



Femoral neck preservation with a short hip stem produced with powder manufacturing: mid-term results of a consecutive case series

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Received: 29 August 2018 / Accepted: 10 January 2019 / Published online: 28 January 2019
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Abstract

Stress shielding and thigh pain are not uncommon after cementless total hip arthroplasty (THA) using conventional hip stems. It has been postulated that short, neck-preserving stems may overcome these disadvantages of standard stems and, hence, further improve clinical outcome. The purpose of our retrospective study was to assess the mid-term performance of a neck-preserving hip stem for which, as of yet, no clinical results have been published. A population of 146 consecutive patients who received 152 neck-preserving stems over a 1.6-year period was retrospectively reviewed. Harris Hip Score (HHS) and the Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC) were collected, along with radiographic data. One hundred and forty-four THAs implanted in 136 patients were available for analysis. After a mean follow-up of 56 months, mean HHS and WOMAC improved significantly versus preoperative values. Aseptic loosening was not observed. Five-year survival with revision of any component for any reason as the endpoint was 99.3% (95% confidence interval, 95.2–99.9%). Excellent mid-term clinical and radiographic outcomes were observed with the study device. We attribute this to the metaphyseal fit in combination with retention of the femoral neck. However, our findings need to be confirmed by multicentre studies with larger patient samples.

Keywords Clinical outcome · Minimally invasive surgery · Neck preservation · Osteoarthritis · Total hip arthroplasty

Introduction

Cementless total hip arthroplasty (THA) is a well-established, cost-effective treatment for degenerative or inflammatory hip disease, with excellent longevity reported for several designs [1]. Adverse outcomes such as stress shielding and thigh pain, however, still frequently occur with the use of cementless hip systems [2, 3]. Contemporary cementless stem designs are further limited by mismatched proximal and distal femoral widths, as well as compromised diaphyseal stem engagement with distal load [4]. Moreover, straight cementless standard stems may alter the native anteversion while being positioned into the femur [5, 6].

The mechanical strength of the cortical bone of the femoral neck and the metaphyseal trabecular bone are believed to facilitate good proximal primary fixation of femoral prostheses [7]. Studies have shown that retaining the femoral neck improves component stability by offering greater rotational strength and stiffness, and better resistance to varus–valgus stress and collapse [8].

The use of a short, neck-preserving stem maintains most of the femoral offset and anteversion and de facto respect, as well as the varying anteversion that exists between the male and female genders [9]. Due to aging of the population, the incidence of fractures around and distal to the femoral stem, with occasional catastrophic consequences, is increasing [10]. A short stem with no or little engagement distal to the lesser trochanter may facilitate the management of both revision or plating, which would diminish most postoperative complications.

Several short, bone-conserving femoral stems with a variety of geometrical designs and fixation principles have been proposed to achieve bone preservation and metaphyseal femoral load transfer [11, 12]. Reported advantages of short

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stems include less blood loss [13], physiological proximal loading of the femur [14], less thigh pain due to the avoidance of diaphyseal interlocking [15], and greater ease of use in minimally invasive surgery, given the more medial entry point of the stem in the femoral neck [16]. Conversely, there are some concerns regarding short-stem prostheses that have hindered their widespread use to date [2]. Positioning of the implant is partly determined by the height of the femoral resection level [17]. In addition, the implant has to follow the native angle and torsion of the femoral neck [17]. A high occurrence of malalignment, subsidence, incorrect sizing, and intraoperative fractures has been reported in literature with their use [2].

The Parva stem (Adler Ortho SRL, Cormano, Italy) was introduced in 2009 to address the limitations of these earlier-generation devices. Although the stem has since been widely adopted, to the best of the authors' knowledge, there have been no peer-reviewed papers describing its clinical outcomes in the published literature. We, therefore, conducted a retrospective study to assess the mid- to long-term performance of this device, with a concentration on survivorship, clinical function, and radiographic outcomes.

