No difference in component migration at five years between the cemented cruciate- retaining ATTUNE and PFC-Sigma knee prosthesis: an update of a randomized clinical radiostereometry trial

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■ KNEE

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Aims

Conflicting clinical results are reported for the ATTUNE Total Knee Arthroplasty (TKA). This randomized controlled trial (RCT) evaluated five-year follow-up results comparing cemented ATTUNE and PFC-Sigma cruciate retaining TKAs, analyzing component migration as measured by radiostereometric analysis (RSA), clinical outcomes, patient-reported outcome measures (PROMs), and radiological outcomes.

Methods

A total of 74 primary TKAs were included in this single-blind RCT. RSA examinations were performed, and PROMs and clinical outcomes were collected immediate postoperatively, and at three, six, 12, 24, and 60 months' follow-up. Radiolucent lines (RLLs) were measured in standard anteroposterior radiographs at six weeks, and 12 and 60 months postoperatively.

Results

At five-year follow-up, RSA data from 61 patients were available and the mean maximum total point motion (MTPM) of the femoral components were: ATTUNE: 0.96 mm (95% confidence interval (CI) 0.79 to 1.14) and PFC-Sigma 1.37 mm (95% CI 1.18 to 1.59) ($p < 0.001$). The PFC-Sigma femoral component migrated more in the first postoperative year, but stabilized thereafter. MPTM of the tibial components were comparable at five-year follow-up: ATTUNE 1.12 mm (95% CI 0.95 to 1.31) and PFC-Sigma 1.25 mm (95% CI 1.07 to 1.44) ($p = 0.438$). RLL at the medial tibial implant-cement interface remained more prevalent for the ATTUNE at five-year follow-up compared to the PFC-Sigma (20% vs 3%). RLL did not progress over time, and varied between patients at different timepoints for both TKA systems. Clinical outcomes and PROMs improved compared with preoperative scores, and were not different between groups.

Conclusion

MTPM migration at five-year follow-up of the femoral and tibial component of the ATTUNE were similar and as low as that of the PFC-Sigma. MTPM migration of both knee implants did not significantly change from one year post-surgery, indicating stable fixation. Long-term ATTUNE performance may be expected to be comparable to the clinically well-performing PFC-Sigma. We have not found evidence of increased tibial component migration as measured by RSA to support concerns about cement debonding and a higher risk of aseptic loosening with the ATTUNE TKA.

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Introduction

Registry data from around the world report mean prosthesis survival at ten years of approximately 95% for total knee arthroplasty (TKA).[1-4] Aseptic loosening is the most common reason for failure of TKA and the need for revision arthoplasty (approximately 31% to 40%).[3,4] Despite high prosthesis survival rates, patient dissatisfaction after TKA has been reported to be as high as 20%.[5,6] With the aim of reducing the risk of aseptic loosening and improving patient satisfaction, innovations in TKA have been introduced.[7] However, introducing new implants or techniques may also lead to less favourable outcomes.

Since the first version of the ATTUNE TKA system (DePuy Synthes, USA) was introduced, concerns have been reported regarding unexpected higher revision rates caused by failure of cement fixation of the tibial component.[8-11] A new design, ATTUNE S+, was introduced with increased prosthesis-surface roughness and a redesigned tibial baseplate for improved cement fixation. The ATTUNE S+ has shown in a cadaver study to have improved tibial component fixation when compared to the ATTUNE.[12]

A phased introduction of new implants has been proposed to safeguard both patient safety and quality of care.[13] Radiostereometric analysis (RSA)-measures prosthesis migration and predicts long-term mechanical loosening. It can be a valuable tool for monitoring the introduction of new implants.[13-16] Despite the reported concerns regarding the ATTUNE design, two RSA studies reported good tibial implant stability at two-year follow-up of the initial version of the ATTUNE TKA.[17,18]

Although aseptic loosening of the femoral component is less common, it still makes up to one-third of the total number of cases undergoing revision for aseptic loosening.[19] Femoral component migration has been studied less frequently than tibial component migration. As a result, knowledge of the clinical consequence of femoral component migration is limited.

Our main study objective was to assess and compare the original ATTUNE femoral component migration in the first five postoperative years with its clinically well-performing predecessor, the PFC-Sigma (DePuy Synthes). A secondary objective was to evaluate the migration between two and five years' follow-up of the original ATTUNE and PFC-Sigma tibial components. Clinical outcomes, patient-reported outcome measures (PROMs), and radiological outcomes of the two TKA designs were included in the study to evaluate clinical performance. We hypothesized that the ATTUNE migration would be similar to or less than the PFC-Sigma migration. Hence, we expected the risk for long-term aseptic loosening of the ATTUNE to be similar as for the well-performing PFC-Sigma TKA.

Methods

This was a single-blind randomized controlled RSA trial on consecutive patients eligible for elective TKA recruited between 2014 and 2015 with five-year follow-up. Operating and cementing techniques were performed according to manufacturer instructions. Neutral mechanical component alignment was performed with manual instrumentation from the manufacturer using bony references. Femoral component alignment was set with external rotation of 3° and 5° valgus using intramedullary alignment jigs. The flexion gap was balanced medially and laterally with the knee in 90° flexion. The tibial component was aligned to the tibial crest with extramedullary jigs. Sagittal alignment was performed with a standard of 3° to 5° posterior slope for the PFC-Sigma and 5° to 6° for the ATTUNE. Cementing was performed in a single stage, starting with the tibial component. A tourniquet was used during cementing. After pulsed lavage and drying of the bone surfaces with dry clean gauzes, clean surgical gloves were donned. Vacuum-mixed bone cement (Palacos; Heraeus Medical, Netherlands) was applied to the exposed tibial cancellous bone using an applicator gun. Cement was applied to the posterior side of the femoral component and the prepared distal femur. After pressurization, impaction of the components, and removal of extruded cement, cement was allowed to cure with the leg fully extended.

