■ **KNEE**

Functional outcome and alignment in computer-assisted and conventionally operated total knee replacements

A MULTICENTRE PARALLEL-GROUP RANDOMISED CONTROLLED TRIAL

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We performed a randomised controlled trial comparing computer-assisted surgery (CAS) with conventional surgery (CONV) in total knee replacement (TKR). Between 2009 and 2011 a total of 192 patients with a mean age of 68 years (55 to 85) with osteoarthritis or arthritic disease of the knee were recruited from four Norwegian hospitals. At three months follow-up, functional results were marginally better for the CAS group. Mean differences (MD) in favour of CAS were found for the Knee Society function score (MD: 5.9, 95% confidence interval (CI) 0.3 to 11.4, p = 0.039), the Knee Injury and Osteoarthritis Outcome Score (KOOS) subscales for 'pain' (MD: 7.7, 95% CI 1.7 to 13.6, p = 0.012), 'sports' (MD: 13.5, 95% CI 5.6 to 21.4, p = 0.001) and 'quality of life' (MD: 7.2, 95% CI 0.1 to 14.3, p = 0.046). At one-year follow-up, differences favouring CAS were found for KOOS 'sports' (MD: 11.0, 95% CI 3.0 to 19.0, p = 0.007) and KOOS 'symptoms' (MD: 6.7, 95% CI 0.5 to 13.0, p = 0.035). The use of CAS resulted in fewer outliers in frontal alignment (> 3° malalignment), both for the entire TKR (37.9% *vs* 17.9%, p = 0.042) and for the tibial component separately (28.4% *vs* 6.3%, p = 0.002). Tibial slope was better achieved with CAS (58.9% *vs* 26.3%, p < 0.001). Operation time was 20 minutes longer with CAS. In conclusion, functional results were, statistically, marginally in favour of CAS. Also, CAS was more predictable than CONV for mechanical alignment and positioning of the prosthesis. However, the long-term outcomes must be further investigated.

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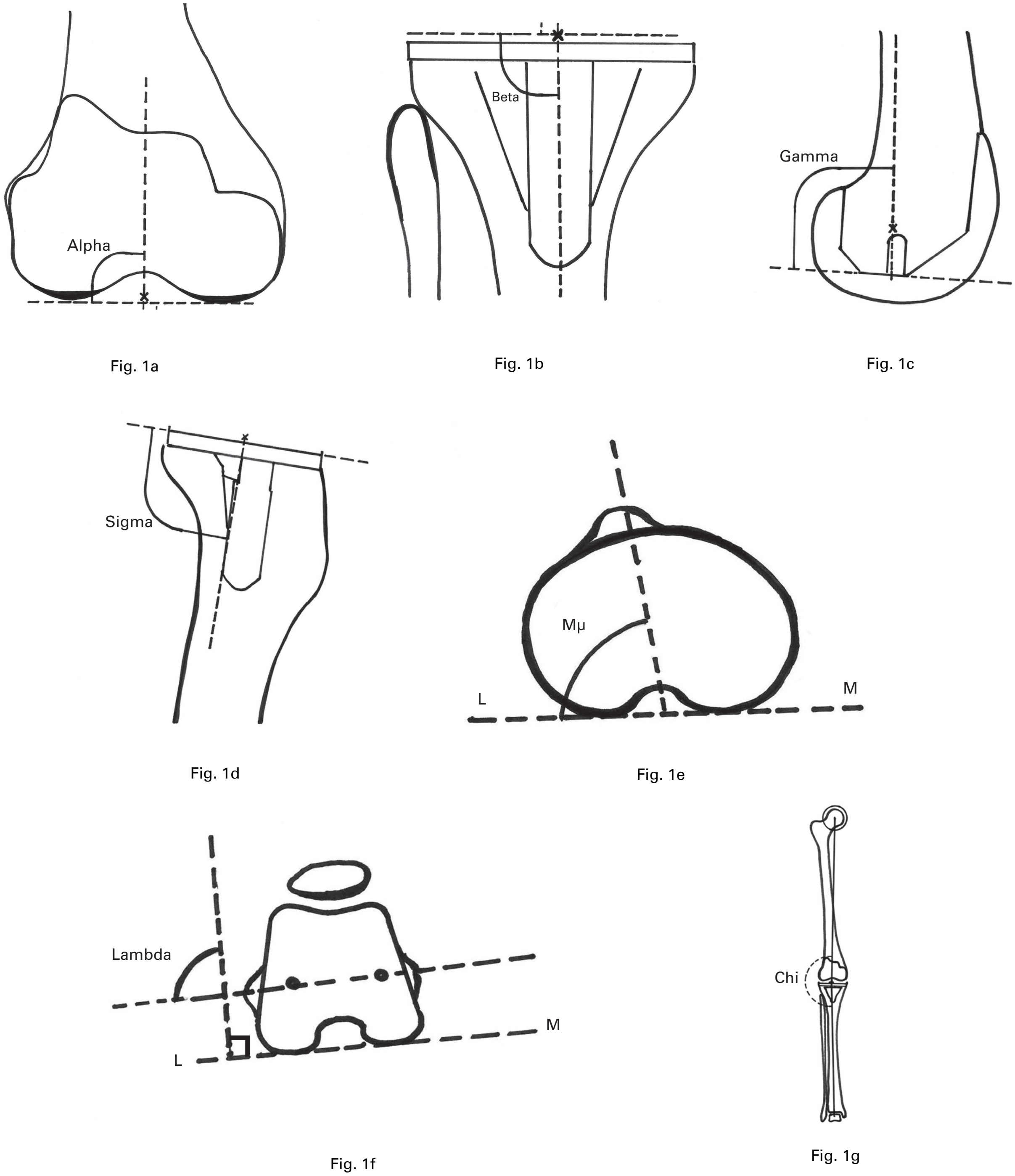
Total knee replacement (TKR) is well documented as being beneficial in patients with osteoarthritis (OA) of the knee.[1,2] However, a substantial number of patients are not satisfied with their outcome, and there is room for improvement.[3] Computer navigation has been used over the past decade in TKR, in the hope of improving the alignment and positioning of the implant. Several authors have reported improved alignment with computer-assisted surgery (CAS),[4-6] and a recent meta-analysis of randomised controlled trials (RCT) concluded that CAS does improve the mechanical leg axis and component orientation in TKR.[7]

It remains controversial, however, whether the improvement of alignment resulting from CAS gives better function[8-10] or longevity.[11] Also, there is an ongoing debate whether perfect alignment really is the target.[12] Choong, Dowsey and Stoney[13] reported that good alignment correlated with good function, and suggested that this correlation was due to the use of CAS, in agreement with the predominant belief that alignment is important for good clinical results and longevity.[14,15] However, they did not compare CAS with conventional surgery (CONV), but rather, well-aligned with malaligned knees. To our knowledge, no trial has shown a direct correlation between the use of CAS and good functional outcomes.

