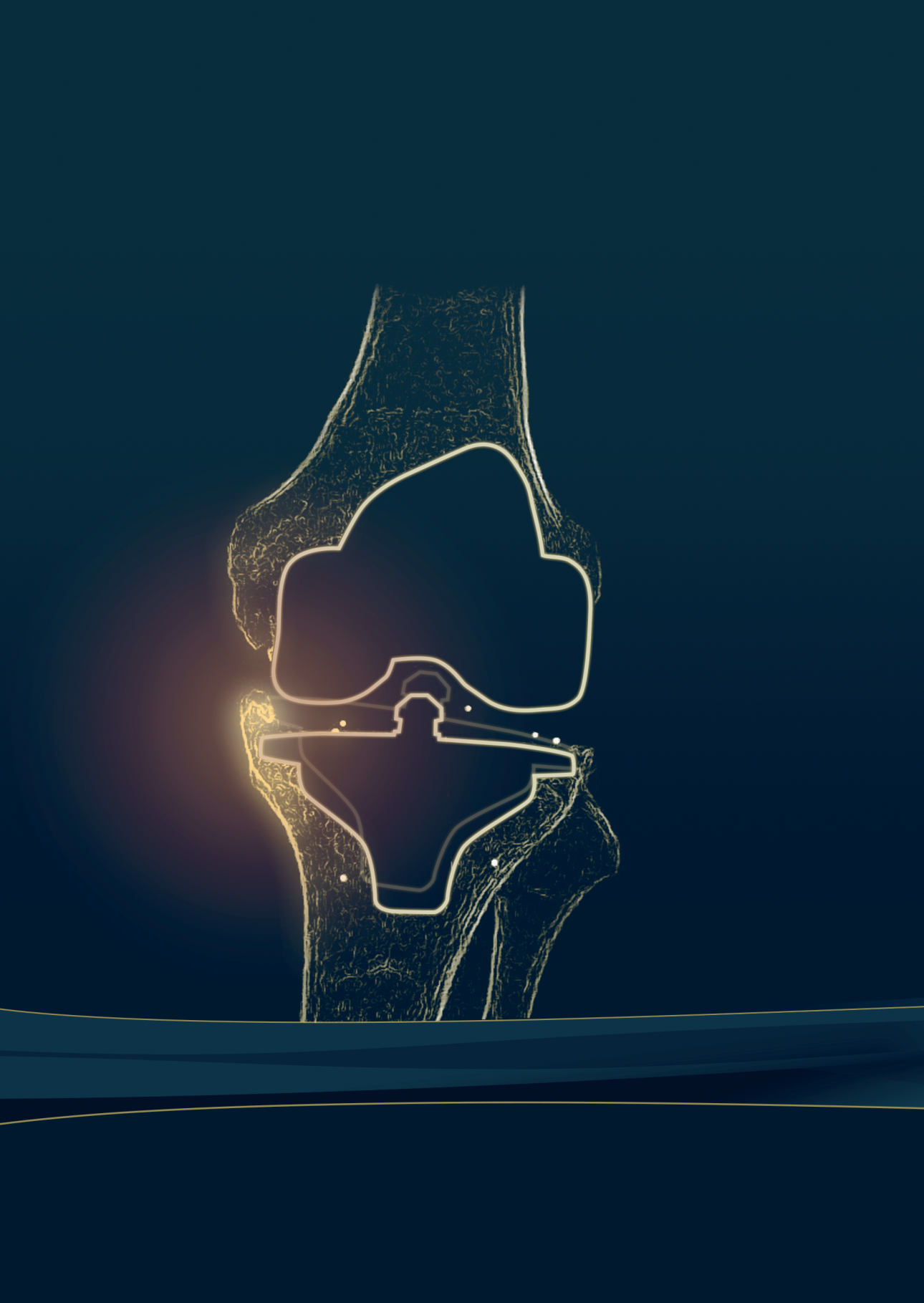
Risk factors for long-term failure of orthopaedic medical devices: taking advantage of RSA as an early detection tool

Hamersveld, K.T. van



4

Fixation and clinical outcome of uncemented peri-apatite-coated *versus* cemented total knee arthroplasty: five-year follow-up of a randomized controlled trial using RSA

KT van Hamersveld
PJ Marang-van de Mheen
R Tsonaka
ER Valstar
S Toksvig-Larsen

The Bone & Joint Journal 2017; 99-B: 1467-76

Abstract

Aims — The optimal method of tibial component fixation remains uncertain in total knee arthroplasty (TKA). Hydroxyapatite coatings have been applied to improve bone ingrowth in uncemented designs, but may only coat the directly accessible surface. As peri-apatite (PA) is solution deposited, this may increase the coverage of the implant surface and thereby fixation. We assessed the tibial component fixation of uncemented PA-coated TKAs *versus* cemented TKAs.

Patients and Methods — Patients were randomised to PA-coated or cemented TKAs. In 60 patients (30 in each group), radiostereometric analysis of tibial component migration was evaluated as the primary outcome at baseline, three months post-operatively and at one, two and five years. A linear mixed-effects model was used to analyse the repeated measurements.

Results — After five years of follow-up, one (cemented) component was revised due to ligament instability. Overall, uncemented PA-coated tibial components migrated significantly more ($p = 0.003$), with the mean maximum total point motion (MTPM) at five years being 0.62 mm (95% confidence intervals (CI) 0.49 to 0.76) for cemented tibial components and 0.97 mm (95% CI 0.81 to 1.15) for PA-coated tibial components in TKA. However, between three months and five years the cemented TKAs migrated significantly more ($p = 0.02$), displaying a MTPM of 0.27 mm (95% CI, 0.19 to 0.36) *versus* 0.13 mm (95% CI, 0.01 to 0.25) for PA-coated tibial components. One implant in each group was considered at risk for aseptic loosening due to continuous migration after five years of follow-up, albeit with different migration patterns for each group (i.e. higher initial migration but diminishing over time for the PA-coated component *versus* gradually increasing migration for the cemented component).

Conclusion — The tibial components of PA-coated TKAs showed more overall migration compared with the tibial components of cemented TKAs. However, *post hoc* analysis showed that this difference was caused by higher migration of PA-coated components in the first three months, after which a stable migration pattern was observed. Clinically, there was no significant difference in outcome between the groups.