The two-year results of this study have been published previously by Kaptein et al.[17] This study, including five-year follow-up, received ethical approval from the local ethics committee: NL48357.058.14 (Clinicaltrials.gov identifier: NCT02256098). A total of 191 patients were eligible for the study; 74 were randomized and 66 were still enrolled in the study at two-year follow-up. Between two- and five-year follow-up, four patients died and one patient did not wish to attend the five-year review. At five-year follow-up, RSA data from 61 patients were available: 26 ATTUNE and 29 PFC-Sigma femoral components, and 27 ATTUNE and 31 PFC-Sigma tibial components (Figure 1).

The first postoperative RSA examination was made after weightbearing, but before hospital discharge. Subsequent RSA examinations were made at three, six, 12, 24, and 60 months' follow-up using a standard RSA protocol, with the patient in supine position above a uniplanar calibration cage.[17] Implant migration was calculated with model-based RSA software (v. 4.2, RSAcore, Netherlands) following the RSA guidelines by Valstar et al.[20] Bone markers used in the migration calculations were well distributed, with a mean condition number of 51 m^{-1} in the femoral bone and 59 m^{-1} in the tibial bone. Markers were stable with a mean error of rigid body fitting of 0.21 mm for the femoral and 0.19 mm for the tibial bone markers, respectively. Double examinations to determine bias and clinical RSA precision were acquired at one-year follow-up (Table I).

The primary outcome was maximum total point motion (MTPM):[21] the length of the translation vector (mm) of a point on the prosthesis with the largest translation. Translations (Tx, Ty, Tz (mm)) and rotations (Rx, Ry, Rz (°)) were calculated along and about the transverse (x-axis), longitudinal (y-axis), and sagittal axes (z-axis) (Figure 2). Migration is calculated for each follow-up moment relative to baseline, and migration rate was defined as the change in migration per year.

Clinical outcome (Knee Society Score (KSS))[22] and adverse events related to the arthroplasty surgery, such as loosening and infection, were recorded during follow-up. PROMs were collected preoperatively and at three, six, 12, 24, and 60 months' follow-up and included: EuroQol five-dimension five-level questionnaire (EQ-5D-5L) and EuroQol visual analogue scale (EQ-VAS), Short form Knee injury and Osteoarthritis Outcome Score (KOOS-PS), numerical rating scale (NRS) pain during rest and activity, Oxford Knee Score (OKS),[23,24] and NRS patient satisfaction score, with 0 representing 'very unsatisfied' and 10 representing