We carried out a RCT in which CAS was primarily evaluated against functional outcome, and secondarily against measures from CT scans and full-length standing radiographs. Our null hypothesis was that there was no difference in functional outcome between CAS and CONV. The trial was designed and conducted according to the CONSORT statement guidelines for reporting parallel-group randomised trials.[16] It was registered on 30 October 2008 in the trial database ClinicalTrials.gov, a service of the United States National Institutes of Health (ClinicalTrials.gov identifier: NCT00782444). The trial was approved by the regional committee for medical and health research ethics, Bergen, Norway, 29 September 2007 (ref.no: 2007/12587-ARS).



Diagrams showing a) Alpha, femoral component relative to mechanical axis of femur in the frontal plane; b) Beta, tibial component relative to mechanical axis of tibia in the frontal plane; c) Gamma, femoral component relative to the mechanical axis of the femur in the sagittal plane; d) Sigma, tibial component relative to the mechanical axis in the sagittal plane; e) Mu, rotation of the tibial component relative to the anteroposterior axis of the tibia; f) Lambda, rotation of the femoral component relative to the transepicondylar axis of the femur, and g) Chi, limb alignment (hip–knee–ankle angle); sum of alpha and beta on CTs, and measured directly on radiographs.

Patients and Methods

Initially patients were randomly parallel-group assigned to either CAS or CONV (allocation ratio 1:1). However, owing to a slow recruitment rate, the age criterion for inclusion was changed after six months, from 60 to 80 years to 50 to 85 years. Ultimately, eligible patients were men and women 50 to 85 years old, in need of a TKR, with primary or other arthritis of the knee, and in the American Society of Anesthesiologists[17] (ASA) category 1 to 3.

Exclusion criteria included severe systemic disease, severe neurological disorder, a history of cancer, dementia, body mass index (BMI) > 35 kg/m^2, previous fractures of the shaft of tibia or femur, severe valgus position of the knee (> 15° from the mechanical axis of the knee), previous

Fig. 2

The hip–knee–ankle angle on full-length radiographs of a prosthetic knee (Chi 2) and a non-operated/native knee (Chi 0).

osteotomy of the tibia or femur, recent knee injury (less than a year pre-operatively), severe stiffness of the ipsilateral hip, ipsilateral hip replacement, and allergy to metals. For patients in need of two knee replacements, only the first knee evaluated in the recruitment period was included in the trial.

The recruitment period was 2009 to 2011, and patients were identified in orthopaedic clinics at four hospitals in Norway. A total of eight surgeons performed the knee replacements. They were all experienced in TKR (defined as having performed > 100 CONVs), and each surgeon had carried out at least ten TKRs with the use of CAS before recruiting patients into the trial.

A cemented CR Profix total knee prosthesis (Smith & Nephew, Memphis, Tennessee) was implanted in all patients using Palacos R+G cement (Heraeus, Hanau, Germany). To match the groups we chose to use the ‘measured bone resection’ technique[18,19] in all cases, and the principles of TKR and ligament balancing according to Whiteside[20] were applied. No patellar resurfacing was performed. The tibial component was implanted with a view to achieving a 4º posterior slope and a neutral alignment in the frontal plane. In the CONV group, conventional instruments and intramedullary rods were used. The femoral component was inserted in a neutral alignment in the frontal plane (referring to the mechanical axis, the surgeon could choose between 5° and 7° cutting blocks with reference to the intramedullary rod) and the sagittal plane (referring to the anatomical axis), or optionally with a 4º flexion of the femoral component. In the CAS group, a neutral alignment was aimed for in the frontal plane and an individualised flexion of the femoral component was allowed in the sagittal plane. The CAS technology used was the VectorVision knee software, version 1.6.93616, with the Kolibri system (BrainLAB, Munich, Germany).

Tranexamic acid 10 mg/kg was administered intravenously ten minutes before surgery, and repeated ten minutes before release of the tourniquet. No drains were applied to the operated knee, which was positioned in 90º flexion for two hours to minimise bleeding. Antithrombotic medication was administered four hours post-operatively and once daily for 17 days (5000 IE dalteparin by subcutaneous injection). Antibiotic medication was administered intravenously within 30 minutes before surgery, after four hours, eight hours and 12 hours, as a prophylaxis against infection (cephalotin 2 g × 4). The skin incision was closed with staples. All patients started weight-bearing and standardised exercises on the first post-operative day.

Outcomes. Patients, nurses, physical therapists, research assistants and outcome assessors were blinded to group assignment. The blinding procedure involved two stab incisions for the CONV patients at the same location as the stab incisions for those with CAS. The computer navigation equipment was present and switched on during every operation to blind the patient. The person measuring the angles on CT scans and radiographs was initially blinded, but sometimes the holes in the tibia and femur made by the fixator pins used to secure the navigation towers were revealed on the images being measured.

The primary outcome was functional scores, Knee Society score (KSS),[21] Knee Injury and Osteoarthritis Outcome Score (KOOS),[22] EQ-5D[23] and a visual analogue scale for pain (VAS) after three months and one year. The VAS was a sheet with a line 100 mm long ranging from 0 (no pain) to 1 (worst pain imaginable), on which the patients were asked to mark their worst knee pain experience during the last week before assessment.