Introduction

Development of uncemented designs in total knee arthroplasty (TKA) started in the 1970s as aseptic loosening was thought to be caused by 'cement disease'[1]. Consistently good long-term survival of cemented TKAs in the decades thereafter shifted the attention, with cemented TKAs being the preferred option. However, concerns have been raised whether the cement-bone interface can endure increased stress now that arthroplasties are performed in increasingly younger, heavier and more active patients[2, 3]. Furthermore, studies have shown a loss of cement-bone interlock due to trabecular resorption as well as deformation and degradation of the cement mantle over the years[4-6].

Uncemented TKAs, at least in theory, can provide strong long-term biological fixation due to bone ingrowth[3, 7, 8]. However, early generations of uncemented designs failed due to experimental modifications of the implant design (e.g. use of screws and metal-backed patellar components)[9]. Consequently, many surgeons are reluctant to perform uncemented TKAs: only 5% of the procedures are uncemented in Sweden[10]; 5% (including hybrid) in England, Wales, Northern Ireland and the Isle of Man[11]; 14% in Australia[12]; and 20% in Canada[13]. Recent meta-analyses comparing the benefit of cemented with cementless fixation show contradictory results depending on selection of trials and outcome measurements[2, 5, 8].

Several biomaterials, like osteoconductive hydroxyapatite (HA) coatings, have been applied to improve bone ingrowth in uncemented TKAs[14-16]. Most HA coatings are plasma sprayed onto the porous implant surface area, thereby only coating the substrate surface in the direct 'line of sight'[17]. In contrast, peri-apatite (PA) HA is solution deposited, which increases the coverage of HA onto the 3D implant surface[18]. The PA-coating is relatively thin with a thickness of 20 µm compared with 50 µm to 75 µm for most HA-coatings[16, 18]. Several studies reported a beneficial effect of PA-coating compared with only porous-coated tibial components with less subsidence and earlier stabilisation[17, 19-21]. Despite cement fixation being the reference standard, there are, to our knowledge, no randomised trials in humans comparing the fixation of PA-coated components with cemented components. We therefore conducted a single blinded, randomised controlled trial to assess the effect of uncemented PA-coated TKAs compared with cemented TKAs on fixation and clinical outcome. We used radiostereometric analysis (RSA) to accurately measure early migration of the tibial component and its predictive value of future loosening as primary outcome[22, 23]. As uncemented prostheses typically show higher initial migration compared with cemented prostheses, the present manuscript is the first to report the short-term outcomes of this trial using five-year follow-up data, rather than the usual two-year data to be able to determine accurately full stabilisation of individual components[3, 24-26].

Patients and Methods

From March 2009 to July 2010, all consecutive patients scheduled to undergo TKA due to primary osteoarthritis at Hässleholm Hospital (Sweden) were asked to participate in this randomised, controlled trial. The study was approved by the local ethics committee (entry no. 445/2005) and registered at ClinicalTrials.gov (NCT02525601, originally part of NCT00436982) before enrolment. Main exclusion criteria were active infection, active malignant disease or not being able to comply with the post-operative scheduled evaluations and prescribed rehabilitation (for example due to long travel time). After informed consent, patients were randomised using a sealed envelope technique and remained blinded to the allocated treatment throughout the entire follow-up. Randomisation was performed using a computer-generated randomisation list and only revealed to the surgeons on the day of surgery.

All patients received a Triathlon implant (Stryker, Mahwah, New Jersey) using either the cemented version (with Refobacin Bone Cement R, Biomet Inc., Warsaw, Indiana) or the uncemented PA-coated version. For both versions, cruciate retaining chrome-cobalt components of similar geometrical shape, with a tibial delta shaped stem and highly crossed-linked polyethylene inserts were used. The only difference with the cemented components is that the undersurface of both the femoral and tibial uncemented components are porous-coated to facilitate bone ingrowth, consisting of (PA-coated) cobalt-chromium sintered beads with a porosity of 35% and mean pore size of 425 μm. All TKAs were performed by three experienced knee surgeons (STL, MM and CFN). Antibiotic prophylaxis (2 g cloxacillin intravenously 15 to 45 minutes before surgery) and tranexamic acid (10 mg/kg intravenously administered prior to incision) were given. A standard midline incision and medial parapatellar arthrotomy was used to enter the joint. No tourniquet was used. Necessary soft-tissue releasing was undertaken with the posterior cruciate ligament retained. The prosthesis was implanted using the appropriate guidance instruments according to manufacturer's instructions. When bone cement was used, pulsatile lavage of the osseous surface was undertaken before applying the cement. Patellar resurfacing was not conducted on any of the patients. A total of eight to nine tantalum markers (0.8 mm diameter; RSA Biomedical, Umeå, Sweden) were inserted into the proximal tibial metaphysis and five markers in the polyethylene tibial insert. Thromboembolic prophylaxis was given for ten days, using low molecular heparin (enoxaparin intramuscular 40 mg/day). Mobilisation was similar for both groups and included immediate bearing of full weight on the day of surgery.

Pre-operatively, the following measurements were conducted: Knee Society Score (KSS)[27]; Knee injury and Osteoarthritis Outcome Score (KOOS)[28]; hip-knee-ankle angle (HKA) measurements (varus < 180° and valgus > 180°)[29]; and severity of osteoarthritis according to the Ahlbäck classification[30]. Post-operative evaluations including conventional radiographs and RSA radiographs were performed after weight-bearing was achieved (on the first post-

operative day in all cases). Subsequent examinations were performed at three months, one year, two years and five years post-operatively. RSA was performed in supine position with the knee in a calibration cage (Cage 10, RSA Biomedical).