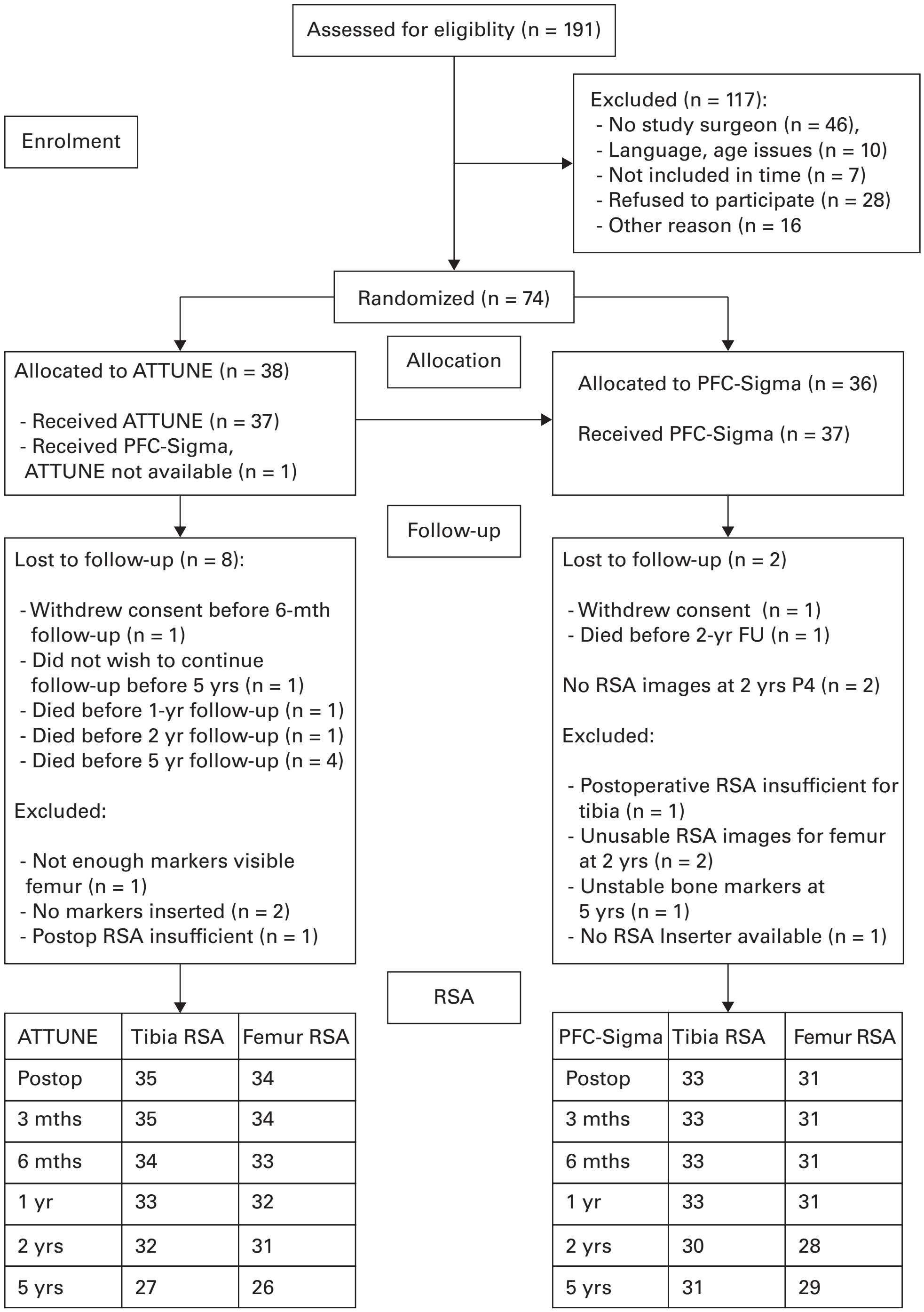

Fig. 1

CONSORT flow diagram of participants through each stage. FU, follow-up; PFC, Press-Fit Condylar; RSA, radiostereometric analysis.

'very satisfied'.[25–28] At five-year follow-up, different versions of the EQ-5D, KOOS, and OKS were used compared with earlier follow-up. Earlier PROM scores were recalculated to the newest version as instructed by the PROM provider.[26,27,29]

Anteroposterior and lateral radiographs of the tibial components acquired at six weeks' and 12 and 60 months' follow-up were scored for the presence, thickness, and progression of radiolucent lines (RLLs). Radiological scoring was performed under the supervision of the lead surgeon (PH) using the Knee Society Clinical Rating System,[30] and a standard PACS viewer (Vital Images, USA) and RadiAnt DICOM Viewer 2020.2.3 (Medixant, Poland).

Statistical analysis. Per-protocol statistical analysis was performed using SPSS v. 25 (IBM, USA) and R v. 4.0.4 (R Foundation for Statistical Computing, Austria). Original sample size calculation was performed on tibial MTPM at two

Table I. Bias and precision of the radiostereometric analysis set-up presented as mean (standard deviation) of the migration between the first and second examination of the double examinations.

Prosthesis	Tx, mm	Ty, mm	Tz, mm	Rx, °	Ry, °	Rz, °	MTPM, mm
Femur							
ATTUNE (n = 31)	0.04 (0.10)	0.01 (0.12)	-0.00 (0.25)	0.01 (0.24)	-0.00 (0.37)	0.01 (0.14)	0.50 (0.25)
PFC-Sigma (n = 34)	0.04 (0.16)	0.03 (0.16)	-0.07 (0.32)	0.05 (0.45)	-0.13 (0.31)	-0.00 (0.16)	0.62 (0.31)
Tibia							
ATTUNE (n = 30)	0.00 (0.13)	-0.05 (0.12)	0.01 (0.21)	0.05 (0.29)	-0.01 (0.35)	0.03 (0.12)	0.41 (0.23)
PFC-Sigma (n = 34)	0.04 (0.13)	-0.00 (0.16)	0.12 (0.40)	0.11 (0.64)	0.07 (0.73)	0.08 (0.18)	0.71 (0.62)

MTPM, maximum total point motion; Rx, Ry, Rz, rotations; Tx, Ty, Tz, translations.

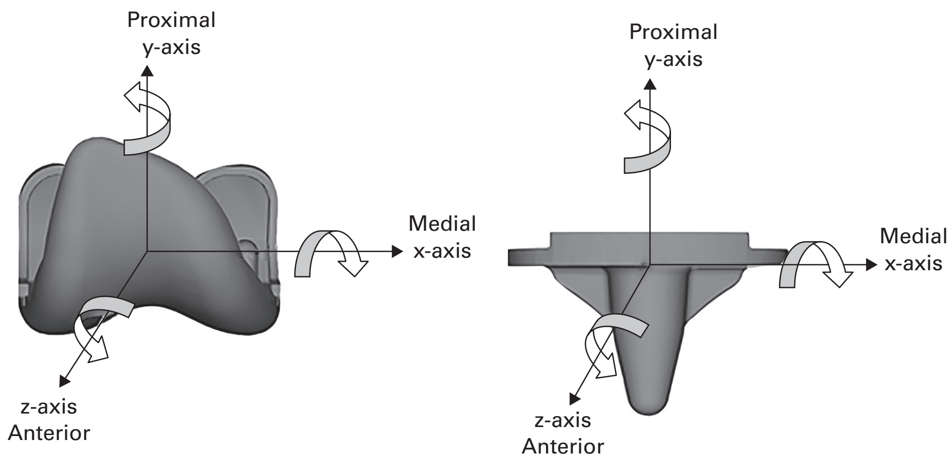

Fig. 2

Translation along the transverse axis (x-axis, Tx) is medial, along the longitudinal axis (y-axis, Ty) is proximal, and along the sagittal axis (z-axis, Tz) is anterior. Rotations (Rx, Ry, Rz) are defined about these axes, according to the right hand rule (for right-handed coordinates, the right thumb points along the z-axis in the positive direction, and the curling motion of the fingers of the right hand represents a motion from the first/x-axis to the second/y-axis). Conventions are for a right-sided knee. Migration of left-sided prostheses were recalculated in order to describe the migration in anatomical terms for a right-sided prosthesis.

years postoperatively.[17] All available data up to five-year follow-up were used for analysis. The significance level was set at $p < 0.05$.

