

Increased migration of uncemented acetabular cups in female total hip arthroplasty patients with low systemic bone mineral density

A 2-year RSA and 8-year radiographic follow-up study of 34 patients

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Background and purpose — Low bone mineral density (BMD) may jeopardize the initial component stability and delay osseointegration of uncemented acetabular cups in total hip arthroplasty (THA). We measured the migration of uncemented cups in women with low or normal BMD.

Patients and methods — We used radiostereometric analysis (RSA) to measure the migration of hydroxyapatite-coated titanium alloy cups with alumina-on-alumina bearings in THA of 34 female patients with a median age of 64 (41–78) years. 10 patients had normal BMD and 24 patients had low systemic BMD (T-score ≤ -1) based on dual-energy X-ray absorptiometry (DXA). Cup migration was followed with RSA for 2 years. Radiographic follow-up was done at a median of 8 (2–10) years.

Results — Patients with normal BMD did not show a statistically significant cup migration after the settling period of 3 months, while patients with low BMD had a continuous proximal migration between 3 and 12 months ($p = 0.03$). These differences in cup migration persisted at 24 months. Based on the perceived risk of cup revision, 14 of the 24 cases were “at risk” (proximal translation of 0.2 to 1.0 mm) in the low-BMD group and 2 of the 10 cases were “at risk” in the normal-BMD group (odds ratio (OR) = 8.0, 95% CI: 1.3–48). The radiographic follow-up showed no radiolucent lines or osteolysis. 2 cups have been revised for fractures of the ceramic bearings, but none for loosening.

Interpretation — Low BMD contributed to cup migration beyond the settling period of 3 months, but the migrating cups appeared to osseointegrate eventually.

which is not uncommon in postmenopausal women with hip osteoarthritis (Glowacki et al. 2003, Mäkinen et al. 2007, Lingard et al. 2010), may jeopardize achievement of immediate press-fit stability of uncemented components. Indeed, we recently found that low bone mineral density (BMD; osteopenia or osteoporosis) and age-related geometric changes of the proximal femur affected initial stability and delayed osseointegration of uncemented femoral stems in THA in female patients (Aro et al. 2012). It is possible that low systemic BMD may also compromise the initial stability of uncemented acetabular cups.

The success of bone ingrowth into or onto the microroughened/porous surface of an acetabular component depends on the degree of initial stability (Illgen and Rubash 2002). If the initial stability is compromised, implant micromotion may delay or even inhibit osseointegration to host bone. Cup stability is dependent on the geometric implant design, close implant-bone apposition, and frictional or interference press-fit fixation (Kraay et al. 2012). The inherent quality of the host bone is arguably equally important in achieving initial stability, although there is little information on the issue.

Patients with supposedly compromised bone quality due to rheumatoid arthritis or sequelae after a fracture of the femoral neck have shown increased migration of both cemented and uncemented cups in radiostereometric analysis (RSA) (Önsten et al. 1993, Snorrason et al. 1993, Digas et al. 2004). Adjunctive screw and spike fixation has been recommended in patients with poor bone quality, but the benefit of additional screw fixation has been questioned in RSA studies of primary THAs (Thanner et al. 2000, Pakvis et al. 2012).

There is no doubt that migration exceeding the detection level of RSA is predictive of clinical implant loosening (Kärrholm 2012). A recent meta-analysis confirmed that excessive

Cementless total hip arthroplasty (THA) was originally designed for middle-aged patients with normal bone quality (Spotorno et al. 1995). However, undiagnosed osteoporosis,

migration of an acetabular cup at 2 years implies an elevated risk of late revision (Pijls et al. 2012). In the present study, we complemented our previous RSA analyses of the femoral stem migration in cementless THA of female patients with primary hip osteoarthritis (Moritz et al. 2011, Aro et al 2012) by investigating the stability of uncemented acetabular cups in the same study population.

Patients and methods

This study was performed as a 2-year, single-center RSA study on female patients who underwent cementless THA between August 2003 and March 2005. The enrolled patients were called in for the radiographic follow-up study, which was performed between October 2012 and January 2013.

Study participants

The main inclusion criteria were female patients aged less than 80 years with advanced primary hip osteoarthritis and without any severe incapacitating systemic disease (class 1–3 according to the Physical Status Classification of The American Society of Anesthesiologists (ASA)). The exclusion criteria were inflammatory arthritis, hereditary skeletal disease, untreated parathyroid disease, osteoporosis-drug therapy or corticosteroid therapy, any other medication affecting bone metabolism, and severe osteoporosis (T-score of less than –3.5).

