Statistical Analysis Plan

Double-bundle versus Single-bundle Anterior Cruciate Ligament reconstruction of the knee, 5-years follow-up of a Randomised Controlled Trial.

Clinical trials ID: NCT01033188

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Background:

The Double bundle(DB) concept considers the Anterior Cruciate Ligament (ACL) divided into the posterolateral and anteromedial bundle.[1,2 3] The Double bundle(DB) ACL reconstruction restores both bundles and thereby normalizes the in situ forces and improves the anterior and rotational stability of the knee compared to traditional Single-bundle(SB) reconstructions.[4-8] The surgical technique reached attention during the last two decades.[9,10] During the same period of time, anatomic ACL reconstruction technique was gradually implemented and transtibial drilling and offset guides were replaced by anteromedial(AM) portal drilling and placement according to anatomic landmarks.[11,12] The DB ACL reconstruction procedure is more expensive and time-consuming and requires relatively high surgical skills compared to SB technique.[13] Despite initial promising findings more studies found that DB ACL reconstruction had little or no superior effect on Patient Related Outcome Measures (PROMs) and other clinical outcomes compared to the anatomic SB technique.[14] Thereby the technique gradually lost interest among orthopaedic surgeons,[9,15,16] allthough more high-quality studies with longer follow-up was needed.[17-19]
Recently more mid-and longterm studies have been published. In a systematic review evaluating three studies with more than 5 years follow-up, they concluded with no difference between the DB and SB surgical technique regarding the development of osteoarthritis, clinical outcome and graft failures.[20]
In a metaanalysis including 40 different studies comparing the SB versus the DB technique, they concluded that the DB technique led to better results when it came to knee laxity and subjective outcomes, but there was no difference in the subgroup analysis of patients reconstructed with anatomic technique through an anteromedial portal.[14] Other studies found significantly fewer graft-ruptures in the DB group compared to the SB group.[17] Although the reason for fewer graft-ruptures remained unclear they assumed that DB reconstructions had some kinematic superiority that could prevent a new trauma and that the thicker grafts and double fixation of the grafts in the DB group could lead to less graft-ruptures.[21]
Posttraumatic osteoarthritis seems to evolve despite surgical intervention after ACL injury.[22,23] On the other hand, kinematic changes in the knee are known to influence on the process of cartilage degeneration together with biological, neuromuscular and structural factors.[24,25] Anatomic SB technique seems to positively affect degenerative cartilage changes in the knee compared to the traditional non-anatomic ACL reconstruction. [26] Howeverit is still uncertain whether reconstructing both bundles anatomically could be of any further benefit, compared to the anatomic SB reconstruction.[26 14]

The aim of this prospective randomized controlled study is to compare anatomic DB versus anatomic SB ACL reconstruction technique more than five years after surgery regarding radiographic imaging and graft failures/revision reconstructions. Also to compare the amount of graft failures and revision surgery between the two groupsm and to look at patient reported outcome measures (PROMs), clinical examinations, activity level and functional tests with the two techniques.

Variables:

Primary objective and outcome:

Primary outcome for the study will be to compare the prevalence of osteoarthritis in the double-bundle(DB) versus the single-bundle(SB) ACL reconstructed knees, 5 years after surgery as judged by the Kellgren-Lawrence classification.

Radiographic imaging:

Radiographic imaging will be performed using standing anterior-posterior (AP) in a Synaflexer™ X-ray positioning frame (Synarc Inc, San Fransisco, CA, US.

Secondary objectives and outcomes:
Compare radiographic outcome between the two groups with the OARSI grading system. Compare the difference in graft ruptures (graft failures) and revision surgeries in both groups. Further, secondary outcomes will be to compare patient reported outcome measurements, functional tests, results from the clinical examination in the double-bundle and single-bundle reconstructions at five years postoperatively.

New injuries/Operations:

Graft ruptures and revision surgery

Patient reported outcomes

1) KOOS subscales:

Pain
Symptoms
Activities of daily living (ADL)
Sports and Recreation
Quality of life (QoL)

2) the subjective International Knee Documentation Committee form (IKDC 2000)

3) the Sports activity scales and return to sport questionnaires:

Tegner activity scale
Sports Activity Scale
Return to previous attended main sports

Clinical examination:

4) Knee laxity test:

Lachmann´s test
Pivot shift test
KT-1000 arthrometer (Knee Laxity Testing Device)

5) Knee joint range of motion (ROM):

Flexion deficit
Extension deficit

Functional performance test:

8) One leg hop test

Adverse Events:

9) Reoperations:
Reoperations because of hematoma, infection or arthrofibrosis.
Menisci surgery including suturing, resection or transplantation.
Reoperations due to cartilage surgery.
Re-arthroscopy because of cyclops removal, donor site morbidity, hardware removal or pain.
Revision surgery first stage operation.