Secondary outcomes were alignment and rotational positioning of the implant measured on CT scans performed three months after surgery (Fig. 1). In addition, full-length radiographs were performed pre-operatively and three months after surgery (Fig. 2) to measure frontal alignment. For CT scans this outcome was the sum of the frontal alignments of the femoral and the tibial component. The radiographic measures were performed by four specially trained assistants (one nurse, one medical student (GD) and two radiologists) according to a specific protocol. Outliers were defined as patients with implant components deviating more than 3° from the target position. The target was defined as alignment of the implant with the mechanical axes of the limb, except the tibial slope was targeted at 4° of flexion of the metal tibial component (7° including the slope of the polyethylene). Rotational position was defined according to the AP axis of the tibia and the transepicondylar line of the femur and additionally, the position of the two components relative to each other was measured. Functional scores were carried out by eight physiotherapists at the four institutions before the operation, after one week (only range of movement (ROM) and VAS), after

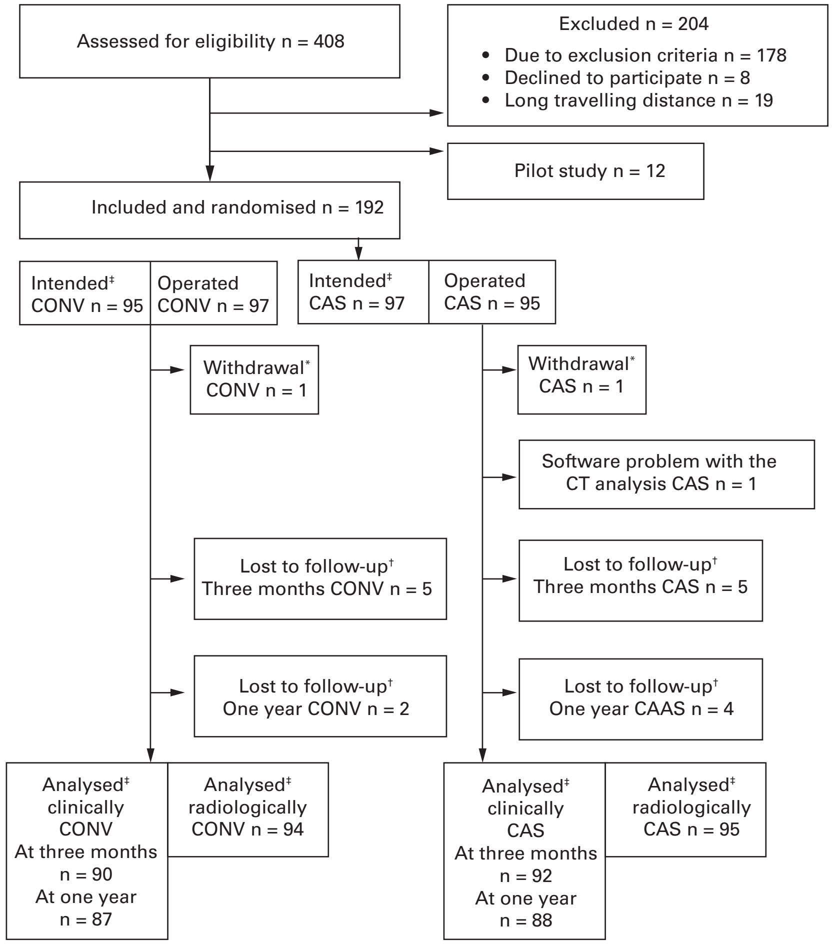


Fig. 3

Flow chart illustrating patient selection for the trial. (*) One patient in the conventional surgery (CONV) group changed his mind after inclusion and refused to participate. One patient in the computer-assisted surgery (CAS) group did not want to continue his participation in the trial owing to a long travelling distance from his home to the hospital. (†) Logistical problems due to sick-leave of a research assistant. (‡) Analysed as intention to treat. Two patients were converted from CAS to CONV because of technical problems with CAS.

three months and after one year. Physiotherapists were previously instructed on how to score the patients in the clinical evaluation part of the KSS. A long-armed goniometer was used, and the anatomical landmarks used were the most prominent parts of the greater trochanter, the lateral epicondyle and the lateral malleolus. ROM was defined as extension lag (degrees of active extension deficit) subtracted from maximum active flexion. All patients were categorised according to Charnley categories, to adjust for potential differences between the groups.

Statistical analysis. All analyses were performed according to the intention-to-treat principle. A difference of ten units in an aggregated and averaged subscale of KOOS was chosen as a minimum important change, as suggested by the developers of KOOS.[24] With a standard deviation (SD) of 20, a sample size of 64 patients per group was necessary to achieve a power of 80% and a 5% level of significance. Alignment in the frontal plane was a secondary outcome, and we calculated a statistical power to reveal an average difference across the groups of 0.5°. According to previous studies we assumed a greater variation of measures in the CONV group (SD 1.3) than in the CAS group (SD 0.9).[4] With a two-sided 5% significance level and a power of 80%, a sample size of 79 patients per group was necessary. A total of 204 patients were included. A pilot study of 12 patients was carried out at the start of the recruitment but this was not included in the final study population.

Separate randomisation lists were created for each of the eight surgeons using the statistical software PASW Statistics v19 (IBM, Armonk, New York). Block randomisation for each participating surgeon with randomly varying block sizes of two and four, was generated to achieve approximate equal numbers in the treatment groups at all times. A central randomisation office performed the computer-generated allocation to the trial groups, with concealment by identical sequentially numbered opaque sealed envelopes.