Migration was analysed using UmRSA software v6.0 (RSA Biomedical). Positive directions along and about the orthogonal axes are, according to RSA guidelines: medial on transverse axis, cranial on longitudinal axis and anterior on sagittal axis for translations and anterior tilt (transverse axis), internal rotation (longitudinal axis) and valgus tilt (sagittal axis) for rotations[31]. Migration was described as translation of the geometric centre of the prosthetic markers and rotation of the rigid body defined by the prosthetic markers about this geometric centre of gravity. The length of the translation vector of the marker (or virtual marker in a rigid body) that has the greatest migration, i.e. the maximum total point motion (MTPM), was used as the primary outcome measure[32]. The post-operative RSA examination served as the reference for the migration measurements. The precision of the local RSA setup as measured by 15 double examinations, described as 1.96 × standard deviation (SD) (i.e. 95% confidence interval (CI)),32 was 0.10 mm, 0.10 mm and 0.09 mm for transverse, longitudinal and sagittal translation, respectively; and 0.20°, 0.20° and 0.24° for transverse, longitudinal and sagittal rotations, respectively. Implants showing continuous migration (more than 0.2 mm of migration (MTPM) in the second post-operative year) are generally considered at risk for aseptic loosening[23, 33]. This threshold was set at 0.3 mm between two and five years[24]. Subsequently, implants with continuous migration in the second post-operative year are considered stabilised if the migration was less than 0.3 mm between two and five years. The mean error of rigid body fitting of the RSA markers was below 0.2 mm. The upper limit for the condition number was set at 100. A high level of precision of migration measurements of the tibial component relative to the bone was thus achieved and marker stability and scatter values were within the limits of RSA guidelines[31].

Statistical analysis

From previous RSA studies, the migration of Triathlon TKAs within the first two years was around 1.0 mm (SD 0.5)[20]. Based on this finding, we undertook a sample size calculation. If the true difference of migration between cemented and PA-coated TKAs is 0.5 mm, we would need 17 patients per group to detect this difference with 80% power and alpha set at 0.05. To account for possible dropouts, 30 patients were randomised to each group.

Mean values and SDs are presented for measured variables; point estimates are presented including the 95% CI. Data were analysed following the intention-to-treat analysis principle. For the primary outcome MTPM, a linear mixed-effects model was used, which deals effectively with missing values during follow-up. MTPM was log-transformed (logMTPM), computed as log10(MTPM+1), given its non-normal distribution. The mean progression of logMTPM is modelled as a function of time and the interaction of time with the type of implant fixation. For the random-effects structure, a random-intercepts term is used and

remaining variability is modelled with a heterogeneous autoregressive order 1 covariance structure using R Software version 3.2.3 with nlme package (R foundation for Statistical computing, Vienna, Austria). To safeguard against multiple testing, differences in migration between groups were only tested for the primary outcome MTPM at two-year follow-up (as prespecified in the protocol) and at final (five-year) follow-up. RSA data describing the direction of migration (i.e. translation along and about the three orthogonal axes) were not tested for significance, but descriptive data is presented to illustrate the directions of migration. *Post hoc* testing was performed to assess between group differences in migration with three months and one year as a baseline to test a possible difference in migration beyond the first post-operative period. A Bonferroni corrected p-value < 0.05 was considered significant. Secondary outcomes (flexion, extension, KSS and KOOS scores) were analysed with a similar mixed-effects model. If the data were non-normally distributed, a log-transformation was performed. If this did not result in a normal distribution, a comparable generalised estimating equations (GEE) approach was used to correct the standard errors via the sandwich estimator. The latter was needed for knee extension and the KSS knee score. IBM SPSS Statistics 23.0 (IBM, Armonk, New York) was used for all secondary outcome measures.

Results

A total of 76 patients were randomised, 16 of which – those operated on between 4 September 2009 and 16 November 2009 – were excluded due to unknown problems with the RSA calibration box, resulting in unmeasurable post-operative RSA images (Figure 1). As expected, the baseline demographic characteristics were similar in the two randomised groups (Table I). Each of the 60 remaining patients were due to have five RSA examinations, giving a possible total of 300 RSA measurements. After five years, five patients were lost to follow-up; two of these patients moved out of the region, two withdrew due to health problems (pulmonary embolism and cardiopulmonary comorbidities, both after one year), and one patient withdrew after two years for reasons unrelated to his knee (family circumstances). One other patient underwent knee revision due to ligament instability. None of the patients died during follow-up. In all lost and revised patients, 12 RSA examinations could not be made. A further ten RSA examinations were missing and two were invalid due to non-matching stereo images, resulting in 276 valid RSA analyses.

RSA migration measurements. Descriptive RSA migration data of the tibial components are presented in Table II. Uncemented PA-coated components migrated significantly more at all follow-up measurements, with a mean migration (MTPM) at five years of 0.62 mm (95% CI 0.49 to 0.76) for the cemented group and 0.97 mm (95% CI 0.81 to 1.15) for the PA-coated group ($p = 0.003$) (Figure 2; Table III). However, differences were primarily due to a

large difference in migration in the first three months. The PA-coated group showed almost no migration from three months onwards (Figure 2; Table III). *Post hoc* testing showed more migration in the cemented group between three months and two years (p = 0.037), and between three months and five years (p = 0.020) (Table III). There were no significant differences between groups from one-year onwards as both groups showed almost no migration (Table III).