ANALYSIS SET:
Full analysis set (FAS)

All subjects randomised to either of the two treatment arms who completed the baseline assessment and the five year assessment and who did not have an ACL-revision surgery.
; independent of the actual intervention they received.

Per protocol (PP) analysis set:

All subjects that received the treatment to which they were randomised, and fulfilled all the required assessments at baseline and at five years follow up and who did not have an ACL-revision surgery.

Exclusion criteria from the PP set relative to the FAS:

- Patients that did not receive the treatment they were randomised to get.

SPECIFICATION OF ENDPOINTS

All primary and secondary outcomes will be analyzed on the full analysis set. In addition, the primary outcome and the secondary outcome graft-rupture (see list below) will be analyzed on the per protocol set.

Primary endpoint:

1. The primary endpoint of the study is the difference between the two treatments in the degree of osteoarthritis in the involved knee, as classified by the Kellgren-Lawrence grade, at five years.

Secondary endpoints:

The difference between the two treatments in the following outcomes:

1. The proportion of osteoarthritis in the involved knee, as classified by the OARSI classification system.
2. Proportion of patients with **Graft-rupture** at five years after the operation.
3. Proportion of patients with **Revision reconstruction** at five years after the operation.
4. The mean value in the **KOOS Symptoms** subscore at five years.
5. The mean value in the **KOOS Pain** subscore at five years.
6. The mean value in the **KOOS Activities of Daily Living** subscore at five years.
7. The mean value in the **KOOS Sports and Recreation** subscore at five years.
8. The mean value in the **KOOS Quality of Life** subscore at five years.
9. The mean value in the **IKDC 2000 subjective score** at five years.
10. Knee laxity as measured by the **Lachman's test** at five years.
11. Knee laxity as measured by the **Pivot shift test** at five years.
12. Knee laxity as measured by the **KT 1000** at five years.
13. Range of motion as measured by the mean **extension deficit** in the involved knee compared to the uninvolved knee at five years.
14. Range of motion as measured by the mean **flexion deficit** in the involved knee compared to the uninvolved knee at five years.
15. The **Tegner activity score** at five years.
16. The **Activity Scale** level at five years.
17. Proportion of patients **Returned to previous sports** at five years.
18. The mean value in the **One leg hop test** at five years.

Radiographic imaging:

Radiographic imaging will be documented by the use of standing radiographs of both legs. The x-rays will be judged by an independent radiologist, not involved in the study and classified according to the Kellgren-Lawrence grading system of osteoarthritis in the joint. Established osteoarthritis is defined as KL grade 2 or more (Grade 2,3 and 4) on front standing radiographs of the knee. The measurements will be performed for the index knee and for the contralateral knee.

Kellgren Lawrence classification[27]:

Grade 0: no radiographic features of OA are present
Grade 1: doubtful narrowing of joint space and possible osteophytic lipping
Grade 2: definite osteophytes and possible narrowing of joint space

Grade 3: moderate multiple osteophytes, definite narrowing of joint space and some sclerosis and possible deformity of bone ends
Grade 4: large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone ends

Scale 0-. Assessment: Baseline and at 1, 2 and 5 years follow-up.

OARSI atlas criteria:

Osteoarthritis research society international(OARSI) criteria: Semiquantitative separate scoring systems for osteophytes and joint space narroewing (JSN) for each comparmtment (medial and lateral) of the knee. The grades 0-3 will be based on imaging provided by the OARSI atlas. On front standing radiographs of the knee the detected osteophytes or Joint Space Narrowing(JSN) will be graded 0-3 point in each compartment (medial and lateral). If the sum of Joint space narrowing (JSN) and osteophytes from the medial and lateral compartment will be grade 2 or more or if grade 1 JSN occurres together with grade 1 osteophytes -tibiofemoral OA will be defined. The measurements will be performed for the index knee and for the contralateral knee.

Graft rupture/reoperations:

Graft ruptures defined as a total rupture of the ACL reconstruction, defined by clinical examination (Lachman 2+ or more and/or pivot shift positive) **and** by MRI or second look arthroscopy.
Revision reconstructions defined as a reoperation with reconstruction of a new ACL graft in the same knee.