Materials and methods

Between July 2009 and February 2011, a total of 709 cementless THAs were completed in two clinics. The study device was used in 152 of these hips (144 patients), which served as the population for the current study. Pathological offset (caput-collum-diaphyseal angle smaller than 125° or larger than 145°), Dorr C "stovepipe" femur morphology [18], poor bone quality, rheumatoid arthritis, or osteoporotic bone found intraoperatively were not considered eligible for short-stem THA. Eight (5.6%) patients underwent THA in both hips. Ethics committee approval was obtained prior to study commencement, and all patients provided written informed consent.

The average \pm standard deviation (SD) age of the study population was 67.8 ± 12.0 years. Eighty-two patients (56.9%) were male.

The Parva stem was designed to allow for high-neck resection, in order to increase the torsional stability of the implant and to avoid damage to the abductor muscle and greater trochanter during implantation. The prosthesis is triple-tapered and collarless, with a lateral flare that conforms to the proximal internal geometry of the metaphysis (Fig. 1). The implant is made of titanium alloy employing the electron beam additive manufacturing (EBM) process, and, to the best of our knowledge, it is the first hip stem produced employing such a technology. EBM also allows for the creation of monolithic, open, three-dimensional macrostructures ("Ti-Por"). The macrostructure covers approximately



Fig. 1 The Parva stem is shown

65% of the stem and has an average porous size of $700 \mu\text{m}$. The macrostructure is built simultaneously with the actual femoral stem, and the integration of these two normally distinct processes provides added implant strength. The stem is available with a modular neck made of Ti-6Al-4 V alloy, and as a monoblock version. Only the modular version has been used in the present study.

All stems were used in combination with the cementless Fixa Ti-Por Cup (Adler Ortho), a cup manufactured with the same technology and with the same 3D, monolithic surface as the Parva stem, in combination with a BioloX Delta head (Ceramtec GmbH, Plochingen, Germany) and a highly crosslinked liner (Adler Ortho) or a Delta liner (Ceramtec GmbH). All implantations from the first site ($n=92$) were performed by one surgeon (MS) using a minimally invasive, posterior approach in all cases. The implantations from the second site ($n=60$) were performed by a single surgeon (LRB) who employed a minimally invasive, anterolateral approach in all cases.

Neck osteotomy level was referenced from the center of the femoral head employing a special jig. The cut was set at approximately 25 mm below the center of rotation of the native femoral head, a reference corresponding to a short neck with a medium-length head in order to avoid any unnecessary limb lengthening, while still allowing for a certain degree of shortening if needed.

Intraoperative axis measurements were performed during sequential broaching in order to prevent implant malalignment.

Fifty-percent partial weight bearing was allowed from the first postoperative day and for four to five postoperative weeks, depending on the patient's weight and general condition. Physiotherapy was initiated on the day of surgery.

Along with the demographic data, comorbidities, the Harris Hip Score [19] and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) [20] were evaluated preoperatively and during follow-up. Any intra- or postoperative complications were recorded. Anteroposterior (AP) and lateral radiographs of the proximal femur were taken preoperatively, immediately postoperatively, and during the follow-up evaluation (with the patient standing in an upright position). All radiographs were analyzed for the presence of radiolucent lines (RLLs), osteolysis, and bone resorption using the Gruen classification [21]. RLLs were defined as regularly shaped zones between the implant and the surrounding bone, usually parallel to the implant surface. Osteolysis was defined as an irregularly shaped, radiolucent zone along the implant-to-bone interface, irregularly demarcated from the surrounding bone and potentially with breaks or signs of resorption [22]. Bone resorption was assumed to be present when the bone appeared darker, thinner, or more osteopenic on follow-up radiographs than on the immediate postoperative radiographs [23]. Stress shielding was defined as the presence of medial and lateral cortical bone thickening with proximal femoral bone resorption and RLL around the tip of the stem. The Brooker classification was used to assess periarticular ossification [24]. Leg-length inequality was determined clinically during the follow-up examination, and radiographically with an AP view of the pelvis in the upright position.

Offset reconstruction was analyzed by comparing the preoperative and postoperative horizontal distance between the femoral axis and the midline of the pelvis at the height of the lateral tip of the greater trochanter [25].