To compare mean angles, means and mean improvements in the KSS, KOOS, EQ-5D and VAS, we used

Table I. Demographic data and pre-operative features of the patients*

	CAS	CONV
n	95	94
Men, n (%)	37 *(40.2)*	35 *(38.0)*
Mean age (years)	68.3 (SD 7.8)	67.7 (SD 6.8)
Right side, n (%)	56 *(60.2)*	57 *(60.6)*
Charnley category, n (%)		
1	31 *(33.0)*	33 *(35.1)*
2	62 *(66.0)*	54 *(57.4)*
3	1 *(1.1)*	7 *(7.4)*
Diagnosis (n) (%)		
Osteoarthritis	83 *(89.2)*	78 *(83.9)*
Other	10 *(10.8)*	15 *(16.1)*
Pre-op mean HKA	182.2 (SD 7.2)	182.7 (SD 6.8)
Pre-op valgus, n (%)	28 *(32.9)*	28 *(32.2)*
Pre-op varus, n (%)	57 *(67.1)*	59 *(67.8)*
Pre-op HKA missing, n (%)	10 *(10.5)*	7 *(7.4)*
Pre-op M/L stability (n)		
< 5 mm	39	46
5 to 10 mm	45	39
> 10 mm	10	7
Missing	0	2
Pre-op A/P stability (n)		
< 5 mm	86	82
5 to 10 mm	8	11
> 10 mm	0	1
Missing	0	0

* CAS, computer-assisted surgery; CONV, conventional technique; HKA, hip–knee–ankle angle (crude mean value measured on radiographs); M/L, mediolateral; A/P, anteroposterior; pre-op, pre-operative; SD, standard deviation

independent samples *t*-tests with 95% confidence intervals (CI). Differences in outliers, age, Charnley category,[25] gender, side and diagnosis were assessed by Pearson's chi-squared test. All tests were two-sided, and p-values < 0.05 were considered statistically significant. Owing to multiple testing with five subscales in the KOOS score, p-values < 0.01 were considered highly statistically significant. The software package IBM SPSS Statistics 20 was used in all analyses and calculations. The correlation of radiological measurements performed by different assistants was assessed by intraclass correlation coefficient (ICC).[26]

Results

A total of 192 patients with a mean age of 68 years (55 to 85) were included in the trial, allocated randomly to CAS (n = 97) or CONV (n = 95) and treated from May 2009 until August 2011. The functional outcome analyses involved 92 CAS and 90 CONV patients at three months' follow-up, and 88 CAS and 87 CONV patients at one year. The radiological analyses involved 95 patients in the CAS group and 94 patients in the CONV group (Fig. 3).

The two groups did not differ with respect to age, gender or side of operation (Table I). Pre-operatively, two-thirds of the patients had a varus position of the knee and one-third a valgus position; these were distributed similarly among the groups. The stability of the knee ligaments was tested pre-operatively in the anteroposterior (AP) and mediolateral directions and showed no differences between the groups (Table I). There were more patients in Charnley category 3 in the CONV group (7 (7.4%) *vs* 1 (1.1%)), but the difference was not statistically significant (p = 0.083, Pearson's chi-squared test).

From the functional scoring at one year (Tables II and III) there were five losses in the CAS group and seven in the CONV group. These patients were drop-outs due to logistical problems at one hospital. The improvements in the Knee Society function score and the KOOS subscales for 'pain', 'sport' and 'quality of life' were significantly better in the CAS group than in the CONV group at three months and for the 'sport' and 'symptoms' subscale, after one year (Table II). No statistically significant differences were detected between the groups with regard to improvements in VAS or EQ-5D, and no differences in anteroposterior (AP) or mediolateral stability at three months or one year (Table II). For all scores, the crude mean values were better in the CAS group at three months' and one year's

Table II. Independent samples *t*-test comparing computer-assisted surgery (CAS) and conventional surgery (CONV) with respect to differences between pre-operative scores and scores at three months' follow-up (Δ 3m), and between pre-operative scores and scores at one year follow-up (Δ 1y). Statistically significant p-values (< 0.05) are bold.

	CONV	CAS	Mean difference (95% CI)	p-value	Number analysed (n) CAS/CONV
Δ 3m KSSfunc	5.6	11.5	5.9 (0.3 to 11.4)	**0.039**	92/90
Δ 1y KSSfunc	20.7	23.6	2.9 (–2.5 to 8.3)	0.290	88/87
Δ 3m KSSsc	8.3	12.6	4.3 (–1.9 to 10.4)	0.173	92/90
Δ 1y KSSsc	22.7	26.4	3.8 (–2.2 to 9.8)	0.214	88/87
Δ 3m ROM	–17.2	–12.5	4.6 (–0.7 to 10.0)	0.090	92/89
Δ 1y ROM	–4.9	–2.3	2.5 (–2.6 to 7.7)	0.328	88/87
Δ 3m KOOS					
Pain	19.7	27.4	7.7 (1.7 to 13.6)	**0.012**	91/90
Symptoms	7.0	13.1	6.0 (–0.4 to 12.5)	0.066	92/90
Activity of daily living	20.9	26.3	5.4 (–0.06 to 10.9)	0.052	92/89
Sports and recreation	7.6	21.1	13.5 (5.6 to 21.4)	**0.001**	87/84
Quality of life	27.8	35.0	7.2 (0.1 to 14.3)	**0.046**	91/89
Δ 1y KOOS					
Pain	34.3	39.8	5.5 (–1.0 to 12.0)	0.096	87/86
Symptoms	21.6	28.3	6.7 (0.5 to 13.0)	**0.035**	88/87
Activity of daily living	30.5	34.8	4.3 (–1.6 to 10.1)	0.153	85/87
Sports and recreation	23.6	34.6	11.0 (3.0 to 19.0)	**0.007**	84/85
Quality of life	41.5	48.6	7.1 (0.0 to 14.3)	0.052	88/87
Δ 3m EQ-5D	14.7	19.3	4.7 (–1.7 to 11.0)	0.151	86/85
Δ 1y EQ-5D	23.8	29.4	5.6 (–1.3 to 12.6)	0.111	83/85
Δ 3m VAS	35.5	41.6	6.2 (–1.9 to 14.3)	0.133	88/89
Δ 1y VAS	45.6	53.4	7.8 (0.0 to 15.7)	0.051	83/83

KSS, Knee Society Score; VAS, visual analogue score; ROM, range of movement; KOOS, knee, injury and osteoarthritis outcome score; EQ-SD, quality of life score from the EURQoL group

follow-up, but the differences were small and most were not statistically significant. Blood loss was similar in the two groups. Operating time was 20 minutes longer in the CAS group.