A cohort of 110 consecutive patients who were scheduled for a cementless THA was invited to participate, and 61 of them consented to screening. They underwent studies for exclusion of undiagnosed primary or secondary osteoporosis (Mäkinen et al. 2007). Of those screened, 43 were eligible for recruitment. Exclusions were due to use of corticosteroid with or without concomitant bisphosphonate therapy (n = 8) or osteoporosis requiring initiation of bisphosphonate therapy (n = 10). Of the 43 patients recruited, 3 were excluded post-operatively due to periprosthetic femoral fracture (7 days, 9 days, and 21 days after surgery) and 6 were excluded for poor visualization of RSA markers. 34 patients were eventually included in the study.

For the data analysis, the patients were divided into groups with normal BMD or low BMD, based on their lowest T-score measured in preoperative dual-energy X-ray absorptiometry (DXA) (Table 1). DXA measurements were performed at the proximal femurs, the lumbar spine, and the distal non-dominant forearm with a Hologic QDR 4500C densitometer (Hologic Inc., Waltham, MA). A T-score value of ≤ -1 at any of the locations studied was used as the criterion for inclusion in the low-BMD group. The average time between the DXA measurements and surgery was 37 (SD 31) days.

Surgery and RSA

All patients received a CE-certified custom-modified cementless THA implant with ceramic-on-ceramic bearings (ABG

Table 1. Baseline demography, preoperative and postoperative Harris hip score (HHS), and Western Ontario and McMaster arthritis index (WOMAC). Values are mean (SD)

Characteristic	Normal BMD n = 10	Low BMD n = 24	p-value
Age, years	58 (11)	66 (6)	0.02 ^a
Body mass index, kg/m ²	29 (7)	31 (6)	0.4 ^a
ASA category			0.4 ^b
ASA 1	3	3	
ASA 2	6	15	
ASA 3	1	6	
BMD, g/cm ²			
Contralateral hip			
Femoral neck	0.92 (0.10)	0.75 (0.06)	0.004 ^c
Total hip	1.03 (0.05)	0.93 (0.10)	0.2 ^c
Non-dominant forearm			
Total (distal radius)	0.58 (0.03)	0.52 (0.05)	0.06 ^c
Lumbar			
Lowest	1.08 (0.01)	0.85 (0.14)	0.004 ^c
Total	1.16 (0.11)	0.94 (0.11)	0.004 ^c
Lowest T-score	–0.33 (0.41)	–2.1 (0.57)	0.004 ^c
HHS			0.5 ^d
Preoperatively	51 (13)	52 (17)	
3 months	70 (22)	75 (17)	
6 months	86 (13)	86 (12)	
12 months	84 (12)	89 (11)	
24 months	82 (22)	86 (13)	
WOMAC			0.5 ^d
Preoperatively	47 (14)	54 (18)	
3 months	28 (23)	25 (14)	
6 months	20 (11)	20 (13)	
12 months	12 (6)	15 (11)	
24 months	13 (8)	19 (17)	

^a Independent-samples t-test.

^b Pearson chi-square test.

^c Independent-samples t-test; p-value Bonferroni-corrected for 7 tests.

^d Repeated-measures ANOVA.

II; Stryker Europe). Both the femoral stem (Aro et al. 2012) and the acetabular cup (Figure 1A) were marked with RSA beads, by the manufacturer. The hemispherical titanium alloy cup had a grit-blasted surface with vacuum plasma-sprayed hydroxyapatite (HA) coating (porosity < 10%, crystallinity > 75%, crystal grain size 20–50 μm , thickness $60 \pm 30 \mu\text{m}$) and 2 circular grooves aimed at promoting osseointegration. The cups had 8 tantalum beads (1.0 mm) on the outer rim (Figure 1A). The 5-hole version of the cup was designed for use with tapered alumina insert and 28-mm alumina head (BioloX; CeramTec AG, Plochingen, Germany). It accommodated additional RSA beads (1.0 mm) on the tips of 5 custom-modified fixation spikes (Figure 1A).

The surgery was performed using an anterolateral Hardinge approach. During the operation, 4–6 tantalum beads (0.8 mm) were inserted into the cancellous bone of the acetabular socket. The cups were inserted using under-reaming with press-fit.