Patient related outcome measurements:

KOOS:

The KOOS was developed to evaluate both short- and long-term outcome after knee injuries in young and active subjects with a knee injury or osteoarthritis in their knee[28]. It is proven as a reliable, valid and responsive score for patients undergoing ACL reconstruction[29](Collins 2016). The KOOS score is preferred to be interpreted as five different subscores[28].
KOOS data are obtained from a questionnaire, where the five dimensions are rated separately: Pain, Symptoms, Activities of daily living, Sports and recreation and Quality of life. The five scales include 42 items with different numbers of elements within each subscore (4-11). Each item can score on a scale from 0 - 4. The five subscores are separately calculated, ranging from 0-100 points where 100 point is the best score possible.. At least 50% of the items within each subscore must be responded to before the score is calculated.
Scale: 0-100 points in each subscore. Assessment: baseline, 1, 2 and five years follow up.

IKDC 2000 subjective score:

The original score was developed by the International Knee Documentation Committee (IKDC) as a standardized form for different knee conditions. The score contents of both clinical assessments and

pathology identified during surgery and the subjective IKDC score is restricted to contain the patient administered form of the total score. The subjective score includes 18 different items that cover three domains: Symptoms, sports, and current knee function. Each item is weighted according to its importance on the total score, and the worst score in each category is carried forward. Range 0-100 points. (A total score of 100 points =normal sports participation with absence of symptoms and no limitation in the daily activity [30,31]).
Scale: 0-100 Assessment: Baseline 1, 2 and five years follow up.

Tegner activity score:

The score was developed complementary to the Lysholm score, and its mission was to detect whether the loss in function could be masked by level of activity[32]. The score is graduated in levels of activity of daily living. The scale ranges from recreational to competitive sports in 11 different levels (0-10). 0 indicates the lowest knee-related level (sick leave or disability), and 11 the highest knee related level (competitive sports at a national level).
Scale: 0-10. Assessment: Before injury, at baseline, 1, 2 and five years follow up.

Activity Scale:

The Activity Scale was based on one of the subjective assessments in the Cincinnati Knee Rating System and is a self-administered score that detects the level of sports activity [33]. The original score (Sports Activity Scale) contains four different levels of sports frequency. Within each level there is a grading from sports performed with "no running, twisting or jumping"(cycling/swimming), to sports with "hard pivoting, cutting, jumping"(basket, football).
In this study, only the frequency of sports participation was recorded, with four different levels frequency (1=sports performed less than one day per month, 4= sports performed more than 4 days per week).
Scale: 1-4. Assessment: Before injury, at baseline, 1, 2 and five years follow up.

Return to previous attended main sports:

The patients recalled the two main sports they participated in the months before the ACL injury. Return to sports was defined as the return to one of the two main sports at one or two years after the reconstruction. If the same sport was recorded in one of the two assessments, the patient was defined as having returned to sports.
Scale: yes (y) or no (n). Assessed: before injury, baseline and at 1, 2 and five years follow up.

Clinical testing:

Lachman's test:

The Lachman's test is a reliable manual laxity test to distinguishing an ACL rupture from an intact ACL. The test has been found to have a higher sensitivity and specificity compared to other manual tests for ACL injury[34,35]. The test can be graded similarly to the anterior drawer test.
With the patient in supine position and 20 degrees of flexion in the involved leg, one hand is stabilizing the femur and the other hand performing a subluxation of the tibia in
the anterior direction. The anterior displacement is recorded in mm and as the difference to the contralateral leg[30].

Grade 3+ = >10mm displacement of the tibia.
Grade 2+ = 6-10mm and
Grade 1+ = 3-5 mm,
Grade 0= 0-2mm

Scale: 0-3, Assessment: Baseline and 1, 2 and five years follow up.

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Pivot shift test:
The Pivot shift test is known as a pathognomonic test for the ACL insufficient knee. The phenomenon is described as the reduction of the tibia from a subluxated position as the knee is extended with the tibia internally rotated [11, 20]. The Pivot shift phenomenon can be graded on a scale from 0 to 3+[36,37] according to the amount of subluxation of the tibia and its the reduction in extension. There has been a discussion among the experts whether a positive test should be recorded as such, or if it should be compared to the contralateral leg.
In the study the Pivot shift was detected by the Slocum`s test and not compared to the contralateral leg[37].