Migration results are presented with descriptive statistics for MTPM, translations, and rotations (mean, 95% confidence interval (CI)), based on linear mixed-effect modelling (LMM).[31] MTPM was log-transformed during statistical modelling to obtain normal distribution, calculated as log(MTPM + 1). The presented values were back-transformed. The LMM model contained a grouping variable (ATTUNE vs PFC-Sigma), a time variable (factor, with baseline and three, six, 12, 24, and 60 months), and an interaction term of group by time (fixed-effects). To ensure model fit, the distribution of the residuals of the variables was visually evaluated.

PROMs and KSS scores are analyzed using a generalized linear mixed model (GLMM).[31] Estimated marginal means were calculated for PROMs and KSS scores with 95% CIs. The model contained a grouping variable (ATTUNE vs PFC-Sigma), a time variable (baseline and three, six, 12, 24, and 60 months), an interaction term of group by time (fixed-effects), and a random-effects term for subject ID.

A correlation term, 'Autoregressive Order-1 covariance matrix', was used to model the remaining variability for both LMM and GLMM. A post-hoc analysis for MTPM was done, stratifying the ATTUNE group into a group with and without radiolucencies.

Results

Migration results at all follow-up timepoints are shown in Table II (femur) and Table III (tibia). Figure 3 (femur and tibia) presents the MTPM data. All translations and rotations along the three orthogonal axes are presented in Supplementary Figures a and b.

Mean femoral component MTPM at five-year follow-up was 0.96 mm (95% CI 0.79 to 1.14) for the ATTUNE and 1.37 mm (95% CI 1.18 to 1.59) for the PFC-Sigma ($p = 0.001$, LMM). The PFC-Sigma femoral component migrated more in the first post-operative year ($p < 0.001$). Mean femoral component MTPM rate between one- and two-year follow-up was not significant and was comparable for both groups: ATTUNE: 0.06 mm/yr (95% CI -0.14 to 0.26) and PFC-Sigma 0.09 mm/yr (95% CI -0.12 to 0.29) ($p = 0.060$, LMM). Similarly, femoral MTPM rates between two- and five-year follow-up were also comparable for both groups and were not significant: ATTUNE mean 0.00 mm/yr (95% CI -0.07 to 0.08) and PFC-Sigma 0.04 mm/yr (95% CI -0.03 to 0.11), ($p = 0.060$, LMM).

Mean internal-external (Ry) rotations of the femoral components at one- and five-year follow-up were significantly

Table II. Femoral translations and rotations.

Mths	Mean, mm (95% CI)			Mean, ° (95% CI)			MTPM, mm
	Tx	Ty	Tz	Rx	Ry	Rz	
ATTUNE Femur							
3	0.01 (-0.10 to 0.12)	0.06 (-0.00 to 0.13)	0.05 (-0.15 to 0.24)	0.05 (-0.14 to 0.25)	-0.10 (-0.28 to 0.09)	0.01 (-0.08 to 0.11)	0.69 (0.56 to 0.83)*
6	0.02 (-0.09 to 0.13)	0.09 (0.02 to 0.15)*	-0.01 (-0.20 to 0.18)	0.11 (-0.08 to 0.31)	-0.12 (-0.30 to 0.07)	0.06 (-0.04 to 0.15)	0.85 (0.70 to 1.01)*
12	0.05 (-0.06 to 0.17)	0.12 (0.05 to 0.19)*	-0.07 (-0.27 to 0.12)	0.24 (0.04 to 0.45)*	-0.13 (-0.32 to 0.06)†	0.07 (-0.03 to 0.17)	0.89 (0.74 to 1.05)*
24	0.04 (-0.07 to 0.16)	0.11 (0.05 to 0.18)*	0.07 (-0.13 to 0.27)	0.18 (-0.02 to 0.38)	0.03 (-0.17 to 0.22)	0.10 (-0.00 to 0.20)	0.96 (0.80 to 1.13)*
60	0.03 (-0.09 to 0.15)	0.10 (0.03 to 0.17)*	-0.00 (-0.21 to 0.20)	0.25 (0.03 to 0.46)*	-0.21 (-0.42 to -0.01)*†	0.01 (-0.10 to 0.11)	0.96 (0.79;1.14)*†
PFC-Sigma							
3	-0.02 (-0.13 to 0.09)	0.15* (0.09 to 0.22)	-0.12 (-0.32 to 0.07)	0.36* (0.15 to 0.56)	-0.00 (-0.19 to 0.19)	-0.03 (-0.13 to 0.07)	1.09 (0.93 to 1.27)*
6	0.00 (-0.11 to 0.11)	0.13* (0.06 to 0.19)	-0.02 (-0.21 to 0.18)	0.30* (0.10 to 0.51)	0.06 (-0.13 to 0.25)	-0.02 (-0.12 to 0.08)	1.03 (0.87 to 1.21)*
12	-0.05 (-0.16 to 0.06)	0.19* (0.12 to 0.26)	-0.11 (-0.31 to 0.09)	0.42* (0.22 to 0.62)	0.16 (-0.04 to 0.35)†	-0.01 (-0.11 to 0.09)	1.23 (1.05 to 1.43)*
24	-0.03 (-0.15 to 0.08)	0.20* (0.13 to 0.27)	0.16 (-0.04 to 0.36)	0.24* (0.03 to 0.45)	0.10 (-0.10 to 0.30)	0.00 (-0.10 to 0.11)	1.27 (1.08 to 1.47)*
60	-0.01 (-0.12 to 0.11)	0.18* (0.11 to 0.25)	0.05 (-0.15 to 0.25)	0.41* (0.21 to 0.62)	0.10 (-0.09 to 0.30)†	0.03 (-0.07 to 0.13)	1.37 (1.18 to 1.59)*†

*Statistically significant difference between baseline and follow-up.
†Statistically significant difference between designs.
CI, confidence interval; MTPM, maximum total point motion.

