

# Fully hydroxyapatite-coated collared femoral stems in direct anterior versus direct lateral hip arthroplasty

Sebastian Heaven, MBCh, MSc  
Maxwell Perelgut, BMSc, MSc  
Edward Vasarhelyi, MD  
James Howard, MD  
Matthew Teeter, PhD  
Brent Lanting, MD

Accepted May 12, 2020

## Correspondence to:

S. Heaven  
Department of Orthopaedics  
London Health Sciences Centre  
339 Windermere Rd  
London ON N6A 5A5  
sebheaven@gmail.com

DOI: 10.1503/cjs.000920

**Background:** Total hip arthroplasty (THA) via the direct anterior approach has increased in popularity in the last decade, with research supporting enhanced early recovery; however, some investigators have reported increased early revision rates in direct anterior THA. We examined outcomes from a single institution's experience with a fully hydroxyapatite-coated collared femoral stem implanted via the anterior or the lateral approach.

**Method:** Patients who had received fully hydroxyapatite-coated collared femoral stems as part of THA surgery performed by 1 of 3 surgeons between January 2012 and September 2017 were identified from our institutional database. We examined revision rates for the 2 approaches and compared them between the 2 groups. We also analyzed outcomes on plain film radiographs obtained immediately postoperatively and at 1 and 2 years.

**Results:** A total of 695 patients received a fully hydroxyapatite-coated collared stem during the study period. Total hip arthroplasty was performed via the direct anterior approach in 281/778 hips (36.1%) and via the direct lateral approach in 497 (63.9%). Nineteen patients (2.5%) underwent subsequent revision surgery; there was no statistically significant difference in the revision rate between the anterior and lateral approaches (2.5% v. 2.4%,  $p = 0.95$ ). The mean subsidence of the stem at 1 year was 1.68 mm (standard deviation 11.7 mm). No statistically significant differences were observed between the cohorts for any of the radiographic measurements at either follow-up time

**Conclusion:** We found no significant difference in revision rates between the direct anterior and direct lateral approach. Stem subsidence levels were in keeping with expected values, and no major changes in stem position occurred during the first postoperative year. Surgical approach did not appear to substantially affect biomechanical stem behaviour.

**Contexte :** L'arthroplastie totale de la hanche (ATH) par voie antérieure directe a gagné en popularité dans les 10 dernières années, la recherche ayant montré qu'elle favorisait un rétablissement rapide; certains chercheurs ont toutefois signalé qu'elle était associée à un taux accru d'opérations de révision précoces. Nous avons étudié les issues de l'installation d'une tige fémorale à collier entièrement recouverte d'hydroxyapatite par voie antérieure ou latérale dans un établissement.

**Méthodes :** Nous avons interrogé la base de données de notre établissement pour y recenser les patients ayant subi, entre janvier 2012 et septembre 2017, une ATH au cours de laquelle 1 de 3 chirurgiens a installé une tige fémorale à collier entièrement recouverte d'hydroxyapatite. Nous avons ensuite examiné le taux d'opérations de révision pour les 2 approches étudiées, et avons comparé les issues des 2 groupes. Nous avons également analysé les clichés radiographiques pris immédiatement après l'intervention, de même de ceux pris aux suivis à 1 et à 2 ans.

**Résultats :** Durant la période à l'étude, 695 patients se sont fait installer une tige fémorale à collier entièrement recouverte d'hydroxyapatite. Sur 778 hanches, 281 (36,1%) avaient subi une ATH par voie antérieure directe, et 497 (63,9%), une ATH par voie latérale directe. Dix-neuf patients (2,5%) ont dû subséquemment subir une opération de révision; aucune différence statistiquement significative n'a été observée entre le groupe voie antérieure et le groupe voie latérale en ce qui a trait au taux de révision (2,5% c. 2,4%;  $p = 0,95$ ). L'affaissement moyen de la tige au suivi à 1 an était de 1,68 mm (écart type 11,7 mm). Les mesures radiographiques des 2 groupes ne présentaient pas de différences statistiquement significatives, quel que soit le moment du suivi.