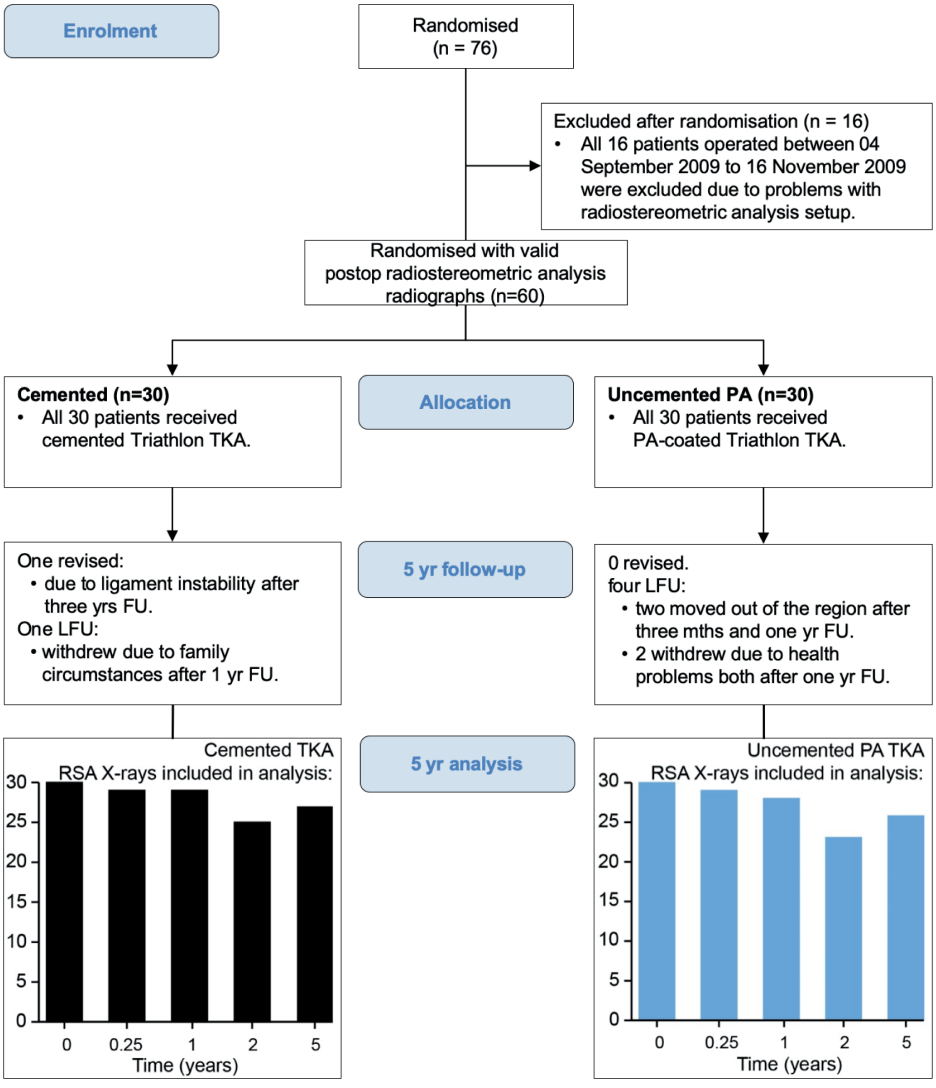


Figure 1. CONSORT flowchart. FU = follow-up, LFU = lost to follow-up, TKA = total knee arthroplasty.

Table I. Baseline demographic characteristics for the two groups of patients

	Cemented (n = 30)	Uncemented PA (n = 30)
Mean age, yrs (SD)	65.7 (6.3)	66.8 *(9.1)*
Mean BMI, kg/m2 (SD)	28.6 (3.6)	28.0 *(3.3)*
Female gender, n (%)	13 *(43.3)*	19 *(63.3)*
Previous knee surgery, n (%)		
None	22 *(73.3)*	23 *(76.7)*
Joint debridement	2 *(6.7)*	2 *(6.7)*
Meniscectomy	4 *(13.3)*	5 *(16.7)*
Other	2 *(6.7)*	0 *(0.0)*
Ahlbäcks grade, n (%)		
II	8 *(26.7)*	5 *(16.7)*
III	20 *(66.7)*	18 *(60.0)*
IV	2 *(6.7)*	7 *(23.3)*
ASA classification, n (%)		
I	7 *(23.3)*	10 *(33.3)*
II	22 *(73.3)*	17 *(56.7)*
III	1 *(3.3)*	3 *(10.0)*
Mean hip-knee-ankle angle, ° (SD)		
Pre-operative	173.2 (5.6)	175.3 (6.3)
Post-operative	180.5 (3.5)	179.9 (3.4)

PA = peri-apatite, BMI = body mass index, ASA = American Society of Anesthesiologists.

Table II. Radiostereometric analysis migration measurements

	3 mths		1 yr		2 yrs		5 yrs	
	Cemented	PA	Cemented	PA	Cemented	PA	Cemented	PA
Mean translation, mm (SD)								
Transverse	0.00 (0.15)	0.03 (0.39)	-0.07 (0.31)	-0.05 (0.41)	-0.11 (0.33)	0.01 (0.44)	-0.09 (0.35)	-0.05 (0.52)
Longitudinal	-0.01 (0.13)	-0.26 (0.30)	-0.01 (0.17)	-0.20 (0.29)	-0.02 (0.18)	-0.17 (0.29)	0.02 (0.24)	-0.13 (0.30)
Sagittal	0.04 (0.14)	-0.05 (0.34)	0.01 (0.26)	-0.09 (0.37)	-0.04 (0.27)	-0.12 (0.36)	-0.03 (0.36)	-0.08 (0.40)
Mean rotation, ° (SD)								
Transverse	0.00 (0.23)	-0.52 (0.76)	-0.16 (0.43)	-0.52 (0.79)	-0.32 (0.65)	-0.62 (0.82)	-0.45 (1.18)	-0.45 (0.77)
Longitudinal	0.04 (0.15)	0.15 (0.31)	0.03 (0.22)	0.15 (0.35)	0.03 (0.24)	0.13 (0.40)	-0.06 (0.25)	0.11 (0.29)
Sagittal	0.04 (0.24)	0.01 (0.76)	0.10 (0.34)	0.05 (0.85)	0.08 (0.36)	0.02 (0.80)	0.07 (0.52)	0.10 (0.96)
Mean MTPM, mm (SD)*	0.34 (0.18)	0.90 (0.44)	0.54 (0.33)	0.97 (0.44)	0.58 (0.35)	0.96 (0.53)	0.68 (0.50)	1.00 (0.56)

*p-values of mean maximum total point motion (MTPM) values derived from a linear mixed-effects model analysis are stated in Table III. PA = peri-apatite.

Continuous migration of > 0.2 mm MTPM in the second post-operative year was seen in three PA-coated components and one cemented component. Between two and five years of follow-up, one of the PA-coated components showed 0.39 mm of migration, the other

two PA-coated components and the cemented component stabilised (i.e. showed less than 0.3 mm of migration). One other cemented component was stable up to two years, after which high migration of 1.32 mm was seen (Figure 2). Migration measurements of the components with continuous migration were not affected by measurement errors as the condition numbers and mean errors were consistent over time and well within limits.

The components with high migration predominantly rotated about the transverse axis (all posterior tilt) and sagittal axis (both varus and valgus tilt) in both groups. However, lateral, medial and posterior translation was also seen (Figure 3). There were no differences in mode of failure between groups. The difference in migration between groups seen in the first three months is primarily due to subsidence and posterior tilt of the PA-coated components, which stabilised beyond three months (Figure 3). Varus and valgus tilt were seen in both pre-operatively varus and valgus aligned knees; subgroup analysis yielded no differences, as the study was not sufficiently powered for subgroup analysis.