Continuous data are presented as a mean \pm standard deviation (SD). Categorical variables are presented as frequencies and percentages. Survivorship was calculated using Kaplan–Meier analysis.

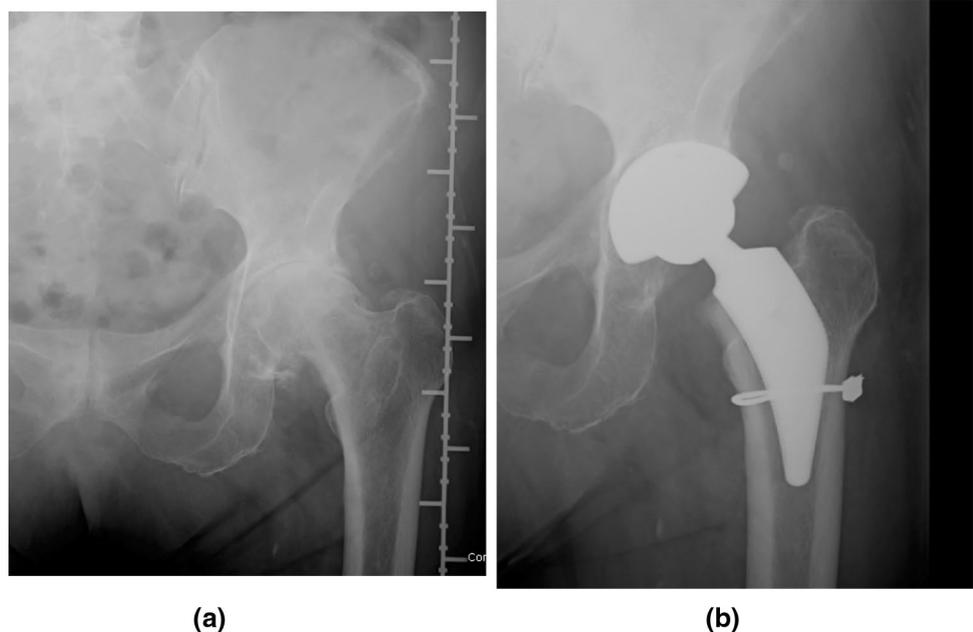
Results

From the original patient cohort, 1 patient (1 hip) was lost to follow-up, and 6 patients (6 hips) had died for causes unrelated with the index procedure. One patient (1 hip) did not attend the final follow-up due to a revision for periprosthetic femoral fracture occurring 1 month postoperatively and not related to the procedure. Hence, the study population comprised 144 hips (136 patients). The study population had a mean follow-up time of 56.2 ± 11.9 months (range, 42.7–71.8 months). The mean HHS had increased from 53.5 ± 15.7 preoperatively to 96.5 ± 6.7 at the final follow-up. The WOMAC score improved from 23.3 ± 1.5 to 1.6 ± 4.4 at the final follow-up. At the last follow-up, 18 patients (12.5%) reported slight pain, and one patient (0.7%) reported mild pain. Only one patient reported moderate pain. None of the patients reported thigh pain.

Among these patients, nine (45.0%) had slight limping and walking difficulties related to multiple joint disease and chronic back pain. Two patients (10.0%) reported discomfort due to leg lengthening; in one patient a leg lengthening of 5 mm and in the other patient a leg lengthening of 18 mm was found.

Except for a periprosthetic fracture treated intraoperatively with cerclages (Fig. 2), a case with Brooker 4 periarticular ossification that required surgical removal of the

Fig. 2 69-year-old female patient. **a** Preoperative anteroposterior radiograph. The patient experienced an intraoperative calcar cracking, which was treated with a cerclage. **b** Anteroposterior radiography at 5-year follow-up. Correct implant position, and a well-osseointegrated stem



ossification, and the previously mentioned postoperative periprosthetic fracture, no major complications occurred.