Table III. Tibial translations and rotations.

Mths	Mean, mm (95% CI)			Mean, ° (95% CI)			MTPM, mm
	Tx	Ty	Tz	Rx	Ry	Rz	
ATTUNE Tibia							
3	-0.02 (-0.15 to 0.12)	0.04 (-0.02 to 0.10)	-0.02 (-0.19 to 0.15)	-0.13 (-0.35 to 0.09)	0.19 (-0.04 to 0.43)	-0.02 (-0.16 to 0.13)	0.86 (0.72 to 1.01)
6	-0.00 (-0.13 to 0.13)	0.04 (-0.02 to 0.10)	-0.09 (-0.26 to 0.08)	-0.22 (-0.44 to 0.00)	0.32* (0.09 to 0.56)	-0.05 (-0.20 to 0.1)	0.96 (0.81 to 1.12)
12	-0.01 (-0.14 to 0.13)	0.03 (-0.03 to 0.09)	-0.24* (-0.41 to -0.06)	-0.38 (-0.60 to -0.15)*	0.28* (0.04 to 0.52)	-0.01 (-0.16 to 0.14)	1.12 (0.96 to 1.30)
24	-0.03 (-0.17 to 0.10)	-0.01 (-0.07 to 0.05)	-0.14 (-0.32 to 0.03)	-0.26 (-0.49 to -0.04)*	0.21 (-0.03 to 0.45)	-0.03 (-0.18 to 0.12)	1.10 (0.93 to 1.27)
60	-0.07 (-0.21 to 0.07)	0.06 (-0.01 to 0.12)	-0.16 (-0.34 to 0.03)	-0.32 (-0.56 to -0.09)*	0.22 (-0.03 to 0.48)†	-0.04 (-0.19 to 0.12)	1.12 (0.95 to 1.31)
PFC-Sigma							
3	-0.07 (-0.21 to 0.06)	0.01 (-0.05 to 0.07)	-0.08 (-0.25 to 0.10)	-0.14 (-0.37 to 0.08)	-0.23 (-0.47 to 0.01)	0.08 (-0.07 to 0.23)	1.03 (0.87 to 1.20)
6	-0.17* (-0.31 to -0.04)	0.01 (-0.04 to 0.07)	0.00 (-0.17 to 0.18)	-0.20 (-0.42 to 0.03)	-0.03 (-0.27 to 0.21)	0.16* (0.01 to 0.31)	1.14 (0.97 to 1.32)
12	-0.15* (-0.28 to -0.01)	0.01 (-0.5 to 0.07)	-0.05 (-0.23 to 0.12)	-0.16 (-0.39 to 0.06)	-0.18 (-0.42 to 0.06)	0.08 (-0.07 to 0.23)	1.13 (0.96 to 1.31)
24	-0.12 (-0.25 to 0.02)	-0.07* (-0.13 to -0.01)	0.08 (-0.10 to 0.26)	0.05 (-0.18 to 0.28)	-0.19 (-0.43 to 0.06)	0.03 (-0.13 to 0.18)	1.19 (1.01 to 1.37)
60	-0.06 (-0.20 to 0.07)	0.3 (-0.03 to 0.9)	0.08 (-0.09 to 0.26)	0.03 (-0.20 to 0.26)	-0.20 (-0.44 to 0.04)†	-0.05 (-0.20 to 0.10)	1.25 (1.07 to 1.44)

*Statistically significant difference between baseline and follow-up.
†Statistically significant difference between groups.
CI, confidence interval; MTPM, maximum total point motion.

different between the designs: ATTUNE -0.13° (95% CI -0.32 to 0.06) and -0.21° (95% CI -0.42 to -0.01), respectively, and PFC-Sigma 0.16° (95% CI -0.04 to 0.35) and 0.10° (95% CI -0.09 to 0.30) respectively (p = 0.039 and p = 0.012 respectively, LMM). All other migration metrics were comparable between the designs.

Mean tibial component MTPM at five-year follow-up was comparable for both groups: 1.12 mm (95% CI 0.95 to 1.31) for the ATTUNE and 1.25 mm (95% CI 1.07 to 1.44) (p = 0.438, LMM) for the PFC-Sigma. Between one- and two-year follow-up, the mean tibial MTPM rate was comparable and not significant for both groups: ATTUNE -0.01 mm/yr (95% CI -0.08 to 0.06) and PFC-Sigma 0.03 mm/yr (95% CI -0.05 to 0.11) (p = 0.740, LMM). Between two- and five-year follow-up, a similar rate was observed: ATTUNE mean 0.00 mm/yr (95% CI -0.01 to 0.02) and PFC-Sigma 0.01 mm/yr (95% CI 0.00 to 0.03) (p = 0.599, LMM).

The mean internal-external rotation of the tibial components at five-year follow-up was significantly different: ATTUNE 0.22° (95% CI -0.03 to 0.48) and PFC-Sigma -0.20° (95% CI -0.44 to 0.04) (p = 0.029, LMM). All other migration metrics were comparable between the two designs.