**Conclusion :** Nous n'avons constaté aucune différence significative dans le taux de révision entre les 2 groupes. L'affaissement observé était dans les valeurs attendues, et la position de la tige n'avait pas changé de façon importante au cours de la première année. La voie chirurgicale utilisée ne semblait pas influencer considérablement le comportement biomécanique de la tige.

**T**otal hip arthroplasty (THA) is one of the most reliable and reproducible procedures in orthopedic surgery today, with a success rate as high as 97%.<sup>1</sup> With recent advances in implant technology enabling surgeons to offer THA to younger patients than ever before, anterior-approach THA is increasingly being used in an attempt to meet the higher demands of younger patients undergoing THA.<sup>2</sup> Although numerous authors have reported accelerated early postoperative recovery in patients who undergo THA with this approach,<sup>3-6</sup> others have suggested that early revision rates are higher with the anterior approach than with other, more traditional approaches.<sup>7-9</sup>

Cost-benefit analyses of using the anterior approach for elective THA showed substantial benefits to the health care system.<sup>10,11</sup> Higher early revision rates in this patient group would dramatically alter and possibly even negate any such benefits. Therefore, the importance of identifying differences in revision rates between surgical approaches cannot be understated.

Radiostereometric analysis (RSA)<sup>12</sup> has become the gold standard protocol for predicting implant failure as early as possible after THA. Although its accuracy has been reported extensively in the literature,<sup>13,14</sup> not all institutions have access to this methodology. In retrospective studies, alternative strategies must be used to increase the sensitivity of standard radiographic examination when considering early implant failure.

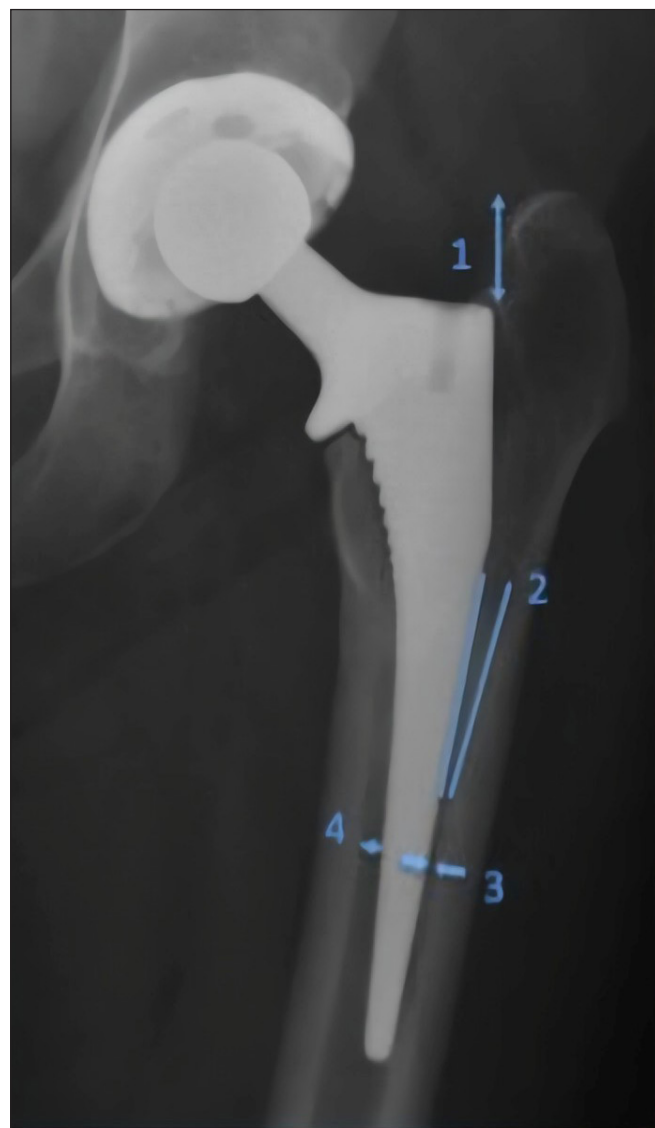
The purpose of this study was to investigate the hypothesis that anterior-approach THA has a higher early revision rate than lateral-approach THA. We used a previously described radiographic analysis technique<sup>15</sup> to examine implant migration in the first 2 postoperative years and compared this variable between the 2 surgical approaches.