Pivot shift:
Grade 0
Grade +1= “trace” positive only in medial/internal rotation of the tibia
Grade +2= “clunk” subluxation in neutral positioning of the tibia
Grade+3= “gross” subluxation in any rotation, laxity due to secondary restraints additional to the ACL injury or in chronic unstable knees.
Scale: 0-3. Assessment: At baseline, and 1, 2 and five years follow up.

KT 1000

The KT 1000 (Knee Laxity Testing Device), is an instrument detecting knee laxity in the anteroposterior direction[38]. It has two sensor pads that are placed in contact with the patella and the greater tuberosity of the tibia during an instrumented Lachman's test of the knee. The instrument detects the motion between those two sensor pads during anterior translation of the tibia towards the femur. Displacements at loads of 134 N and maximal manual load (MM) are detected. Displacement in the involved compared to the uninvolved knee will be detected[38].
Range: - 20 till +20mm. Assessment: Baseline and 1, 2 and five years follow up.

Range of motion (ROM)

As the knee joint is a hinge joint, the range of motion can be detected as both the extension/flexion movement and by internal/external rotation. In this study, only the extension/flexion movements are detected. The normal flexion is widely individual from 120-150 degrees, and therefore the flexion deficit was compared to the uninvolved knee. If any extension- or flexion-deficit was detected, a goniometer was used for exact measurement of the deficit and recorded. The extension deficit of the involved knee was compared both to 0(zero) degrees of extension and to contralateral knee extension.
Scale:
Extension: -20 (hyperextension) to 150 degrees
Flexion: 0-150 degrees.
Assessment: At baseline, and at 1, 2 and five years follow up.

Functional tests:

The functional tests were performed to evaluate the functional capacity of the knee. The tests revealed both the clinical assessments and the patient´s perception of their knee.

One leg hop test

The "one leg hop test" is a functional test often used as part of a performance test for ACL deficient knees[39,40]. The test is known to be highly correlated to the clinically assessed instability of the knee[41]. The test was performed with two attempts at each leg, the best of the two scores were documented and the percentage difference from the uninjured knee presented:

Operated knee hop distance/Non operated knee hop distance X 100

Scale: 0-100 %. Assessment: Baseline, and 1, 2 and five years follow up.
Table: Summary of the primary and secondary endpoints

Outcome	**Scale**	**Method***
Primary outcome		
Kellgren-Lawrence grade	0,1,2,3,4	Wilcoxon-Mann-Whitney
Secondary outcomes		
OARSI medial	0,1,2,3	Wilcoxon-Mann-Whitney
OARSI lateral	0,1,2,3	Wilcoxon-Mann-Whitney
Graft-rupture	Dichotomous	Newcombe/Fisher mid-P
Revision reconstruction	Dichotomous	Newcombe/Fisher mid-P
KOOS symptoms	0-100	Linear mixed model
KOOS pain	0-100	Linear mixed model
KOOS activities of daily living	0-100	Linear mixed model
KOOS sports and recreation	0-100	Linear mixed model
KOOS quality of life	0-100	Linear mixed model
IKDC	0-100	Linear mixed model
Lachman's test	0,1,2,3	Wilcoxon-Mann-Whitney
Pivot shift test	0,1,2,3	Wilcoxon-Mann-Whitney

KT1000	-20 to 20 mm	Linear mixed model
Range of motion: extension	-20 to 150°	Linear mixed model
Range of motion: flexion	0 to 150°	Linear mixed model
Tegner activity score	0-10	Wilcoxon-Mann-Whitney
Activity scale	1,2,3,4	Wilcoxon-Mann-Whitney
Return to sport (yes/no)	Dichotomous	Newcombe/Fisher mid-P
One leg hop test	0-100	Linear mixed model

* See below for details

SAMPLE SIZE CALCULATION:

The sample size was calculated for the initial study based on the KOOS QoL subscore, A minimal important change (MIC) in KOSS QoL of 8 points, has been considered sufficient [28]. With equal allocation in both arms, a standard deviation of 15 points, power of 80%, and assuming a two-sided significance-level of 0.05, the sample size was calculated to be 56 patients in each treatment group.

To allow for 5% drop-outs, the final sample size was set to 60 patients in each arm, and 120 patients in total. The five years FU used the same cohort.