At three months' follow-up, we detected more outliers in the CONV group for the hip–knee angle (HKA) ('Chi 1', 36/94 (38.3%) *vs* 17/95 (17.9%), p = 0.008) (Fig. 4), the femoral component frontal plan position ('Alpha', the tibial component frontal plane position ('Beta 1', 27/94 (28.7%) *vs* 6/95 (6.3%), p < 0.001) and the tibial slope ('Sigma', defined as outside 86º (SD 3) (56/94 (59.6%) *vs* 25/95 (26.3%), p < 0.001)). For the other angles measured there were no significant (p < 0.01) differences in outliers between the two groups. The mean angles of the frontal plane and the tibial slope were, statistically, significantly closer to the target in the CAS group (Table IV). Mean angle measurements and outliers on full-length radiographs in the frontal plane ('Chi 2, Alpha 2, Beta 2') were similar to those on the CT scans. However, fewer outliers were detected on radiographs than on CT scans (Table V).

Sub-analysis. A sub-analysis was performed to investigate the functional results of outliers independent of CAS or CONV. Internal malrotation of the femoral component (> 3º) resulted in inferior results in KSS function score, the KOOS subscale for sport and recreational activities and VAS at three months. However, these differences were no longer statistically significant at one year. Patients with a tibial posterior slope < 1º, or an anterior slope, had worse KSS scores and worse KOOS subscale scores for quality of life at three months, and in KSS function score and VAS at one year follow-up. Outliers of the other angles measured did not show any statistically significant differences in functional results compared with the well-aligned knees. The ICCs for inter- and intra-observer analysis of the CT scan measures, with a two-way mixed-effects model, showed good correlation using an absolute agreement definition for single measures (Table IV).

Complications. These were evenly distributed between the two groups (Table VI). Infection was the cause of revision in three cases. Two of these were treated with a two-stage operation and one with debridement and exchange of the polyethylene component. One of the patients (CONV group) with a two-stage revision recovered and is now functioning well with his new prosthesis. The other one (CAS group) did not recover well and required above-knee amputation to eradicate the infection.

Discussion

Some functional scores were marginally better with CAS than with CONV at both three months and one year follow-up. The clinical significance of this marginal

Table III. Independent sample *t*-test comparing crude mean values of conventional surgery (CONV) *vs* computer-assisted surgery (CAS) with respect to ROM, KSS, KOOS, EQ-5D, VAS, haemoglobin drop, number of patients in need of transfusions and operating time. Chi-squared test comparing post-operative stability mediolaterally (M/L) and anteroposteriorly (A/P) in the two groups at three months and one year. Statistically significant p-values (< 0.05) are bold*

	CONV	CAS	Mean difference (95% CI)	p-value	Numbers analysed (n), CAS/CONV
ROM pre-op (°), (95% CI)	110.4	109.1	1.3 (–3.7 to 6.2)	0.609	93/94
ROM post-op (°), (95% CI)	65.2	66.0	0.8 (–3.2 to 4.8)	0.696	92/91
ROM three months (°), (95% CI)	93.2	96.7	3.4 (–0.5 to 7.3)	0.084	92/89
ROM one year (°), (95% CI)	105.7	106.7	1.1 (–2.4 to 4.6)	0.550	88/87
Knee score pre-op	41.2	38.3	2.9 (–7.4 to 1.6)	0.205	93/94
Knee score three months	49.2	50.9	1.6 (–3.2 to 6.5)	0.510	92/90
Knee score one year	63.8	65.1	1.3 (–3.6 to 6.2)	0.610	88/87
Function score pre-op	59.1	60.8	1.7 (–2.9 to 6.3)	0.479	93/94
Function score three months	64.9	72.3	7.4 (1.8 to 13.1)	**0.009**	92/90
Function score one year	79.6	84.1	4.5 (–0.7 to 9.7)	0.092	88/87
Post-op M/L stability three months (n)				0.283	93/89
< 5 mm	69	66			
5 to 10 mm	15	20			
> 10 mm	5	4			
Missing	0	3			
Post-op M/L stability one year (n)				0.264	88/87
< 5 mm	69	62			
5 to 10 mm	18	23			
> 10 mm	0	2			
Missing	0	1			
Post-op A/P stability three months (n)				0.265	93/89
< 5 mm	78	79			
5 to 10 mm	10	11			
> 10 mm	1	0			
Missing	0	3			
Post-op A/P stability one year (n)				0.213	88/87
< 5 mm	75	72			
5 to 10 mm	12	13			
>10 mm	0	0			
Missing	0	3			
KOOS three months					
Pain	65.7	72.2	6.5 (1.3 to 11.6)	**0.014**	91/90
Symptoms	61.8	65.9	4.0 (–1.1 to 9.2)	0.124	92/90
Activity of daily living	71.4	75.2	3.8 (–1.0 to 8.5)	0.117	92/89
Sports and recreation	23.6	33.5	9.9 (3.0 to 16.9)	**0.005**	87/85
Quality of life	54.3	59.7	5.4 (–0.8 to 11.6)	0.088	91/89
KOOS one year					
Pain	80.1	83.8	3.7 (–2.1 to 9.4)	0.209	87/86
Symptoms	76.4	80.8	4.4 (–0.3 to 9.1)	0.067	88/87
Activity of daily living	80.4	83.4	3.0 (–2.3 to 8.3)	0.263	85/87
Sports and recreation	39.7	46.8	7.1 (–0.8 to 14.9)	0.077	84/85
Quality of life	67.8	73.1	5.3 (–1.3 to 11.8)	0.115	88/87
EQ-5D three months	72.3	76.3	4.0 (–0.9 to 8.9)	0.109	88/86
EQ-5D one year	81.4	84.2	2.9 (–2.9 to 8.6)	0.325	85/86
VAS three months	29.6	23.6	6.0 (–0.6 to 12.6)	0.074	89/90
VAS one year	19.4	11.9	7.5 (1.2 to 13.8)	**0.019**	84/84
Drop in S-haemoglobin (95% CI)	2.6	2.5	0.1 (–0.2 to 0.4)	0.380	88/89
Blood loss women (ml)	893	829	63 (–126 to 253)	0.508	42/44
Blood loss men (ml)	1215	1033	182 (–68 to 432)	0.150	27/30
Blood transfusions (no. of patients)	4	4			
Operating time (min)	86.0 (81.5 to 90.5)	106.3 (102.7 to 109.9)		**< 0.001**	