## METHODS

In this retrospective study, after obtaining research ethics board approval, we extracted anonymized data on all patients who had received a fully hydroxyapatite-coated collared femoral stem (Corail AMT collared, DePuy Synthes) as part of primary THA surgery between January 2012 and September 2017 from the database of our tertiary care academic centre. The index arthroplasty procedure was performed by 1 of 3 consultant surgeons from our institution (B.L., J.H. or E.V.).

The postoperative radiographs were examined by 2 reviewers (S.H. and M.P.). They assessed the radiographs for the first 100 patients together and compared agreement between their values using the Pearson correlation coefficient. Each reviewer was then assigned half of the remaining data to analyze independently. Patients who received revision surgery were identified, and the reason for revision was recorded.

Three postoperative radiographs were examined for each patient: the radiograph obtained immediately after surgery, the 1-year follow-up radiograph and the 2-year follow-up radiograph. These radiographs were retrieved and viewed with our institution's Centricity picture archiving and communication system (GE Healthcare). Analysis of each radiograph included the following measurements:<sup>15</sup> 1) the distance from the tip of the greater trochanter to the shoulder of the femoral component, 2) the angle formed between the lateral border of the component and the lateral cortex, 3) the distance from the midpoint of the femoral component to the medial cortex and 4) the distance from the midpoint of the femoral component to the lateral cortex (Figure 1).



**Fig. 1.** Radiographic analysis parameters. 1: distance from tip of greater trochanter to implant shoulder; 2: angle portended between lateral cortex and lateral implant surface; 3: distance between lateral cortex and lateral implant surface; 4: distance between medial cortex and medial implant surface.

We defined the midpoint of the femoral component as the point on the stem halfway between the distal tip and the shoulder of the component. Measurement 1 has previously been validated.<sup>15</sup> Measurements 3 and 4 are 2-dimensional extrapolations of the x-axis measured in RSA radiographs and therefore are validated as part of RSA measurements. Measurement 2, although not validated, provides a more clinically relevant assessment of measurements 3 and 4: when discussing varus tilt of a component, degrees of tilt are easier to describe and more readily understood than changes in distance from medial and lateral cortices.

### Statistical analysis

The data were formatted into a Microsoft Excel spreadsheet. We analyzed the data statistically using an unpaired *t* test for continuous data (e.g., the radiographic analysis parameters) and the  $\chi^2$  test for nominal data (e.g., revision rate, reasons for revision). Values for the surgical approach cohorts were calculated and compared for statistical significance, set at  $p < 0.05$ .

## RESULTS

The database search identified 809 hips in 734 patients in whom a fully hydroxyapatite-coated femoral stem was used. We excluded 31 hips that had a surgical approach other than anterior or lateral, leaving 778 cases for analysis (281 direct anterior approach and 497 direct lateral approach). A total of 734 hips (94.3%) had retrievable postoperative and 1-year radiographs, and 275 (35.3%) had postoperative, 1-year and 2-year radiographs available for analysis.

For the 100 cases analyzed in tandem, the Pearson correlation coefficient for measurement 1 was 0.97, for measurement 2, 0.75, for measurement 3, 0.81, and for measurement 4, 0.92, indicating good to excellent agreement between the reviewers' measurements.

Table 1 shows the patients' demographic and clinical characteristics, and Table 2 shows a comparison of characteristics between the 2 cohorts. There was a significant difference in mean body mass index between the anterior and lateral groups (28.1 v. 30.3,  $p = 0.04$ ).

Between the postoperative radiograph and the 1-year follow-up radiograph, the mean stem subsidence (as indicated by measurement 1) was 1.68 mm  $\pm$  SD 11.7 mm (median 1.12 mm [range 0–34.8 mm]). At 2 years, the mean stem subsidence from the postoperative radiograph was 1.89 mm  $\pm$  SD 8.1 mm (median 2.14 mm [range 0–26.34 mm]).