Randomisation:

A nurse not involved in the research project performed a computer-generated block randomization, ten patients in each block. The allocation sequence was generated by a software program: (http://randomization.com) and was conducted with a 1:1 ratio between the treatment arms. With 60 patients within each intervention group, twelve blocks of ten patients was needed. 120 sequentially numbered, opaque, sealed envelopes, containing a label describing one of the two interventions, were placed in the operating theatre at operation. One of the assisting nurses would open the envelopes at the request of the surgeon. The envelope was only opened if the patient fulfilled the inclusion criteria and the baseline assessments and after the ACL rupture was verified by arthroscopy and the hamstring tendon grafts sizes were sufficient. (The minimal desired hamstring graft sizes were 5.0 mm for the PL bundle and 6.0 mm in diameter for the AM bundle.)

Level and method for blinding:

Initially, the trial participants were not intentionally blinded for the intervention, but the outcome assessor was blinded and ensured that the PRO from the patients were complete.
The level of blinding was changed during the enrollment, and after a discussion between the co-authors, the study participants number 62 – 120 were consequently blinded for the intervention. Unblinding was performed after the assessments of the two years follow-up.

Functional tests at five years: The outcome assessor that completed the functional tests, was not blinded for the intervention.

Clinical assessment at five years: The clinical assessments were performed by the assisting orthopedic surgeon (CA). The surgeon was not blinded.

Radiographic imaging at five years: The radiologist was not blinded, as the intervention was visible at the standing radiographic imaging.

Data analysis: The statistical advisor will be blinded when performing the analysis.

STATISTICAL METHODS:

Presentation of observed data

All continuous variables will be summarized with means and standard deviations (SD) within each treatment. Categorical data will be summarized with counts and percentages within each category and treatment arm.

Primary hypothesis setup

Null hypothesis: Double bundle ACL reconstruction is equal to single bundle ACL reconstruction, regarding the presence of degenerative changes (osteoarthritis) at five years follow-up.

Alternative hypothesis: Either double bundle ACL reconstruction is superior to single bundle ACL reconstruction or single bundle ACL reconstruction is superior to double bundle ACL reconstruction, regarding the presence of degenerative changes (osteoarthritis) at five years follow-up.

STATISTICAL ANALYSIS

Primary outcome

The **Kellgren-Lawrence classification** at five years will be analyzed with the Wilcoxon-Mann-Whitney test for ordered 2xc tables.[42] The number and percentage of each treatment in each category will be presented together with a P-value for the null hypothesis that the two treatments have equal distributions across the categories.

Secondary outcomes

Ordered categorical outcomes (OARSI medial, OARSI lateral, Lachman's test, pivot shift test, Tegner activity score, and the activity scale) will be analyzed with the Wilcoxon-Mann-Whitney test, in a similar manner as the primary outcome.

Dichotomous outcomes at 5 years (graft ruptures, revision surgeries, and return to sport) will be analyzed with a Newcombe hybrid score 95% CI for the difference between the treatment probabilities and a Fisher mid-P test for the null hypothesis of equal probabilities.[42]

Continuous outcomes (all KOOS dimensions, IKDC, KT1000, range of motion extension & flexion, one-leg hop test) will be analyzed with a linear mixed model with treatment, time point (baseline, 1

year, 2 years, 5 years), and treatment x time point interaction as fixed effects. A random intercept will be used. Based on the fitted model, we will estimate the mean baseline, 1 year, and 2 years, and 5 years values (with 95% CIs) for each treatment, and the between-treatment difference in values at 5 years (with 95% CI and a P-value for the null hypothesis of no difference).

Figures/diagram:
Two diagrams of affected knees KL grading and OARSI score (Medial and lateral compartment together) and their CI, will be presented.
The observed mean values of the five KOOS subscores will be presented in a figure as two curves (one for each treatment) plotted at four different time points (baseline, one, two and five years). Vertical lines at each time point for each treatment will represent the standard deviation.

Adverse events
Descriptive data of adverse events including graft rupture and revision surgery will be presented.

The timing of analysis:

The final analysis will be performed after the five years follow-up of all study candidates and after finalization and approval of the statistical analysis plan by all coauthors (MAR, SJ, IT, SH and LE) and the statistical advisor (MWF).
The data will then be prepared and presented to the statistician as blinded data.

MISSING DATA:

Reasons for not participating at five years FU has not been recorded.

All continuous outomes will be analyzed with linear mixed models. These models account for missing data on individual time points, thus obviating the need to impute missing values.