Baseline RSA imaging was performed within 7 days after surgery, with follow-up at 3, 6, 12, and 24 months. The accuracy of the RSA setup was validated with a phantom model

(Mäkinen et al. 2004) and the international RSA guidelines were used (Valstar et al. 2005).

The RSA images were analyzed for migration relative to the baseline using UmRSA version 6.0.3.7 software (RSA BioMedical Innovations AB, Umeå, Sweden). The linear and angular movements were determined on 3 axes (x, y, and z) (Figure 1B and Table 2). The stability of individual markers and sufficiency of distribution were evaluated through mean error of rigid body fitting (ME) and condition number (CN) (Table 3, see Supplementary data). The cutoff points for ME and CN were kept at around 0.35 and 150, respectively. All patients were subjected to a double examination at least once, with repositioning between examinations, resulting in a total of 82 double measurements. The precision of the RSA measurements was calculated based on the differences measured in double examinations for each axis. The precision (the upper limit of 95% confidence interval (CI)) of the RSA measurements for translational migration was 0.35 mm for the x-axis, 0.25 mm for the y-axis, and 0.46 mm for the z-axis, and for rotational migration it was 1.79 degrees for the x-axis, 2.03 degrees for the y-axis, and 1.20 degrees for the z-axis.

In a recent meta-analysis of RSA studies (Pijls et al. 2012), acetabular cups with proximal translation of 1.0 mm or more at 2 years were considered to be at high risk of revision. Proximal translations of 0.2–1.0 mm and ≤ 0.2 mm were considered to indicate an elevated risk of revision and a low rate of revision, respectively. To this effect, we assigned each individual patient a risk classification of “high”, “at risk”, or “low” based on the extent of proximal translation at 24 months.

Functional recovery

Western Ontario and McMaster arthritis index (WOMAC) and Harris hip score (HHS) were collected at baseline and at each follow-up. The scores were subsequently evaluated for differences between the 2 BMD groups.

Conventional radiography

Conventional 2-plane radiographs were obtained postoperatively and at 6, 12, and 24 months. Of the 34 study patients, 23 took part in the radiographic follow-up at a median time of 9 (7–10) years. 4 patients had died of other comorbidities and 7 patients were unable to attend the follow-up visit, but they could be interviewed by telephone. In these 11 cases (3 with normal BMD and 8 with low BMD), cup survival was confirmed based on review of electronic medical records and the latest hip radiographs taken at a median of 3 (2–10) years. None of the patients were lost to follow-up. The serial radiographs were reviewed for postoperative appearance of radiolucent or reactive lines, or of osteolysis.

Statistics

The primary outcome measure was the relationship between the BMD group assigned and the migration measured by RSA at 24 months.

All relevant data were tested for normality using the Kolmogorov-Smirnov test. Parametric statistical tests were preferred. The equality of variances was established using Levene's test. Student's t-test was used as the independent-samples t-test.

The relationship between the BMD group assigned (normal BMD or low BMD) and cup migration on different axes at 24 months was evaluated using independent-sample t-test or, alternatively, the Mann-Whitney U-test when the assumption of normality was breached. The extent of any statistically significant difference between the BMD groups was further evaluated using age- and BMI-controlled multiple linear regression. Age was controlled for due to a minor but statistically significant difference in the mean ages of the 2 BMD groups (Table 1).

Fisher's exact test was used to evaluate the relationship between the BMD group and the perceived risk of revision as determined by the risk classification system (Pijls et al. 2012). Repeated-measures ANOVA was used for comparison of WOMAC and HHS between the normal-BMD group and the low-BMD group, followed by paired-samples t-test as the post-hoc test in the comparison of time-related changes.

In order to delineate the outcome of the whole patient population, 1-sample t-test was used to detect statistically significant deviations of the mean movement from zero migration during the first 3 months after surgery. Any further migrations were evaluated using either Friedman test or repeated-measures ANOVA based on the normality of the data.

Data were analyzed as of the date of last data collection (July 2015). Statistical significance was assumed from a p-value ≤ 0.05 after Bonferroni correction for multiple tests, where applicable. All statistical analyses were done using IBM SPSS Statistics for Windows v. 21.0.

Ethics

The study had ethical approval from the Ethics Committee, Hospital District of Southwest Finland (entries 4/2002 §76 and 9/2012 §271).