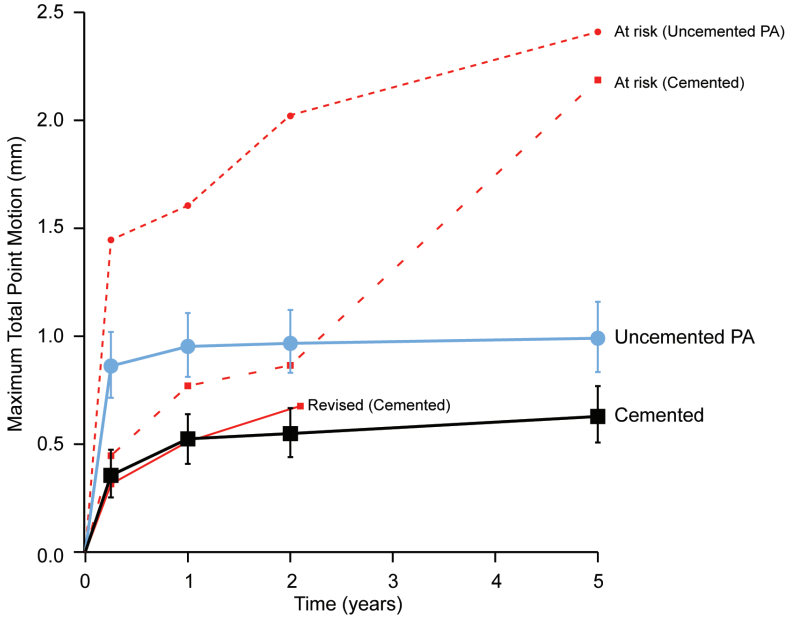


Figure 2. Maximum total point motion during the five years of follow-up (mean and 95% confidence interval for the groups in the original scale in mm, derived from the linear mixed-model analysis). The individual lines excluded from the groups are shown for one revised (ligament instability) and two high migrating components at risk for aseptic loosening.

Clinical results

Post-operatively, no significant differences in improvement in flexion, extension, KSS Knee Score, KSS Function Score and all KOOS subscales were found between groups (Table IV).

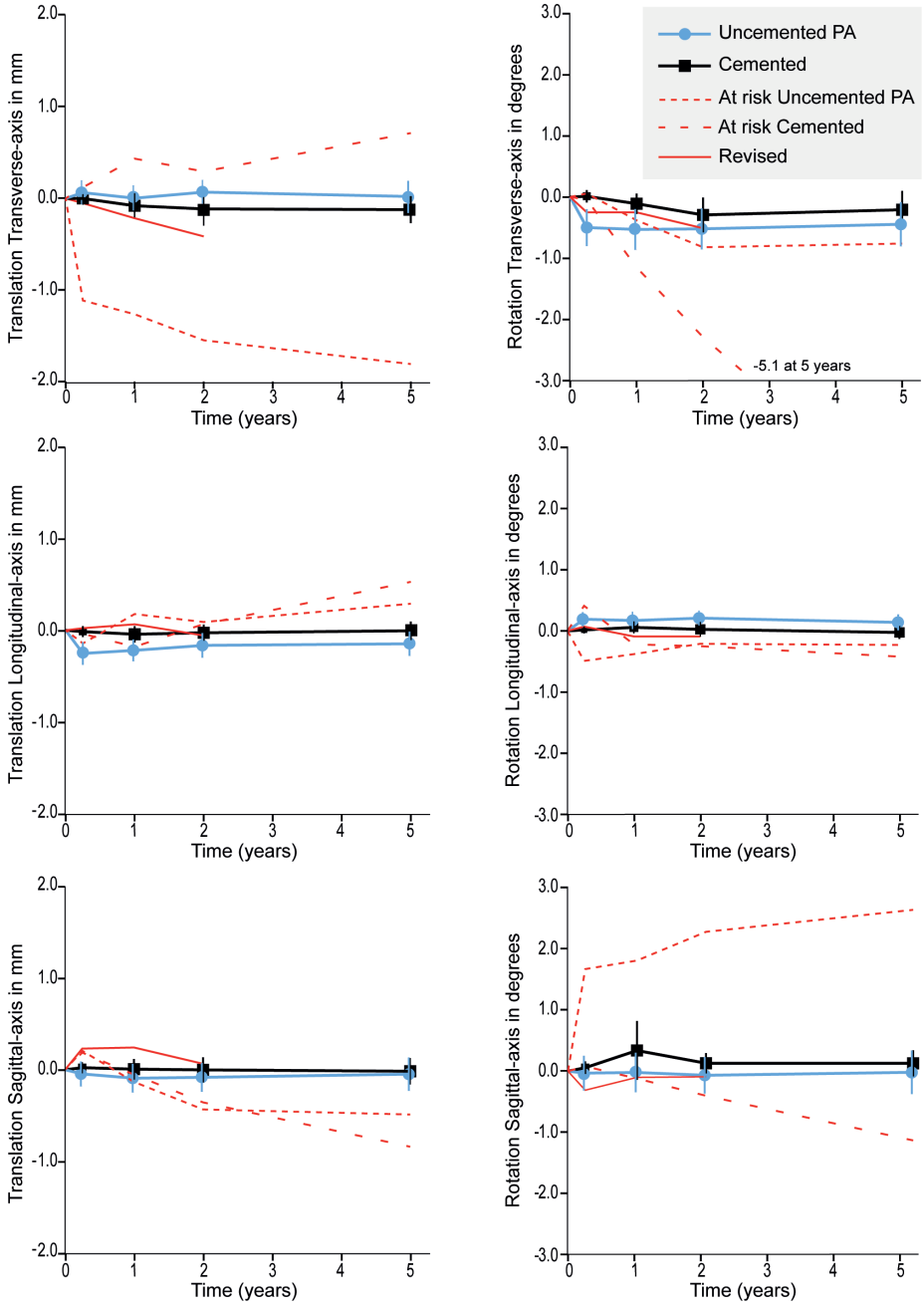


Figure 3. Translations in mm **(left side)** and rotations (°) **(right side)** of the transverse axis **(top)**, longitudinal axis **(middle)** and sagittal axis **(bottom)** for both groups (mean and 95% confidence intervals, descriptive data). The individual lines excluded from the groups are shown for one revised and two high migrating components at risk for aseptic loosening.

