the pre-clinical testing of the studied joint-specific knee distraction method, human cadaver knees were used. During the clinical evaluation in this study, it appeared that a human cadaver model lacks anticipated, but in retrospect essential, active muscular activity and pain sensation, which effect the joint motion even during passive flexion. Although this was anticipated, it was not considered to be as relevant as we now observed. The limitations of the models that are intended for reduction of risks of new technology in the clinic, should therefore be critically examined for its specific purpose, and subsequent critical clinical evaluation remains essential in assessing risks of new technology.

Conclusions

The goal of this study was to test the clinical feasibility of the joint-specific articulating knee distractor validated in pre-clinical studies, which unfortunately could not be demonstrated. This is primarily due to pain that patients experienced at the pin tracts during joint motion. Although this effect can be reduced by shifting pin locations to anatomically less favorable positions, the risk of neuro-vascular damage and compromising the area for total knee arthroplasty is not favoring such an approach. The possible benefits of articulation during distraction are as yet considered to be of lower impact on patients than the risks that are accompanied with alternative approaches.

Ethical approval: "All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (University Medical Center of Utrecht, Utrecht and The Netherlands (NL48424.041.14)) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards."

Informed consent: "Informed consent was obtained from all individual participants included in the study."

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