Results

RSA migration

There was a statistically significant difference in cup migration between patients with normal BMD and those with low BMD. At 24 months, the patients belonging to the low-BMD group showed greater translation along the y-axis (proximal translation), while other modes of translation or rotation did not differ significantly between the groups (Table 2). Linear regression between the assigned BMD group and proximal translation was statistically significant even after age and BMI had been controlled for ($\beta = 0.60$, $p = 0.001$). Age did not predict proximal translation at a statistically significant level ($\beta = -0.007$, $p = 0.2$) whereas BMI did ($\beta = 0.40$, $p = 0.01$). The overall adjusted multiple linear regression model fit was $R^2 = 0.39$.

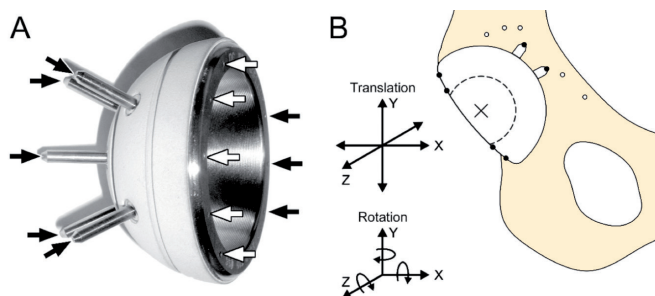


Figure 1. A. The custom-modified acetabular cup with 8 RSA beads (arrows) inserted in the opening and additional RSA beads inserted at the tips of the 5 fixation spikes of the cup. B. The anatomical orientation of the coordinate system used to evaluate the translational and rotational migration of the cup.

Table 2. Acetabular cup migration in patients with normal BMD or low BMD at 24 months

Migration	Normal BMD	Low BMD	p-value
Translation, mm			
Lateral–medial (x-axis)			
Mean value	0.14	0.16	1.0 ^b
95% CI ^a	–0.11 to 0.39	0.01 to 0.31	
Range	–0.26 to 0.78	–0.34 to 1.20	
Distal–proximal (y-axis)			
Mean value	0.08	0.29	0.04 ^b
95% CI	–0.04 to 0.19	0.20 to 0.39	
Range	–0.21 to 0.31	–0.01 to 0.69	
Posterior–anterior (z-axis)			
Mean value	0.27	0.05	0.8 ^b
95% CI	–0.06 to 0.61	–0.09 to 0.19	
Range	–0.23 to 1.19	–0.65 to 0.51	
Rotation, degrees			
Anterior tilt (x-axis)			
Mean value	–0.67	0.24	0.3 ^b
95% CI	–1.31 to –0.02	–0.33 to 0.82	
Range	–2.33 to 0.56	–2.04 to 3.10	
Internal rotation (y-axis)			
Mean value	0.50	–0.01	1.0 ^c
95% CI	–0.19 to 1.18	–0.56 to 0.53	
Range	–0.66 to 2.49	–3.20 to 2.57	
Adduction (z-axis)			
Mean value	0.45	0.28	1.0 ^b
95% CI	–0.25 to 1.15	–0.26 to 0.81	
Range	–0.60 to 2.62	–2.62 to 3.32	

^a CI: confidence interval.

^b Independent-samples t-test; p-value Bonferroni-corrected for 6 tests.

^c Mann-Whitney U-test; p-value Bonferroni-corrected for 6 tests.

The difference in proximal cup migration between the patients with normal BMD and those with low BMD appeared to progress after the settling period of 3 months (Figure 2 and 3). An extra analysis was therefore performed. Patients with low BMD had statistically significant proximal translation (paired-samples t-test, $p = 0.03$) between 3 and 12 months but not between 12 and 24 months (paired-samples t-test, $p = 1.0$). Patients in the normal-BMD group did not show statistically significant proximal migration at any time after 3

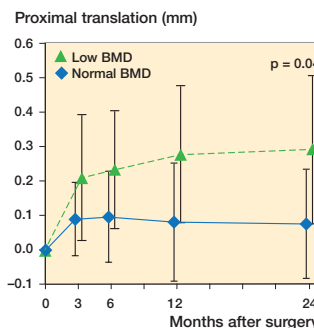


Figure 2. The proximal translation (mean \pm SD) of the acetabular cups in patients with normal or low BMD during the first 24 months after surgery.