* ROM, range of movement; KSS, Knee Society score; KOOS, Knee Injury and Osteoarthritis Outcome Score; EQ-5D, quality of life score from the EuroQol group; VAS, visual analogue scale (pain). Blood loss formula based on serum pre- and post-operative haematocrit values, gender, height and weight

improvement is uncertain. Only the KOOS subscale for sports and recreational activities exceeded the predefined minimal important change. CAS seems to be a more precise method than CONV when performing TKR, in that we found fewer outliers in the CAS group for alignment of the hip–knee–ankle angle, and for the tibial slope. The improved positioning may have an impact on implant survival in the long term. However, CAS is more time-consuming.

The functional results of well-aligned and misaligned knees must not be confused with the results of computer

Table IV. Angles and outliers in the CAS *vs* the CONV group, measured by CT scan at three months. P-values < 0.01 are marked in bold script. 'Alpha 1' alignment of the femoral component, 'Beta 1' alignment of the tibial component, 'Gamma' flexion/extension of the femoral component (< 90° means flexion), 'Sigma' slope of the metal tibial component (< 90° means posterior slope), 'Lambda' rotation of the femoral component, 'Mu' rotation of the tibial component, 'Omega' mis-match between tibial and femoral components, 'Chi' sum of the Alpha and Beta angles. Statistically significant p-values (< 0.05) are bold

	CAS (n = 95)		CONV (n = 94)						
Angle measured	Mean (SD)	Outliers (%)	Mean (SD)	Outliers (%)	MD (95%CI)	Independent samples *t*-test comparing means, p-value	Chi-squared test comparing number of outliers, p-value	Inter-class correlation coefficient*	Intra-class correlation coefficient*
Alpha 1	89.0 (1.7)	13 (*13.7*)	90.0 (2.4)	18 (*19.1*)	1.0 (0.4 to 1.6)	**0.001**	0.310	0.93	0.92
Beta 1	91.1 (1.4)	6 (*6.3*)	91.8 (1.7)	27 (*28.7*)	0.8 (0.3 to 1.2)	**0.001**	**< 0.001**	0.82	0.75
Gamma 1	87.9 (3.6)	46 (*48.4*)	88.6 (3.6)	31 (*33.0*)	0.7 (–0.4 to 1.7)	*0.204*	0.031	0.90	0.83
Sigma 1	87.6 (2.2)	25 (*26.3*)	89.3 (2.8)	56 (*59.6*)	1.8 (1.0 to 2.5)	**< 0.001**	**< 0.001**	0.85	0.91
Lambda 1	91.2 (2.6)	26 (*27.4*)	91.3 (3.6)	42 (*44.7*)	0.1 (–0.8 to 1.0)	0.858	0.013	0.69	0.80
Mu 1	78.8 (6.1)	51 (*53.7*)	79.0 (6.0)	64 (*68.1*)	0.1 (–1.6 to 1.9)	0.872	0.043	0.70	0.90
Omega 1	1.1 (3.0)	35 (*36.8*)	1.3 (3.0)	33 (*35.1*)	0.3 (–0.6 to 1.1)	0.536	0.804	0.85	0.93
Chi 1	180.0 (2.1)	17 (*17.9*)	181.8 (3.0)	36 (*38.3*)	1.8 (1.1 to 2.5)	**< 0.001**	**0.008**		

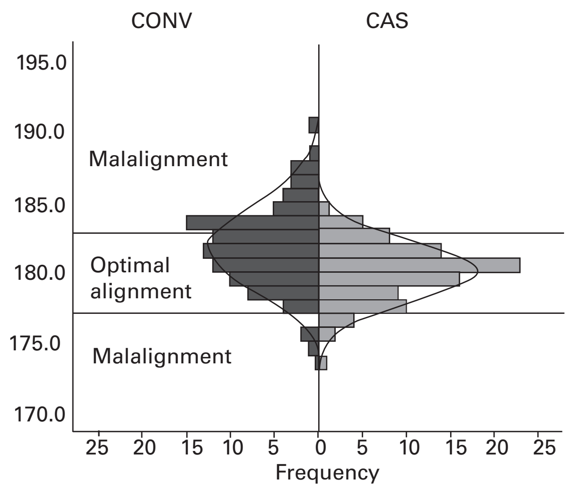


Fig. 4

A graphical illustration of the numbers of outliers for hip–knee–ankle angle (Chi 1), defined as < 177 ° or > 183° for each method of implanting. The area between the lines defines the target area. Values above and below these lines are defined as outliers. To the left of origo on the x-axis are the conventionally operated knees (left-hand bars); to the right are the computer navigated knees (right-hand bars). Y-axis in degrees.

navigation and conventional techniques, and we agree with Harvie, Sloan and Beaver[27] that those data should be dealt with separately. There could be reasons other than good alignment to explain the functional results in navigated knees, including the fact that CAS allows the surgeon to perform accurate ligament balancing, and that the sizing of implant components might be different using CAS; the tissue insult might also be less extensive. Theoretically, an improved alignment might require less surgical balancing of the ligaments, thereby minimising the tissue insult, post-operative pain and bleeding. The extent of ligamentous release was not registered in this study, but the stability of the knee was tested pre- and post-operatively and revealed no differences between the groups.