Between two- and five-year follow-up, no patient required revision surgery. Clinical outcomes (KSS) and patient-reported outcome measures (PROMs) improved over time for both groups (generalized linear mixed-effects model (Table IV and Supplementary Table i)). No differences were found for KSS and PROM scores between groups. At five-year follow-up, medial implant-cement interface RLLs were present in 20% of the ATTUNE and 3% of the PFC-Sigma tibial components. These RLLs did not progress between one- and five-year follow-up.

In a post-hoc analysis, the ATTUNE group was stratified into a group without radiolucency (n = 21) and a group with radiolucency (n = 11) at five-year follow-up. There was no difference in any of the migration parameters between these groups.

Discussion

At five-year follow-up, the ATTUNE femoral component MTPM was significantly lower compared to that of the PFC-Sigma. This difference originated in the first postoperative year; thereafter, the migration rate of both designs was comparable. For the tibial components, MTPM at five-year follow-up

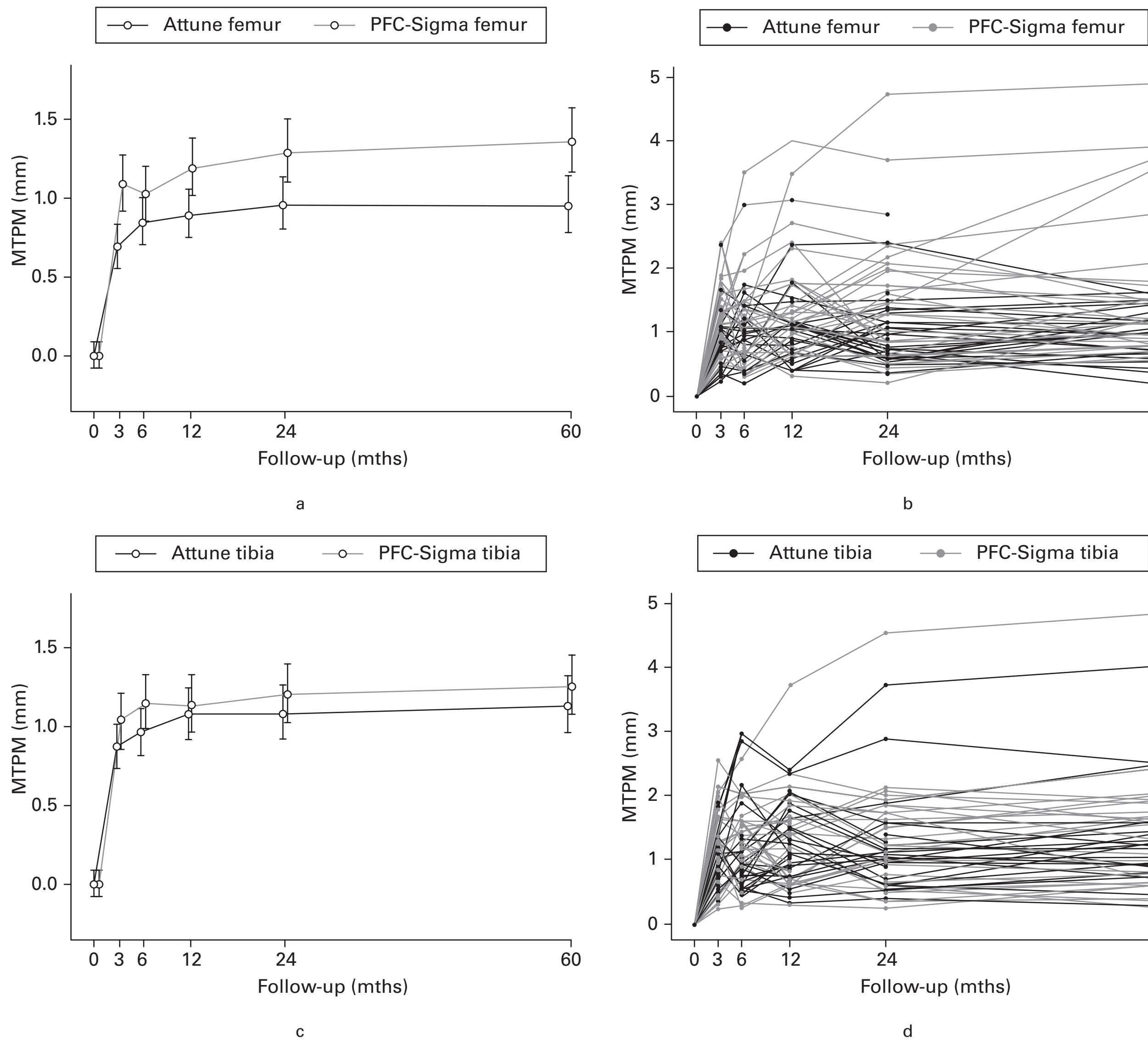

Fig. 3

Five-year mean maximum total point motion (MTPM) (mm) (linear mixed effects model). Error bars indicate 95% confidence interval (CI) of the mean. a) Mean MTPM femoral component. b) Individual MTPM femoral component. c) Mean tibial component. d) Individual MTPM tibial component.

and the migration rate between one- and five-year follow-up were comparable.

Our results support that the conclusion of our previous study,[17] that at two-year follow-up the ATTUNE TKA was not inferior to the PFC-Sigma with regard to overall tibial migration, and this maintained at five-year follow-up. Important additional findings of this five-year follow-up study are that the ATTUNE femoral component migration is similar to the PFC-Sigma component, and that mean tibial and femoral MTPM of both TKA designs do not significantly change after one-year follow-up.