Table III. RSA migration analysis of maximum total point motion (MTPM) in the cemented group and the uncemented PA-coated group (back-transformed in the original scale in mm) with different time points as baseline, as derived from a linear mixed-effects model analysis

Baseline	Duration	Cemented, mean MTPM, mm (95% CI)	Uncemented PA, mean MTPM, mm (95% CI)	p-value*
Post-operative as baseline	3 mths	0.34 (0.23 to 0.47)	0.84 (0.69 to 1.01)	NS
	1 yr	0.50 (0.39 to 0.63)	0.93 (0.78 to 1.09)	NS
	2 yrs	0.53 (0.42 to 0.66)	0.95 (0.81 to 1.11)	0.000
	5 yrs	0.62 (0.49 to 0.76)	0.97 (0.81 to 1.15)	0.003
Three-months as baseline	1 yr	0.16 (0.09 to 0.23)	0.09 (-0.01 to 0.18)	NS
	2 yrs	0.19 (0.12 to 0.26)	0.11 (0.01 to 0.20)	0.037
	5 yrs	0.27 (0.19 to 0.36)	0.13 (0.01 to 0.25)	0.020
One-year as baseline	2 yrs	0.03 (-0.02 to 0.08)	0.02 (-0.05 to 0.09)	0.721
	5 yrs	0.11 (0.04 to 0.19)	0.04 (-0.06 to 0.14)	0.421

*The (Bonferroni-corrected) p-values stated in this column indicate testing the between-group mean differences with different baselines at two and five years of follow-up, as derived from a linear mixed-effects model analysis. PA = peri-apatite, NS = not stated.

Adverse events

One cemented TKA was revised after three years due to ligament instability. No other revisions were performed. One patient in the cemented group had a deep vein thrombosis during hospital admission. One patient in the PA-coated group suffered a myocardial infarction ten months after discharge but continued to participate in the study. Patients with components showing high migration are clinically still asymptomatic; no revisions due to aseptic loosening have been performed yet.

Table IV. Functional outcome compared between the two groups

	Cemented	Uncemented PA	p-value*
Mean flexion, º (SD)			
Pre-operative	116.3 (9.6)	116.0 (12.3)	NS
1 yr	121.3 (12.3)	122.6 (10.1)	NS
5 yrs	127.6 (10.0)	125.8 (8.5)	0.514
Mean extension, º (SD) †			
Pre-operative	-0.8 (7.0)	-1.8 (5.9)	NS
1 yr	-0.3 (2.9)	-0.3 (1.3)	NS
5 yrs	-0.3 (1.3)	0.0 (0.0)	0.656
Mean KSS – Knee Score (SD)			
Pre-operative	36.5 (11.8)	37.9 (8.5)	NS
1 yr	93.1 (7.7)	95.0 (5.1)	NS
5 yrs	94.3 (11.7)	91.2 (13.6)	0.297
Mean KSS – Function Score (SD)			
Pre-operative	57.3 (13.1)	62.5 (14.4)	NS
1 yr	90.2 (13.0)	94.8 (9.9)	NS
5 yrs	90.0 (12.8)	86.4 (20.9)	0.089
Mean KOOS – Symptoms (SD)			
Pre-operative	37.8 (14.5)	45.9 (13.6)	NS
1 yr	81.3 (15.8)	82.5 (16.2)	NS
5 yrs	82.1 (14.5)	86.6 (13.2)	0.307
Mean KOOS – Pain (SD)			
Pre-operative	29.9 (10.2)	38.7 (9.7)	NS
1 yr	83.2 (15.2)	83.4 (15.5)	NS
5 yrs	84.3 (15.1)	86.1 (17.9)	0.114
Mean KOOS – ADL (SD)			
Pre-operative	35.5 (11.5)	43.5 (11.5)	NS
1 yr	82.7 (17.6)	82.1 (16.3)	NS
5 yrs	80.5 (17.2)	82.9 (17.2)	0.193
Mean KOOS – Sports (SD)			
Pre-operative	3.1 (7.1)	6.0 (9.3)	NS
1 yr	44.1 (23.1)	41.0 (19.7)	NS
5 yrs	37.9 (28.7)	38.5 (25.6)	0.719
Mean KOOS – QOL (SD)			
Pre-operative	29.6 (5.5)	33.4 (8.8)	NS
1 yr	54.6 (13.2)	58.3 (12.8)	NS
5 yrs	71.0 (22.8)	74.0 (19.2)	0.867

*The p-values stated in this column indicate testing the between-group mean differences of improvement between baseline and five years of follow-up, derived with a linear mixed-effects model analysis. Note that three-months and two-year values are not stated, but results from all follow-up measurements were used in the linear mixed-effects model to test for differences. †Negative extension means no full extension possible. PA = peri-apatite, NS = not stated, KSS = Knee Society Score, KOOS = Knee injury and Osteoarthritis Outcome Score, ADL = Activities of Daily Living, QOL = Knee-related Quality of Life.

Discussion

The present study shows that uncemented PA-coated tibial components migrate more compared with cemented components over five years of follow-up. However, this difference was caused by higher migration of PA-coated components in the first post-operative weeks (i.e. settling into the bone bed). From three months onwards, the migration in both groups showed minor progression especially in the PA-coated group, suggesting a durable biological fixation might have been achieved despite high initial migration.

Both excessive initial migration in the first year, as well as high continuous migration after one year is believed to be detrimental to implant fixation and longevity[23, 34]. Yet, in most uncemented tibial trays, high initial migration in the first months appears benign and merely part of a typical biphasic migration pattern followed by stabilisation[3, 24-26, 35]. Long-term RSA studies have shown that despite substantial initial migration, highly porous and hydroxyapatite-coated uncemented components remain firmly fixated to the bone up to at least ten years of follow-up[25, 26]. In contrast, cemented tibial trays typically display little initial migration in the first months as the cement provides instant fixation, is capable of filling irregularities of the cut surface of the prepared tibial bone and evenly distributes weight[3, 36]. Continuous bone resorption at the cement-bone interface may, however, prohibit stabilisation[3]. In our study, the migration pattern suggests stabilisation of uncemented PA-coated components within three months, while cemented components appear to continue to migrate up to one year of follow-up or even longer. Carlsson et al[37] found similar migration patterns over five years of follow-up and hypothesised that cemented TKAs would eventually show more migration than the hydroxyapatite coated TKAs. Unfortunately, no long-term follow-up data are published to confirm this. The Australian registry reported comparable implant survival rates up to seven years of follow-up of cemented (97.0%) and uncemented (96.7%, not discriminating between porous-coated or PA-coated) Triathlon CR implants[12]. Given these comparable rates and the results of our study, we agree with Henricson and Nilsson[25], who concluded that the magnitude of the initial migration is not as important as the migration pattern over time, particularly for implants relying on bone ingrowth. However, future registry reports with long-term results should confirm our prediction that PA-coated implants achieve a durable biological fixation. Furthermore, future research should also focus on whether peri-apatite clinically provides any benefit over conventional 'line of sight' hydroxyapatite coating techniques.