On radiographs, neutral stem alignment was achieved in all but 2 hips (1.4%). In two instances, the stem had been positioned in slight varus. In both cases, this was associated with the cervico-diaphyseal angle below 125°. In most cases, it had been possible to preserve a large part of the neck, and in all cases, an isthmic fixation was obtained (Fig. 3). Six hips (4.2%) showed non-progressive radiolucent lines of less than 2 mm width at the lateral stem edge/bone interface. Stress shielding was not observed in any of the patients. In 16 hips (11.1%), periarticular ossification (Brooker 1) was observed. Brooker 2 was identified in 5 hips (3.5%), Brooker 3 in 4 hips (2.8%), and Brooker 4 in 1 hip (0.7%). No patients had a femoral offset greater or less than 5 mm from native femoral offset.

The five-year Kaplan–Meier survival for stem revision for aseptic loosening was 100%. Five-year Kaplan–Meier survival for revision of any component for any reason was 99.3% (95% CI, 95.2–99.9%).

Discussion

Bone-conserving stem designs have become increasingly popular in THA during recent years, with encouraging mid-term results noted that are comparable with those of more traditional cementless stems [26, 27]. Retention of the femoral neck, in combination with metaphyseal fixation of the prosthesis, provides excellent component stability, although several requirements must be fulfilled [8]. Firstly, the proximal femoral bone must be of good quality as the primary stability relies on the cervico-metaphyseal area. Secondly, the recipient's hip anatomy may be compromised on the epiphyseal side only and should not be affected on the cervical area. One of the purposes of the surgery is to preserve a larger part

of the femoral neck in order to increase torsional resistance for additional primary stability and to extend the surface area for secondary bone ongrowth. The authors, therefore, believe a short stem must allow for proper neck preservation because by shortening the stem length, we only diminish the area of bone contact, which reduces both primary and secondary stability. This is the main difference between a short stem designed for the purpose of cervical and metaphyseal fixation and an ordinary short stem; the latter de facto reduces its bone contact (and ongrowth area) and does not provide any additional torsional stability.

The stem used in this study retains a large part of the femoral neck and does not lock below the lesser trochanter in order to minimize the problem of stress shielding and thigh pain. These are problems which may occur even in conventional short stems, which find their stability in an area around and below the lesser trochanter (i.e., the isthmus level) [28].

Despite this, to the best of the authors' knowledge, there are only very few short stems available designed according to the same concept as the study device.

This is the first paper describing clinical outcomes with the bone-conserving, modular, triple-tapered stem manufactured with a powder technology process. Our study showed that good clinical and radiographic results were obtained with a calcar-loading short stem with lateral flare after an average follow-up of 56 months. Stress shielding, implant tilting, subsidence, and aseptic loosening were not noted in our study population, which is indicative of the load transfer and the good primary and secondary fixation of the device.

Our results are in agreement with publications with conventionally manufactured (forged) neck-preserving stems. Toth et al. reported good preliminary results and no device loosening with a device with a similar fixation principle in a young cohort of patients [29]. Kim et al. found no reported loosening, minimal stress shielding, and a mean Harris