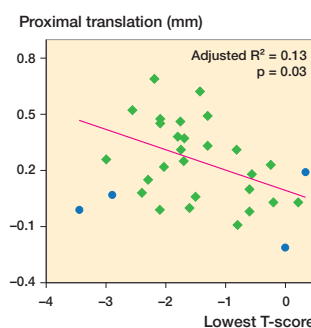


Figure 3. Proximal migration of the acetabular cups at 24 months plotted against the lowest T-score of each individual patient (diamonds). Outliers excluded from the linear regression (due to elevated Cook’s distance) are marked with round dots.

months (repeated-measures ANOVA, $p = 0.9$) as a sign of cup stability.

When the patients with low BMD and those with normal BMD were analyzed as 1 group, the cup showed statistically significant migration only during the first 3 months. By 3 months, translation occurred on the x-axis (0.14 mm, CI: 0.06–0.22; $p = 0.006$) and the y-axis (0.17 mm, CI: 0.11–0.23; $p = 0.003$). The initial rotation occurred on the z-axis alone (0.44°, CI: 0.20–0.68; $p = 0.006$).

Perceived risk of cup revision

By 24 months, there were no cases of high proximal translation (1 mm or more). In the low-BMD group, there were 14 (out of 21) cases “at risk of revision” (proximal translation of 0.2–1.0 mm), while in the normal-BMD group there were only 2 (out of 10) such cases, with the difference between the BMD groups being statistically significant (OR = 8.0, CI: 1.3–48; $p = 0.02$). The low-BMD group had a mean proximal translation of 0.29 (SD 0.21) mm, which lay within the classification limits of “at risk of revision”. The mean proximal translation in the normal-BMD group was 0.08 (SD 0.16) mm, corresponding to the classification “at low risk of revision”.

Functional recovery and radiographic outcome

The cup migration measured by RSA had no effect on the subjective or functional recovery from the hip replacement (Table 1). Both groups showed a significant improvement in the outcome measures postoperatively ($p < 0.001$ for both).

During the median follow-up time of 8 (2–10) years, cups of 2 patients in the low-BMD group were revised for fracture of a ceramic liner at 3 years and fracture of a ceramic head at 4 years. None of the cups were revised for loosening. Conventional radiographs did not show a postoperative appearance of either radiolucent or reactive lines, or of periprosthetic osteolysis. 2 patients have reported occasional audible squeaking.

Discussion

Confirming our hypothesis, patients with normal preoperative BMD did not show statistically significant cup migration after the settling period of 3 months, while patients with low BMD had minor but sustained proximal cup migration for up to 12 months.

The results of the whole patient population are in line with those of previous RSA studies of cementless acetabular cups (Önsten et al. 1996, Thanner et al. 2000, Digas et al. 2004, Rohrl et al. 2006, Zhou et al. 2006, Pakvis et al. 2012). The current study, like a recent meta-analysis (Pijls et al. 2012), showed that the migration occurs mainly along the y-axis (proximal translation). Interestingly, the increased migration in patients with low BMD was not evident statistically when the study patients were analyzed as 1 group. This finding suggests that the effect of low BMD does not become apparent in RSA studies without subgroup analysis of patients with defined BMD status. To our knowledge, this is the first study to report the RSA migration of the acetabular cup as a function of DXA-measured systemic BMD. Our results confirm the observations of Digas et al. (2004), who reported increased migration of uncemented cups (as measured with RSA) in patients with osteoporosis suggested by their diagnosis (rheumatoid arthritis, failed femoral neck fracture, or being on cortisone treatment). These authors stratified and randomized patients based on preoperative DXA measurements, but they did not report the influence of preoperative DXA status on migration. In a randomized study of bisphosphonate treatment, Saari et al. (2014) followed the changes in acetabular BMD and measured RSA migration of revision cups, but preoperative systemic DXA was not investigated as a predictor of cup migration.

3 patients were excluded due to early periprosthetic fracture of the proximal femur, which is a characteristic complication of the ABG II stem (Mäkelä et al. 2010). In line with the arthroplasty register records (Eskelinen et al. 2006, Mäkelä et al. 2010), our radiographic follow-up results of the ABG II acetabular cup were unremarkable, with no signs of radiolucent lines or osteolysis—resembling the “radiological silence” reported by Nourissat et al. (2013). To date, 2 cups have been revised due to fracture of a ceramic head and a liner. 2 patients have complained of occasional squeaking. These complications are annoying unresolved problems with ceramic-on-ceramic bearings (Park et al. 2015, Hamilton et al. 2015).