A strength of this study is that both the cemented and the PA-coated components were of similar geometrical shape, thus differences in migration can be fully attributed to the mode of fixation. Three earlier RSA studies comparing the effect of cemented *versus* cementless fixation on migration used different designs between groups, with modular stemmed tibial trays in cemented components and either monoblock trays with two pegs[25, 33] or modular trays with a short stem and multiple spikes in uncemented components[3].

Several limitations can be noted. First, migration was based on markers inserted in the polyethylene insert. Previous studies have demonstrated small movements in the transverse plane between the polyethylene insert and the metal tray in fixed bearing TKAs[38, 39]. Nilsson et al[39] conclude that when measuring marker-based migration of modular tibial components, only out-of-plane measurements are reliable. In our study, however, a similar tibial tray and locking mechanism was used in both groups, thus insert migration with respect to the tibial tray, if any, is expected to be similar. Furthermore, the migration predominantly comprised of transverse and sagittal rotations moving out of the transverse plane. Second, the study was underpowered to perform subgroup analysis on preoperative alignment. Dunbar et al[33] reported a significant difference in rotation about the sagittal axis depending on the pre-operative alignment of the knee. They found that pre-operatively aligned varus knees tilted into valgus and *vice versa*, but only in the uncemented Trabecular Metal knees (Zimmer Biomet, Warsaw, Indiana). Previous studies have shown that pre-operative varus or valgus alignment is associated with a lower bone mineral density in one compartment and that this might influence component migration[40, 41]. Pooling data of several RSA studies, while properly adjusting for slight differences in implant design, may increase the power to further explore these failure mechanisms. Third, because cement can be seen on radiographs, migration measurements could not be blinded, making it a single blinded study. However, a single straightforward and therefore objective interpretation of RSA data can be expected when using standardised analysing methods in accordance with the RSA guideline[26, 32].

In conclusion, PA-coated tibial components showed more initial migration compared with cemented components. However, *post hoc* analysis showed that a stable migration pattern was observed from three months onwards, especially in the PA-coated group, suggesting subsequently durable biological fixation might have been achieved. Clinically, there was no significant difference in outcome between the two methods of fixation.

Take home message:

- Compared with cemented tibial components, PA-coated tibial components show higher initial migration as part of a biphasic migration pattern, characteristic for uncemented components.
- Despite high initial migration of PA-coated tibial components, a stable migration pattern was achieved.
- Both the number of tibial components showing continuous migration and the clinical outcomes were comparable between cemented and PA-coated TKAs.

Note: the authors would like to thank Prof. Dr. R. Nelissen for his valuable input in the preparation of this manuscript. We also thank study coordinator M. Davidsson, Dr M. Molt (MM) and C. Feldborg-Nielsen (CFN) for their assistance with this project in patient monitoring, inclusion of patients and surgeries.

References

1. Vince KG, Whiteside LA. Point-counterpoint. Fixation for primary total knee arthroplasty: cemented versus cementless. *Journal of Arthroplasty* 1996; 11: 123-9.
2. Voigt JD, Mosier M. Hydroxyapatite (HA) coating appears to be of benefit for implant durability of tibial components in primary total knee arthroplasty. *Acta orthopaedica* 2011; 82: 448-59.
3. Nilsson KG, Henricson A, Norgren B, Dalen T. Uncemented HA-coated implant is the optimum fixation for TKA in the young patient. *Clinical orthopaedics and related research* 2006; 448: 129-39.
4. Freeman MA, Tennant R. The scientific basis of cement versus cementless fixation. *Clinical orthopaedics and related research* 1992; 19-25.
5. Gandhi R, Tsvetkov D, Davey JR, Mahomed NN. Survival and clinical function of cemented and uncemented prostheses in total knee replacement: a meta-analysis. *J Bone Joint Surg Br* 2009; 91: 889-95.
6. Miller MA, Terbush MJ, Goodheart JR, Izant TH, Mann KA. Increased initial cement-bone interlock correlates with reduced total knee arthroplasty micro-motion following in vivo service. *Journal of biomechanics* 2014; 47: 2460-6.
7. Hofmann AA, Heithoff SM, Camargo M. Cementless total knee arthroplasty in patients 50 years or younger. *Clinical orthopaedics and related research* 2002; 102-7.
8. Nakama GY, Peccin MS, Almeida GJ, Lira Neto Ode A, Queiroz AA, Navarro RD. Cemented, cementless or hybrid fixation options in total knee arthroplasty for osteoarthritis and other non-traumatic diseases. *Cochrane Database Syst Rev* 2012; 10: CD006193.
9. Meneghini RM, Hanssen AD. Cementless fixation in total knee arthroplasty: past, present, and future. *J Knee Surg* 2008; 21: 307-14.
10. Swedish Knee Arthroplasty Register. Annual Report 2014. *Lund: SKAR* 2014.
11. National Joint Registry for England, Wales, Northern Ireland and the Isle of Man: 13th Annual Report 2016. 2016.
12. Australian Orthopaedic Association National Joint Replacement Registry. Annual Report 2016. *Adelaide: AOA* 2016.
13. Canadian Institute for Health Information. Hip and Knee Replacements in Canada: Canadian Joint Replacement Registry 2015 Annual Report. *Ottawa, ON: CIHI* 2015.
14. Geesink RG. Osteoconductive coatings for total joint arthroplasty. *Clinical orthopaedics and related research* 2002; 53-65.
15. Nelissen RG, Valstar ER, Rozing PM. The effect of hydroxyapatite on the micromotion of total knee prostheses. A prospective, randomized, double-blind study. *The Journal of bone and joint surgery American volume* 1998; 80: 1665-72.
16. Søballe K, Hansen ES, Brockstedt-Rasmussen H, Bunger C. Hydroxyapatite coating converts fibrous tissue to bone around loaded implants. *J Bone Joint Surg Br* 1993; 75: 270-8.
17. Hansson U, Ryd L, Toksvig-Larsen S. A randomised RSA study of Peri-Apatite HA coating of a total knee prosthesis. *The Knee* 2008; 15: 211-6.
18. Serekian P. Hydroxyapatite: from plasma spray to electrochemical deposition. In: Epinette J, Manley MT, editors. Fifteen years of clinical experience with hydroxyapatite coatings in joint arthroplasty: Springer, France; 2004. p. 29-33.
19. van der Linde MJ, Garling EH, Valstar ER, Tonino AJ, Nelissen RG. Periapatite may not improve micromotion of knee prostheses in rheumatoid arthritis. *Clinical orthopaedics and related research* 2006; 448: 122-8.