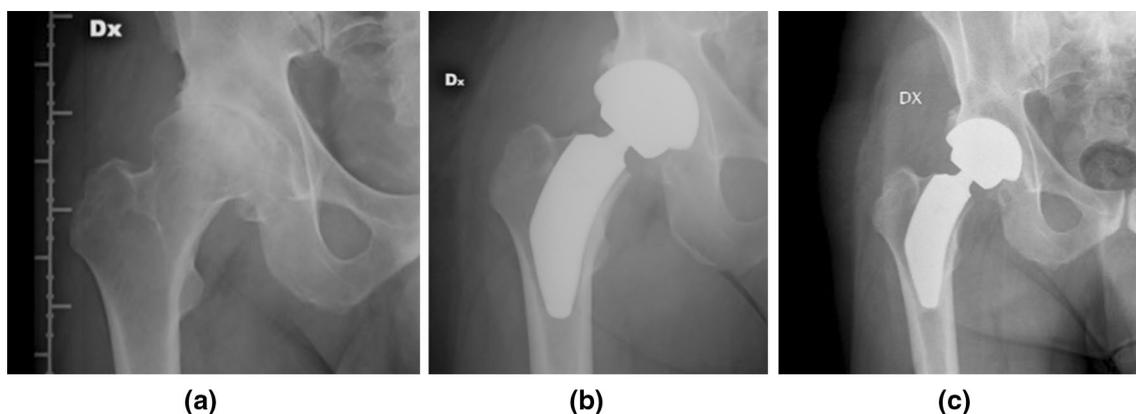


Fig. 3 58-year-old male patient with short hip-stem implant is shown. **a** Preoperative anteroposterior radiograph. **b** Immediate postoperative radiograph. Note the correct implant position. **c** Anteroposterior radiography at 5-year follow-up shows a stable, well-osseointegrated stem

Hip Score of 96 points at a mean follow-up of 4.5 years after implantation of a device with similar fixation principle [29]. Notably, we did not engage in any age restrictions for the device in our study population, with almost 20% older than 75 years at time of surgery.

In the current study, we selected our patients according to bone quality, and good results were obtained in both Dorr A and Dorr B proximal femoral types. The results from the present study are supported by Kim et al. [15]. The authors reported good radiographic and clinical outcomes at 7 years using a metaphyseal-fitting (non-femoral, neck-retaining) cementless anatomic stem, with results in patients with osteoporotic (Dorr C) bone being non-inferior [15].

The stem used in our study offers modularity at the neck–stem junction. This allows for the patient’s individual biomechanics to be reconstructed by restoring the unique physiological offset and rotation of the proximal femur while avoiding postoperative leg-length inequalities. Recent studies have shown that using non-modular, standard cementless femoral components led to high pre- and postoperative variability of femoral anteversion and neck-shaft angles, as well as a reduction in offset in nearly 30% of patients [30]. In our series, femoral offset was restored in all cases.

This short hip stem aims to preserve femoral bone stock, including the femoral neck. Consequently, the stem should follow the anatomy of the femoral neck [17]. Early neck-sparing stem designs reported a high percentage of postoperative leg-length discrepancies, which has been attributed to the higher femoral resection level [17]. The surgical technique of the study device has been conceived in a way that this issue is avoided. The neck osteotomy level is referenced from the center of the femoral head at a level where leg-length adaption according to patient’s anatomy is still possible. The prevalence of leg-length discrepancy in the study population was low—only one patient had a leg-length discrepancy exceeding 5 mm.

Several studies have reported breakages and failures due to corrosion at the neck-stem junction [31]. Corrosion has been determined to be induced by coupling of two different metal (Ti–6Al–4 V and Co–Cr–Mo) alloys [32]—a combination that has not been used for the product used in our study. Good results with titanium-on-titanium TiAl6V4 modular necks have previously been reported by Ollivier et al. [33] and Omlor et al. [34], without elevation of systemic titanium ion levels in the medium term when compared to non-modular stems [34]. However, long-term data from larger registries will need to confirm these preliminary findings.

Our study is limited by its non-randomized, observational nature, which leaves it open to selection bias. The uncontrolled study design does not allow for inferences about differences in performance between neck-preserving and standard hip stem designs. Furthermore, relying on data from our

two centers means we cannot conclude that our findings are applicable to other institutions, where other eligibility criteria, surgical techniques, and rehabilitation protocols may be employed. The relatively short follow-up time and small number of patients for which clinical data were available also complicates our ability to draw firm conclusions regarding the efficacy of this device compared with conventionally manufactured neck-preserving stem designs. The size of the patient cohort is not uncommon for studies of this length and type [27]. However, larger patient series with a longer follow-up will be necessary to assess the extent of the benefits and limitations of this device and this manufacturing technology in total hip arthroplasty.

The current study has shown that implantation of the Parva stem leads to good clinical and radiographic outcome after a mean follow-up of 56 months. No implant malalignment was observed, and stress shielding and aseptic loosening were also not seen.

We believe that the rationale of a stem providing a metaphyseal fit coupled with femoral neck retention should be taken into consideration now that a larger part of our patient population faces a longer life expectancy and high activity level.