At five-year follow-up, the ATTUNE femoral component had rotated externally, whereas the PFC-Sigma rotated internally. For the tibial component, component rotation was in the opposite direction: the ATTUNE rotated internally and the PFC-Sigma rotated externally. The opposite directions of femur and tibia rotation are caused by the forces and moments between them. A moment causing the femur to rotate internally triggers an external rotation on the tibial component. These rotation differences may be related to the initial positioning of the femoral and tibial components, but since we did not have CT measurements to compare, this cannot be verified.[32] More importantly, these rotations stabilized and did not change further after two-year follow-up.

At two-year follow-up, we found more backward tilting of the ATTUNE tibial component (Rx), longitudinal axis rotation (Ry), and sagittal translation (Tz).[17] The backward tilting about the transverse axis has been suggested to be a good predictor for the aseptic loosening of individual components.[33] However, the difference in migration along the transverse axis between the

Table IV. Estimated means (from generalized linear mixed-effects model) of clinical outcome and patient-reported outcome measures. All scores are given as means and standard errors.

Follow-up	KSS	Pain rest	Pain activity	EQ-5D-5L	EQ-VAS	KOOS-PS	OKS	Satisfaction
ATTUNE								
Preoperative	52 (2.8)	5 (2.9)	7 (4.0)	0.80 (0.07)	68 (8.4)	50 (6.8)	26 (3.3)	N/A
3 mths	81 (4.4)	2 (1.4)	2 (1.7)	0.86 (0.08)	77 (9.5)	70 (9.4)	36 (4.6)	5 (0.7)
6 mths	85 (4.6)	2 (1.2)	2 (1.4)	0.89 (0.08)	78 (9.6)	71 (9.6)	39 (5.1)	6 (0.7)
1 yr	92 (5.0)	1 (0.9)	1 (1.2)	0.87 (0.08)	74 (9.2)	74 (10.0)	40 (5.1)	6 (0.7)
2 yrs	94 (5.1)	1 (0.8)	1 (1.1)	0.90 (0.09)	78 (9.7)	77 (10.4)	42 (5.4)	6 (0.7)
5 yrs	93 (5.1)	0 (0.6)	1 (0.8)	0.93 (0.09)	76 (9.4)	80 (10.8)	45 (5.8)	8 (1.0)
PFC-Sigma								
Preoperative	53 (2.9)	5 (2.9)	8 (4.2)	0.78 (0.07)	68 (8.4)	48 (6.4)	25 (3.1)	N/A
3 mths	86 (4.7)	1 (1.0)	3 (1.2)	0.87 (0.08)	80 (9.9)	70 (9.4)	38 (4.9)	5 (0.7)
6 mths	90 (4.9)	1 (0.8)	2 (1.4)	0.89 (0.08)	70 (8.6)	72 (9.7)	38 (4.8)	6 (0.7)
1 yr	94 (5.1)	0 (0.7)	1 (1.1)	0.91 (0.08)	78 (9.6)	73 (9.9)	41 (5.3)	6 (0.7)
2 yrs	94 (5.1)	1 (0.7)	1 (0.9)	0.92 (0.08)	79 (9.8)	76 (10.4)	42 (5.4)	6 (0.8)
5 yrs	90(4.9)	1 (0.8)	1 (0.9)	0.88 (0.08)	77 (9.6)	75 (10.2)	43 (5.5)	8 (1.1)

EQ-5D-5L, EuroQol five-dimension five-level questionnaire; EQ-5D-VAS, EuroQol visual analogue scale; KOOS-PS, Knee injury and Osteoarthritis Outcome Score Physical Function Short Form; KSS, Knee Society Score; N/A, not applicable; OKS, Oxford Knee Score; SE, standard error of estimation.

two designs as reported in the two-year follow-up paper was not present at five-year follow-up. Additionally, backward tilting stabilized between one- and five-year follow-up.

Clinical outcome (KSS) and PROMs were comparable between both groups. All PROM scores changed significantly up to three-month follow-up, after which a plateau was reached. This ceiling and floor effect is commonly found in PROMs.[34] Apart from one liner exchange for periprosthetic infection at two-year follow-up, revision surgery was neither needed nor planned. At five-year follow-up, the ATTUNE showed more RLLs than the PFC-Sigma, similar to the amount we reported at two-year follow-up (17% ATTUNE vs 3% PFC-Sigma).[17] However, neither a progression in RLLs was observed nor an association between RLL and migration were found. Other studies report inconclusive results on the presence and clinical relevance of RLLs.[10,30,35–37] In a post-hoc analysis, the presence of RLLs along the ATTUNE tibial components did not affect the five-year migration results. As we reasoned in a previous study,[17] this is most likely due to the non-biological nature of these non-progressive RLLs.

There are no published RSA data for femoral component migration for the ATTUNE design. Koster et al[38] reported femoral migration for the Persona PS and NexGen LPS designs (both from Zimmer Biomet, USA), Henricson et al[39] reported on the NexGen CR design, and Teeter et al[40] reported on the Triathlon PS design (Stryker, USA). In these studies, the femoral component stabilized after the initial migration, similar to our results. Additionally, Teeter et al[40] reported no differences in migration between measured resection, the technique we used, and gap balancing for femoral component migration.

No literature on RSA data for femoral component migration exists about the ATTUNE design. Koster et al[38] reported femoral migration of the Persona PS and NexGen LPS designs, Henricson et al[39] reported on the NexGen CR design, and Teeter et al[40]reported on the Triathlon PS design. In these studies, the femoral component stabilized after the initial migration, similar to our results. Additionally, Teeter et al[40] reported no differences in migration between measured resection, the technique we used, and gap balancing for femoral component migration.