Our study design did not include determination of the local acetabular BMD. We applied the lowest T-score from any of the DXA-measured skeletal sites as the indicator of systemic bone quality, because osteoarthritis may interfere with local BMD measurements and cause false-negative results (Mäkinen et al. 2007). In fact, using systemic BMD has advantages over using local BMD, as osteoporosis may go unnoticed unless BMD measurements are performed at sites distant from joints affected by osteoarthritis (Lingard et al. 2010).

The current analyses were part of a clinical study designed to evaluate the frequency of osteoporosis in female patients scheduled for cementless THA, and to determine the effect of reduced BMD on THA. At the time the study was initiated, systemic BMD status in female patients with primary hip osteoarthritis had not been studied systematically. This base study can provide the necessary data for power analyses when designing future studies.

Consecutive patients were recruited without any attempt to control the number of patients recruited in each BMD group, so the sizes of the groups were different. Although the normal-BMD group was small, we believe that it was representative. There were no outliers in the normal-BMD group, which showed stable cups after the settling period of 3 months. This is in line with the expected healing period (i.e. osseointegration). Another limitation of the recruitment methodology was that, for ethical reasons, patients with severe osteoporosis were put on osteoporosis medication and were therefore excluded.

The value of proximal migration in predicting long-term failure rates of acetabular cups was confirmed recently (Pijls et al. 2012), but little is known about the mechanisms and causes thereof. Anti-resorptive therapy with intravenous zoledronic acid may prevent cup migration (Friedl et al. 2009). The surgical procedure per se (THA with an uncemented cup) causes a decrease in periprosthetic acetabular BMD (Digas et al. 2006) and a single intravenous dose of pamidronate can reduce the loss of periprosthetic bone (Wilkinson et al. 2001). If the loss of periprosthetic bone is inevitable, our RSA results in patients with normal BMD suggest that such an adverse remodeling does not affect cup stability. Indeed, in support of this hypothesis, negative findings on the benefits of anti-resorptive treatment have also been reported, at least with revision acetabular cups (Saari et al. 2014). It is important to recognize that patients with low BMD are prone to periprosthetic bone loss in the proximal femur (Alm et al. 2009). A similar response is possible in the acetabular region. We cannot exclude the possibility that the increased cup migration in patients with low BMD was in part related to the increased postoperative loss of periprosthetic acetabular bone and not only a result of the impaired preoperative bone quality.

The main strengths of our study were the highly screened homogenous patient population and the application of custom-modified RSA implants. Major potentially confounding factors such as corticosteroid therapy and inflammatory arthritis were used as exclusion criteria. The homogenous patient population enabled the use of a fairly small sample size recommended for RSA studies (Valstar et al. 2005, Derbyshire et al. 2009).

The ceramic-on-ceramic bearings were chosen over other options in order to avoid the side effects of released metal ions and polyethylene wear particles (Malviya et al. 2010, Nich et al. 2013). The use of non-elastic ceramic-on-ceramic bearings may have added to the peak impact forces transmitted to the bone-implant interface. Theoretically, the increased impact

forces could have worsened the proximal cup migration in the presence of compromised bone quality. However, a comparative RSA study has shown no statistically significant difference in cup migration between ceramic-on-ceramic bearings and metal-on-polyethylene bearings (Zhou et al. 2006).

One could argue against the use of uncemented cups, especially in patients with impaired bone quality (Hailer et al. 2010). The clinical value of bioactive HA coating remains unclear. Routine HA coating of uncemented cups may not be indicated (Lazarinis et al. 2010) but, based on preclinical studies, HA coating should be beneficial in helping incorporation of implants in osteopenic bones (Soballe et al. 1991).

In conclusion, our study has produced the first evidence of increased migration of uncemented cups in female patients with low systemic BMD. It appears that the normal settling period of 3 months was only extended, and that the migrating cups eventually osseointegrated with the host bone. Further research is certainly needed to establish what—if any—effect the increased proximal migration of uncemented cups in patients with low BMD has on the long-term clinical results.

Supplementary data

Table 3 is available on the Acta Orthopaedica website at www.actaorthop.org, identification number 8878.

SF analyzed the data and prepared the manuscript. NM performed the RSA measurements and prepared the manuscript. ES helped with the DXA measurements. JJA helped in data gathering and prepared the manuscript. HTA designed the study, operated on patients, and prepared the manuscript.

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