For the categorical outcomes, we will use the full analysis set, where only the observed data at 5 years will be included If the amount of missing data is more than 10% for an outcome, a sensitivity analysis will be performed, wherein the missing data will be imputed according to three scenarios:

1. The 5 year (missing) measurements will be given the values of the last observed measurement (at two years, one year, or baseline).
2. The 5 year (missing) measurements will be imputed as the most favourable score for patients who received the double bundle treatment, and the least favourable score for patients who received the single bundle treatment.
3. The 5 year (missing) measurements will be imputed as the least favourable score for patients who received the double bundle treatment, and the most favourable score for patients who received the single bundle treatment.

SAFETY ANALYSIS:

Adverse events:

Any reoperation any other injury will be reported and listed in the summary tables of adverse events (Table 3).
An adverse event refers to an untoward occurrence during the trial, which may or may not be causally related to the intervention or other aspects of trial participation [43]. The study participants were questioned whether they "had observed any adverse events related to the treatment during the last year," at the 1, 2 and five years follow-up. The recorded adverse events were further categorized as listed in Table 3.
Each subject will be counted once in each category of AE, but each participant can have more than one AE. Any repetition of the same event in one patient was ignored (Table 4). Additional information was obtained from the patient`s journal if necessary.

PROTOCOL DEVIATIONS:

Study design:
The hypothesis in the original study protocol was formulated as in a non-inferiority study. Although further evaluations and sample size calculations of the study were designed as in a superiority study design, with the hypothesis questioning if the Double bundle technique was superior to the Single bundle method regarding the KOOS, QoL subscore.
Double bundle reconstructions are more cost demanding, time-consuming and require higher skills of the performing surgeon compared to Single bundle surgery; therefore a superiority study was considered as the preferred design for this study[44].

Study period – primary end point:
The study endpoint changed to the two years follow-up instead of the five years result, because of a prolonged inclusion period.

Study settings:
Martina Hansens Hospital was in 2013 implemented as an additional recruiting hospital, because of the prolonged inclusion period and because of the first author worked at both hospitals during this time. The interventions were performed at Oslo University Hospital but were changed to Martina Hansens Hospital as the operating theatres at Oslo University Hospital were closed down due to rehabilitation, (1st March 2013). The operating surgeon(SJ) continued to perform the intervention, and the same equipment and fixation devices were used for the operations at both hospitals. (The equipment was transported to Martina Hansens Hospital during the last two years of inclusion.)

Interventions:

The inclusion criteria for the hamstring tendon graft sizes were changed from 5.5 mm for both bundles to 5.0 mm for the PL bundle and 6.0 mm for the AM bundle, due to the arising difficulties with inclusion.

Secondary endpoints:
The Activity scale as one of the PROM`s was added after the protocol was made but before inclusion of the first patient.

Level and method of blinding:
A subgroup of patients (randomization number 62-120) were blinded to the intervention until they completed the two years follow up, to improve the quality of the study. The reason for blinding the patients was to prevent the patients from biasing the results unintentionally, as not blinded studies are known to give larger treatment effects than non-blinded studies.

Clinical trials, history of changes:
Published at https://clinicaltrials.gov 15th of December 2009, (ID: NCT01033188).

5th July 2011:
The name of location has been modified from Ullevaal University Hospital to Oslo University Hospital.

2nd June 2014:
The surgical procedure: Anatomic ACL reconstruction technique was described in detail, and the name of the fixation devices was changed to the devices that was used on the study participants. The minimum hamstring graft size was adjusted from minimum 5.5 mm to 5.0 mm. The sample-size was changed to 112 patients according to the initial sample size calculation.

12th May 2015:
The description of the surgical procedure was further improved to aim the actual anatomic reconstruction that the surgeons performed during the study period. The sample size was enlarged to 120 patients because of the block-randomisation and the anticipated end of study date, changed to 2017.

6th August 2015:
Study status was changed from recruiting to active, not recruiting. The minimum hamstring tendon sizes required for inclusion, were changed to 5.0 mm for the PL bundle and 6.0 mm for the AM bundle.

4th April 2017:
Update on recruitment.

IMPLEMENTATION OF ANALYSIS PLAN:

The statistical analysis will be performed blinded by the statistical advisor, and not by the other investigators on this project. A data collection form will be outlined; the data will have anonymous

coding into "treatment 1" and "treatment 2". Analysis of the primary and secondary outcome will be performed blinded and then presented for the other authors.

OTHERS:

Registration numbers:

ClinicalTrials.gov ID: NCT01033188

Ethical approval: REK no: S-09108b

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