The use of a stem built and designed according to the concepts presented in this paper may diminish many of the technical difficulties related to stem revision or related to the management of periprosthetic femoral fractures that may occur within a life span. Multi-center studies with larger patient samples alongside results from national joint registries are warranted to confirm our findings.

Funding Funding for manuscript development was provided by Adler Ortho, Cormano, Italy. The sponsor had no involvement in the writing of the report or in the decision to submit the results for publication.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval Ethics committee approval was obtained prior to study commencement.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Daigle ME, Weinstein AM, Katz JN, Losina E (2012) The cost-effectiveness of total joint arthroplasty: a systematic review of published literature. *Best Pract Res Clin Rheumatol* 26(5):649–658

2. Khanuja HS, Banerjee S, Jain D, Pivec R, Mont MA (2014) Short bone-conserving stems in cementless hip arthroplasty. *J Bone Joint Surg Am* 96(20):1742–1752
3. Lavernia C, D'Apuzzo M, Hernandez V, Lee D (2004) Thigh pain in primary total hip arthroplasty: the effects of elastic moduli. *J Arthroplasty* 19(7 Suppl 2):10–16
4. Noble PC, Alexander JW, Lindahl LJ, Yew DT, Granberry WM, Tullos HS (1988) The anatomic basis of femoral component design. *Clin Orthop Relat Res* 235(235):148–165
5. Sendtner E, Tibor S, Winkler R, Wörner M, Grifka J, Renkawitz T (2010) Stem torsion in total hip replacement. *Acta Orthop* 81(5):579–582
6. Worlicek M, Weber M, Craiovan B, Wörner M, Völlner F, Springorum HR, Grifka J, Renkawitz T (2016) Native femoral anteversion should not be used as reference in cementless total hip arthroplasty with a straight, tapered stem: a retrospective clinical study. *BMC Musculoskelet Disord* 17:399
7. Rajakulendran K, Field RE (2012) Neck-preserving femoral stems. *HSS J* 8(3):295–303
8. Nunn D, Freeman MA, Tanner KE, Bonfield W (1989) Torsional stability of the femoral component of hip arthroplasty. Response to an anteriorly applied load. *J Bone Joint Surg Br* 71(3):452–455
9. Traina F, De Clerico M, Biondi F, Pilla F, Tassinari E, Toni A (2009) Sex differences in hip morphology: is stem modularity effective for total hip replacement? *J Bone Joint Surg Am* 91(Suppl 6):121–128
10. Lindahl H (2007) Epidemiology of periprosthetic femur fracture around a total hip arthroplasty. *Injury* 38(6):651–654
11. Budde S, Seehaus F, Schwarze M, Hurschler C, Floerkemeier T, Windhagen H, Noll Y, Ettinger M, Thorey F (2016) Analysis of migration of the Nanos(R) short-stem hip implant within 2 years after surgery. *Int Orthop* 40(8):1607–1614
12. Yan SG, Woiczinski M, Schmidutz TF, Weber P, Paulus AC, Steinbrück A, Jansson V, Schmidutz F (2017) Can the metaphyseal anchored Metha short stem safely be revised with a standard CLS stem? A biomechanical analysis. *Int Orthop* 41(12):2471–2477
13. Hochreiter J, Hejkrlik W, Emmanuel K, Hitzl W, Ortmaier R (2017) Blood loss and transfusion rate in short stem hip arthroplasty. A comparative study. *Int Orthop* 41(7):1347–1353
14. Dabirrahmani D, Hogg M, Kohan L, Gillies M (2010) Primary and long-term stability of a short-stem hip implant. *Proc Inst Mech Eng H* 224(9):1109–1119
15. Kim YH, Park JW, Kim JS (2013) Is diaphyseal stem fixation necessary for primary total hip arthroplasty in patients with osteoporotic bone (Class C bone)? *J Arthroplasty* 28(1):139–146.e131
16. McElroy MJ, Johnson AJ, Mont MA, Bonutti PM (2011) Short and standard stem prostheses are both viable options for minimally invasive total hip arthroplasty. *Bull NYU Hosp Jt Dis* 69(Suppl 1):S68–S76