Our sub-analysis of outliers compared with well-aligned knees, independent of CAS or CONV, indicates that excessive internal rotation of the femur might cause inferior functional results. The 'Lambda' angle outliers were defined as an inward malrotation of the femoral component of > 3º. These outliers had inferior KOOS sport/rec subscale (mean difference (MD): 10.0, 95% CI 2.3 to 17.7, p = 0.011), KSS function score (MD: 7.6, 95% CI 1.3 to 13.9, p = 0.018), and VAS (MD: 9.3, 95% CI 2.0 to 16.5, p = 0.013), at three months follow-up. After one year there were no longer any differences between the groups. Also, a tibial slope < 1º or an anterior slope might affect the functional results. Statistically, there was a non-significant tendency towards fewer outliers with CAS with respect to

Table V. Angles and outliers in the CAS *vs* the CONV group, measured on full-length radiographs at three months. Statistically significant p-values (< 0.05) are bold*

	CAS (n = 95)		CONV (n = 92)				
Angle measured	Mean (SD)	Outliers (%)	Mean (SD)	Outliers (%)	MD (95% CI)	Independent samples *t*-test comparing means, p-value	Chi-squared test comparing outliers, p-value
Alfa 2	89.2 (1.7)	11/95 (*11.6*)	90.0 (2.5)	15/94 (*16.0*)	0.8 (0.2 to 1.4)	**0.010**	0.135
Beta 2	90.9 (2.0)	18/95 (*18.9*)	91.9 (2.1)	32/94 (*34.0*)	1.0 (0.4 to 1.6)	**0.001**	**0.010**
Chi 2	180.1 (2.6)	25/95 (*26.3*)	182.0 (3.5)	36/94 (*38.3*)	1.9 (1.0 to 2.7)	**< 0.001**	0.034

Table VI. Complications (number of cases for each treatment group)

	CONV	CAS
Deep infection	2	1
Superficial infection	1	1
Arthrofibrosis	1	
Femoral fracture		1
Tibial fracture	2	
Lung embolism	1	
Paroxysmal atrial fibrillation	1	1
Necrosis of femoral head		1
Decubitus heels		1
Technical errors with the computer		2
Stiffness of the knee calling for mobilisation under general anaesthesia	4	2
Total	12	10

CONV, conventional technique; CAS, computer-assisted surgery

malrotation of the femoral component, and there was a statistically significantly better achievement of an optimal tibial slope with CAS. The combination of these effects might explain the marginally superior functional results found in the CAS group, as previously suggested by others.[28-31]

In a large CT-controlled trial by Kim, Park and Kim[32] both knees were replaced sequentially under one anaesthetic by one experienced surgeon, using CAS in one knee and CONV in the other. Two different implant designs were used. The navigation system was similar to the one used in our trial. No differences were found regarding alignment, function or mid-term survival. Our trial involved eight surgeons with unequal experience, thereby giving a better external validity. When sequential operations are performed under the same anaesthetic, there might be a transfer of information from the computer-navigated knee to the conventionally operated knee, thus guiding the surgeon. However, this is not the normal situation for most surgeons performing TKR. The excellent results of Kim et al[32] might show that great experience with both methods and a sequential operation under the same anaesthetic negates the need for a more precise instrument such as CAS.

A trial by Chauhan et al[33] was stopped for ethical reasons when the authors, in an interim analysis, found a greater improvement in alignment with CAS. The two- and five-year functional results have since been published and were similar across the groups.[27,34] However, the numbers were too low to reach definitive conclusions, as only 60 patients were able to be assessed, 30 in each group. Our power calculations suggested that at least 64 patients in each group are required in order to show a clinically relevant difference in KOOS score (> 10 points on any subscale).

In most studies on CAS and alignment, the definition of malalignment is based on the early assumptions of Jeffery, Morris and Denham in 1991[35] suggesting that good survival was related to alignment within 3º of the mechanical axis. This assumption has been questioned by others, and other values have been suggested.[36] In the absence of a clear definition, we have accepted 3º as the limit value of alignment. Good alignment is probably not the only factor leading to good longevity. A recent study from the Norwegian Arthroplasty Register reported inferior short-term survival for certain implants when CAS was used.[37]

In terms of limitations, this was a multicentre study with a number of surgeons involved, which may have produced differences regarding surgical procedures, unequal experience and skills, selection of patients suitable for surgery, a large number of clinical evaluators, different rehabilitation programmes and different evaluating tools and procedures. Thorough preparations were carried out prior to the study in order to balance these differences. Other navigation systems and other implants may, of course, have different results.

In conclusion, we found that some functional scores were statistically significantly better with CAS, but for the patient this effect was marginal and probably sub-clinical in the short term. CAS was more predictable than conventional TKR in providing consistent mechanical alignment of the limb. The effect on implant survival and cost-effectiveness must be further investigated.

Supplementary material

A table comparing outliers (O) with well-aligned knees (W), independent of CAS or CONV, as well a radiological measurements protocol are available with the electronic version of this article on our website at http://www.boneandjoint.org.uk