20. Molt M, Toksvig-Larsen S. Peri-Apatite™ Enhances Prosthetic Fixation in Tka-A Prospective Randomised RSA Study. *Journal of Arthritis* 2014; 3: 134.
21. Therbo M, Lund B, Jensen KE, Schroder HM. Effect of bioactive coating of the tibial component on migration pattern in uncemented total knee arthroplasty: a randomized RSA study of 14 knees presented according to new RSA-guidelines. *J Orthop Traumatol* 2008; 9: 63-7.
22. Karrholm J. Roentgen stereophotogrammetry. Review of orthopedic applications. *Acta orthopaedica Scandinavica* 1989; 60: 491-503.
23. Ryd L, Albrektsson BE, Carlsson L, Dansgard F, Herberts P, Lindstrand A, et al. Roentgen stereophotogrammetric analysis as a predictor of mechanical loosening of knee prostheses. *J Bone Joint Surg Br* 1995; 77: 377-83.
24. Wilson DA, Richardson G, Hennigar AW, Dunbar MJ. Continued stabilization of trabecular metal tibial monoblock total knee arthroplasty components at 5 years-measured with radiostereometric analysis. *Acta orthopaedica* 2012; 83: 36-40.
25. Henricson A, Nilsson KG. Trabecular metal tibial knee component still stable at 10 years. *Acta orthopaedica* 2016; 1-7.
26. Pijls BG, Valstar ER, Kaptein BL, Fiocco M, Nelissen RG. The beneficial effect of hydroxyapatite lasts: a randomized radiostereometric trial comparing hydroxyapatite-coated, uncoated, and cemented tibial components for up to 16 years. *Acta orthopaedica* 2012; 83: 135-41.
27. Insall JN, Dorr LD, Scott RD, Scott WN. Rationale of the Knee Society clinical rating system. *Clinical orthopaedics and related research* 1989; 13-4.
28. Roos EM, Roos HP, Ekdahl C, Lohmander LS. Knee injury and Osteoarthritis Outcome Score (KOOS)--validation of a Swedish version. *Scandinavian journal of medicine & science in sports* 1998; 8: 439-48.
29. Cooke TD, Sled EA, Scudamore RA. Frontal plane knee alignment: a call for standardized measurement. *The Journal of rheumatology* 2007; 34: 1796-801.
30. Ahlbäck S. Osteoarthrosis of the knee. A radiographic investigation. *Acta Radiol Diagn (Stockh)* 1968; Suppl 277:7-72.
31. Valstar ER, Gill R, Ryd L, Flivik G, Borlin N, Karrholm J. Guidelines for standardization of radiostereometry (RSA) of implants. *Acta orthopaedica* 2005; 76: 563-72.
32. ISO 16087:2013(E). Implants for surgery - Roentgen stereophotogrammetric analysis for the assessment of migration of orthopaedic implants. *International Organization for Standardization, Geneva, Switzerland* 2013.
33. Dunbar MJ, Wilson DA, Hennigar AW, Amirault JD, Gross M, Reardon GP. Fixation of a trabecular metal knee arthroplasty component. A prospective randomized study. *The Journal of bone and joint surgery American volume* 2009; 91: 1578-86.
34. Pijls BG, Valstar ER, Nouta KA, Plevier JW, Fiocco M, Middeldorp S, et al. Early migration of tibial components is associated with late revision: a systematic review and meta-analysis of 21,000 knee arthroplasties. *Acta orthopaedica* 2012; 83: 614-24.
35. Kendrick BJ, Kaptein BL, Valstar ER, Gill HS, Jackson WF, Dodd CA, et al. Cemented versus cementless Oxford unicompartmental knee arthroplasty using radiostereometric analysis: a randomised controlled trial. *The bone & joint journal* 2015; 97-b: 185-91.
36. Toksvig-Larsen S, Ryd L. Surface characteristics following tibial preparation during total knee arthroplasty. *J Arthroplasty* 1994; 9: 63-6.
37. Carlsson A, Bjorkman A, Besjakov J, Onsten I. Cemented tibial component fixation performs better than cementless fixation: a randomized radiostereometric study comparing porous-coated,

hydroxyapatite-coated and cemented tibial components over 5 years. *Acta orthopaedica* 2005; 76: 362-9.

38. Hansson U, Toksvig-Larsen S, Jorn LP, Ryd L. Mobile vs. fixed meniscal bearing in total knee replacement: a randomised radiostereometric study. *The Knee* 2005; 12: 414-8.
39. Nilsson KG, Henricson A, Dalen T. In vivo determination of modular tibial insert micromotion. *Trans Orthop Res Soc* 2003; 28: 1402.
40. Petersen MM, Nielsen PT, Lebech A, Toksvig-Larsen S, Lund B. Preoperative bone mineral density of the proximal tibia and migration of the tibial component after uncemented total knee arthroplasty. *J Arthroplasty* 1999; 14: 77-81.
41. Regner LR, Carlsson LV, Karrholm JN, Hansson TH, Herberts PG, Swanpalmer J. Bone mineral and migratory patterns in uncemented total knee arthroplasties: a randomized 5-year follow-up study of 38 knees. *Acta orthopaedica Scandinavica* 1999; 70: 603-8.