17. Schmidutz F, Beirer M, Weber P, Mazoochian F, Fottner A, Jansson V (2012) Biomechanical reconstruction of the hip: comparison between modular short-stem hip arthroplasty and conventional total hip arthroplasty. *Int Orthop* 36(7):1341–1347
18. Dorr LD, Faugere MC, Mackel AM, Gruen TA, Bognar B, Mal-luche HH (1993) Structural and cellular assessment of bone quality of proximal femur. *Bone* 14(3):231–242
19. Harris WH (1969) Traumatic arthritis of the hip after dislocation and acetabular fractures: treatment by mold arthroplasty. An end-result study using a new method of result evaluation. *J Bone Joint Surg* 51-A:737–755
20. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW (1988) Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol* 15(12):1833–1840
21. Gruen T, McNeice G, Amstutz H (1979) “Modes of failure” of cemented stem-type femoral components: a radiographic analysis of loosening. *Clin Orthop Relat Res* 141:17–27
22. Zweymüller K (2007) Good results with an uncoated grit-blasted tapered straight stem at 10 years. *Interactive Surgery* 2(3):197–205
23. Bugbee WD, Culpepper WJ 2nd, Engh CA Jr, Engh CA Sr (1997) Long-term clinical consequences of stress-shielding after total hip arthroplasty without cement. *J Bone Joint Surg Am* 79(7):1007–1012
24. Brooker A, Bowerman J, Robinson R, Riley LJ (1973) Ectopic ossification following total hip replacement. Incidence and a method of classification. *J Bone Joint Surg (Am)* 55(8):1629–1632
25. Kjellberg M, Englund E, Sayed-Noor AS (2009) A new radiographic method of measuring femoral offset. *The Sundsvall method*. *Hip Int* 19(4):377–381
26. Falez F, Casella F, Panegrossi G, Favetti F, Barresi C (2008) Perspectives on metaphyseal conservative stems. *J Orthop Traumatol* 9(1):49–54
27. Rometsch E, Bos P, Koes B (2012) Survival of short hip stems with a “modern”, trochanter-sparing design—a systematic literature review. *Hip Int* 22(4):344–354
28. Burchard R, Braas S, Soost C, Graw JA, Schmitt J (2017) Bone preserving level of osteotomy in short-stem total hip arthroplasty does not influence stress shielding dimensions—a comparing finite elements analysis. *BMC Musculoskelet Disord* 18:343
29. Kim YH, Kim JS, Joo JH, Park JW (2012) A prospective short-term outcome study of a short metaphyseal fitting total hip arthroplasty. *J Arthroplasty* 27(1):88–94
30. Muller M, Abdel MP, Wassilew GI, Duda G, Perka C (2015) Do post-operative changes of neck-shaft angle and femoral component anteversion have an effect on clinical outcome following uncemented total hip arthroplasty? *Bone Joint J* 97-b(12):1615–1622
31. Nawabi DH, Do HT, Ruel A, Lurie B, Elpers ME, Wright T, Potter HG, Westrich GH (2016) Comprehensive analysis of a recalled modular total hip system and recommendations for management. *J Bone Joint Surg Am* 98(1):40–47
32. Kop AM, Swarts E (2009) Corrosion of a hip stem with a modular neck taper junction: a retrieval study of 16 cases. *J Arthroplasty* 24(7):1019–1023
33. Ollivier M, Parratte S, Galland A, Lunebourg A, Argenson JN (2015) Are titanium-on-titanium TiAl6V4 modular necks safe in total hip arthroplasty for non-overweight patients? Results of a prospective series at a minimum follow-up of 7 years. *Eur J Orthop Surg Traumatol* 25(7):1147–1152
34. Omlor GW, Kretzer JP, Reinders J, Streit MR, Bruckner T, Gotterbarm T, Aldinger PR, Merle C (2013) In vivo serum titanium ion levels following modular neck total hip arthroplasty—10 year results in 67 patients. *Acta Biomater* 9(4):6278–6282

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