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References

1. **Robertsson O, Dunbar M, Pehrsson T, Knutson K, Lidgren L.** Patient satisfaction after knee arthroplasty: a report on 27,372 knees operated on between 1981 and 1995 in Sweden. *Acta Orthop Scand* 2000;71:262–267.
2. **Carr AJ, Robertsson O, Graves S, et al.** Knee replacement. *Lancet* 2012;379:1331–1340.
3. **Bourne RB, Chesworth BM, Davis AM, Mahomed NN, Charron KD.** Patient satisfaction after total knee arthroplasty: who is satisfied and who is not? *Clin Orthop Relat Res* 2010;468:57–63.
4. **Bäthis H, Perlick L, Tingart M, et al.** Alignment in total knee arthroplasty. A comparison of computer-assisted surgery with the conventional technique. *J Bone Joint Surg [Br]* 2004;86-B:682–687.
5. **Chauhan SK, Scott RG, Breidahl W, Beaver RJ.** Computer-assisted knee arthroplasty versus a conventional jig-based technique. A randomised, prospective trial. *J Bone Joint Surg [Br]* 2004;86-B:372–377.
6. **Lüring C, Bäthis H, Tingart M, Perlick L, Grifka J.** Computer assistance in total knee replacement - a critical assessment of current health care technology. *Comput Aided Surg* 2006;11:77–80.
7. **Cheng T, Zhao S, Peng X, Zhang X.** Does computer-assisted surgery improve postoperative leg alignment and implant positioning following total knee arthroplasty? A meta-analysis of randomized controlled trials? *Knee Surg Sports Traumatol Arthrosc* 2012;20:1307–1322.
8. **Bauwens K, Matthes G, Wich M, et al.** Navigated total knee replacement. A meta-analysis. *J Bone Joint Surg [Am]* 2007;89-A:261–269.
9. **Kim YH, Kim JS, Choi Y, Kwon OR.** Computer-assisted surgical navigation does not improve the alignment and orientation of the components in total knee arthroplasty. *J Bone Joint Surg [Am]* 2009;91-A:14–19.
10. **Longstaff LM, Sloan K, Stamp N, Scaddan M, Beaver R.** Good alignment after total knee arthroplasty leads to faster rehabilitation and better function. *J Arthroplasty* 2009;24:570–578.
11. **Parratte S, Pagnano MW, Trousdale RT, Berry DJ.** Effect of postoperative mechanical axis alignment on the fifteen-year survival of modern, cemented total knee replacements. *J Bone Joint Surg [Am]* 2010;92-A:2143–2149.
12. **Bellemans J.** Neutral mechanical alignment: a requirement for successful TKA: opposes. *Orthopedics* 2011;34:507–509.
13. **Choong PF, Dowsey MM, Stoney JD.** Does accurate anatomical alignment result in better function and quality of life? Comparing conventional and computer-assisted total knee arthroplasty. *J Arthroplasty* 2009;24:560–569.
14. **Fehring TK, Odum S, Griffin WL, Mason JB, Nadaud M.** Early failures in total knee arthroplasty. *Clin Orthop Relat Res* 2001;392:315–318.
15. **Ritter MA, Faris PM, Keating EM, Meding JB.** Postoperative alignment of total knee replacement. Its effect on survival. *Clin Orthop Relat Res* 1994;299:153–156.
16. **Schulz KF, Altman DG, Moher D, CONSORT Group.** CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;340:332.
17. **Dripps RD.** New classification of physical status. *Anesthesiol* 1963;24:111.
18. **Dennis DA, Komistek RD, Kim RH, Sharma A.** Gap balancing versus measured resection technique for total knee arthroplasty. *Clin Orthop Relat Res* 2010;468:102–107.
19. **Whiteside LA, Arima J.** The anteroposterior axis for femoral rotational alignment in valgus total knee arthroplasty. *Clin Orthop Relat Res* 1995;321:168–172.
20. **Whiteside LA.** Soft tissue balancing: the knee. *J Arthroplasty* 2002;17 (4 Suppl 1):23–27.
21. **Insall JN, Dorr LD, Scott RD, Scott WN.** Rationale of the Knee Society clinical rating system. *Clin Orthop Relat Res* 1989;248:13–14.
22. **Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD.** Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. *J Orthop Sports Phys Ther* 1998;28:88–96.
23. **EuroQol Group**. EuroQol - a new facility for the measurement of health-related quality of life. *Health Policy* 1990;16:199–208.
24. **Roos EM, Lohmander LS.** The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes* 2003;1:64.
25. **Charnley J.** The long-term results of low-friction arthroplasty of the hip performed as a primary intervention. *J Bone Joint Surg [Br]* 1972;54-B:61–76.
26. **Shrout PE, Fleiss JL.** Intraclass correlations: uses in assessing rater reliability. *Psychol Bull* 1979;86:420–428.
27. **Harvie P, Sloan K, Beaver RJ.** Computer navigation vs conventional total knee arthroplasty: five-year functional results of a prospective randomized trial. *J Arthroplasty* 2012;27:667–672.
28. **Barrack RL, Schrader T, Bertot AJ, Wolfe MW, Myers L.** Component rotation and anterior knee pain after total knee arthroplasty. *Clin Orthop Relat Res* 2001;392:46–55.
29. **Luring C, Perlick L, Bäthis H, Tingart M, Grifka J.** The effect of femoral component rotation on patellar tracking in total knee arthroplasty. *Orthopedics* 2007;30:965–967.
30. **Shi X, Shen B, Kang P, et al.** The effect of posterior tibial slope on knee flexion in posterior-stabilized total knee arthroplasty. *Knee Surg Sports Traumatol Arthrosc* 2013;21:2696–2703.
31. **Berger RA, Crossett LS, Jacobs JJ, Rubash HE.** Malrotation causing patellofemoral complications after total knee arthroplasty. *Clin Orthop Relat Res* 1998;356:144–153.
32. **Kim YH, Park JW, Kim JS.** Computer-navigated versus conventional total knee arthroplasty a prospective randomized trial. *J Bone Joint Surg [Am]* 2012;94-A:2017–2024.
33. **Chauhan SK, Clark GW, Lloyd S, et al.** Computer-assisted total knee replacement. A controlled cadaver study using a multi-parameter quantitative CT assessment of alignment (the Perth CT Protocol). *J Bone Joint Surg [Br]* 2004;86-B:818–823.
34. **Spencer JM, Chauhan SK, Sloan K, Taylor A, Beaver RJ.** Computer navigation versus conventional total knee replacement: no difference in functional results at two years. *J Bone Joint Surg [Br]* 2007;89-B:477–480.
35. **Jeffery RS, Morris RW, Denham RA.** Coronal alignment after total knee replacement. *J Bone Joint Surg [Br]* 1991;73-B:709–714.
36. **Sikorski JM.** Alignment in total knee replacement. *J Bone Joint Surg [Br]* 2008;90-B:1121–1127.
37. **Gøthesen O, Espehaug B, Havelin L, Petursson G, Furnes O.** Short-term outcome of 1,465 computer-navigated primary total knee replacements 2005-2008. *Acta Orthop* 2011;82:293–300.