In our study, the PFC-Sigma tibial component initially migrated more than reported by Schewelov et al,[41] but the change in MTPM from three months to five years is comparable: 0.23 mm in our study and 0.24 mm in Schewelov et al.[41] Mean MTPM of the ATTUNE tibial component in the study by Turgeon et al[18] was < 0.2 mm six months postoperatively, whereas in this study we measured 0.96 mm. This is due to the difference in design, as well as the use of a different baseline MTPM measurement: Turgeon et al[18] used a Posterior Stabilized (PS) design and baseline RSA acquisition at six weeks postoperatively, while we used a cruciate-retaining (CR) design and direct postoperative reference.

Since our previous study, two further publications have reported revisions of the ATTUNE TKA, related to potential problems with cement adherence at the ATTUNE tibial tray.[10,11] Lachieiwcz et al[10] found a higher rate of revisions performed and a higher rate of revisions pending for the ATTUNE compared to a control group of 13 other TKAs. In 17 of 19 knees revised, and in 10 of 12 knees with revisions pending, the indication for revision was aseptic loosening (debonding) of the tibial component. Bhalekar et al[11] found significantly less cement adherence for the ATTUNE and NexGen tibial trays compared to Triathlon and PFC-Sigma in their retrieval study (median cover of 0% vs 50%, respectively; p < 0.001), and in a supplementary dataset from an Australian retrieval unit. Despite less adherence to the tibial tray, all of the ATTUNE TKAs from their dataset and 18 of the 23 from the supplementary dataset were revised for reasons other than a tibial component loosening. Our cementing technique is similar to the most optimal method described by Rodríguez-Collell,[42] which is associated with deep cement penetration and good cement interdigitation.

Two national joint registers do not report a difference in revision rate between the ATTUNE and PFC-Sigma. The 2020 report of the National Joint Registry (NJR) for England, Wales, Northern Ireland, Isle of Man, and the States of Guernsey states that the cemented, fixed-bearing CR ATTUNE had a five-year revision rate of 2.38% (95% CI 1.94 to 2.92) and 2.03% (95% CI 1.95 to 2.10) for the cemented CR PFC-Sigma. Furthermore, the Australian Orthopaedic Association National Joint Replacement Registry reported a five-year revision rate of 3.0% (95% CI 2.7 to 3.5) for the ATTUNE and 2.5% (95% CI 2.3 to 2.7) for the PFC-Sigma.[3,43] The ten-year revision rates of the PFC-Sigma in joint registries is 3% to 4%.[3,43] Up to the present, apart from one liner exchange, no revisions were required in our study, or are scheduled, contributing to the registry data that revision rates of the ATTUNE are indeed low at five years.

This study had some limitations, some of which were noted in our two- year study.[17] First, some patients were lost to follow-up (n = 10), mostly due to death (n = 8), which is a consequence of the age of the patients at inclusion. None of these deaths were related to the implants or surgery. Moreover, the number of enrolled patients still meets the calculated sample size for the two-year tibial MTPM outcome.[17] Second, not all RSA images could be analyzed due to obscured or unstable markers at the RSA radiographs, resulting in missing data. However, using a linear mixed-effects model statistical technique, all available data are included in the analysis and missing data are taken into account with repeated measures. Third, this study is underpowered for meaningful analysis of PROM scores. PROM scores vary between different studies for ATTUNE and PFC TKA.[18,41] However, regarding the association between implant migration and PROMs, preliminary results of a study presented at the seventh RSA conference indicated that patients with continuously migrating implants do not have inferior PROM scores.[44] This study suggests that RSA and PROMs are instruments that measure different domains of outcome in implant surgery: RSA measures the exact fixation of the implant within the bone and the effect of biomechanical forces on migration, while PROMs measure the perception of the patients on outcome after TKA.

In conclusion, overall MTPM migration at five-year follow-up of the femoral and tibial components of the ATTUNE TKA is low and similar to that of the PFC-Sigma. More importantly, MTPM migration of both knee implants does not significantly change from one year onwards, indicating a stable implant and fixation. Long-term ATTUNE performance is expected to be similar to that of the well-performing PFC-Sigma TKA design. PROMs and clinical findings do not differ between the designs in this study. Despite persisting concerns about cement debonding of the ATTUNE tibial component and a high revision rate secondary to aseptic loosening for the ATTUNE TKA in the literature, we did not find evidence of increased tibial or femoral component migration as measured by RSA for the ATTUNE knee when compared to the PFC-Sigma. We advise a ten-year follow-up RSA study to enable long-term analyses of the ATTUNE TKA.

Take home message

- Short-term tibial implant migration is predictive for long-term aseptic loosening.
- This study shows that the tibial and femoral components of the ATTUNE and PFC-Sigma designs remained well-fixated at medium-term follow-up after initial migration, and with good clinical outcomes.
- Reporting femoral component migration is important to increase knowledge about femoral migration, patient-reported outcome measures, and clinical outcomes.

Supplementary material

Original data of clinical outcome and patient-reported outcome measures; Figures of all migration results for the femoral and tibial component.

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Ethical review statement:
The trial was performed in compliance with the Declaration of Helsinki and Good Clinical Practice guidelines. The study was approved by the Committee for Medical Ethics (CME) of Leiden University Medical Center (LUMC) (NL48357.058.14) and was registered in Clinical Trials (ClinicalTrials. gov ID NCT02256098). Informed consent was obtained from all patients. Reporting of the trial was in accordance with the CONSORT statement.

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