For measurement 2, the mean difference between the postoperative radiograph and the 1-year radiograph was 0.2°  $\pm$  SD 0.28° (median 0.1° [range 0°–7.9°]), indicating a very minor varus change of the overall com-

**Table 1. Demographic and clinical characteristics of patients who underwent total hip arthroplasty with the direct anterior or direct lateral approach**

Characteristic	No. (%) of patients* n = 695
Age at time of surgery, mean $\pm$ SD, yr (range)	70 $\pm$ 12 (21–95)
Mean body mass index $\pm$ SD (range)	30 $\pm$ 6.9 (15–74)
Sex	
Male	337 (48.5)
Female	358 (51.5)
Side (n = 778)	
Left	359 (46.1)
Right	419 (53.9)
Surgical approach (n = 778)	
Direct anterior	281 (36.1)
Direct lateral	497 (63.9)
Indication (n = 778)	
Osteoarthritis	677 (87.0)
Osteonecrosis/avascular necrosis	21 (2.7)
Posttraumatic	20 (2.6)
Fracture	5 (0.6)
Hip dysplasia	3 (0.4)
Inflammatory arthritis	3 (0.4)
Tumour	2 (0.2)
Perthes disease	2 (0.2)
Osteopetrosis	1 (0.1)
Not recorded	44 (5.7)

SD = standard deviation.  
\*Except where noted otherwise.

**Table 2. Comparison of age, sex, body mass index and side operated between the 2 cohorts**

Characteristic	Approach; no. (%) of hips*		
	Direct anterior n = 281	Direct lateral n = 497	<i>p</i> value
Age, mean $\pm$ SD, yr	69.1 $\pm$ 11.4	70.6 $\pm$ 14.5	0.2
Sex			0.98
Male	128 (45.6)	225 (45.3)	
Female	153 (54.4)	272 (54.7)	
Body mass index, mean $\pm$ SD	28.1 $\pm$ 15.7	30.3 $\pm$ 8.0	0.04
Side			0.1
Left	143 (50.9)	229 (46.1)	
Right	138 (49.1)	268 (53.9)	

SD = standard deviation.  
\*Except where noted otherwise.

ponent alignment. The mean difference between the postoperative radiograph and the 2-year radiograph was 0.44°  $\pm$  SD 0.25° (median 0.5° [range 0°–4.3°]).

These alignment findings were confirmed by the results of analysis of measurements 3 and 4. Between the postoperative radiograph and the 1-year radiograph, the distance from the midpoint of the femoral component to the medial cortex had increased by a mean of 0.15 mm  $\pm$  SD 0.54 mm (median 0.23 mm [range 0–5.74 mm]). It had

**Table 3. Mean change in radiographic measurements between the postoperative film and the 1-year film, and between the postoperative film and the 2-year film for the 2 cohorts**

Time; cohort	Measurement; mean change ± SD, mm			
	1	2	3	4
<b>1 yr</b>				
Direct anterior	1.88 ± 18.5	0.176 ± 0.45	-0.463 ± 2.79	0.116 ± 2.12
Direct lateral	0.47 ± 7.03	0.418 ± 0.16	-0.435 ± 1.44	0.027 ± 1.48
<i>p</i> value*	0.3	0.9	0.7	0.3
<b>2 yr</b>				
Direct anterior	3.99 ± 11.7	0.427 ± 0.96	-0.614 ± 3.84	0.499 ± 1.83
Direct lateral	2.89 ± 4.01	0.661 ± 1.25	-0.699 ± 0.90	0.327 ± 0.68
<i>p</i> value*	0.2	0.2	0.8	0.2

SD = standard deviation.  
\*Unpaired *t* test.

increased further on the 2-year radiograph, by a mean of 0.11 mm ± SD 0.16 mm (median 0.2 mm [range 0–4.9 mm]). The distance from the midpoint of the femoral component to the lateral cortex had decreased by a mean of 0.67 mm ± SD 0.2 mm (median 0.1 mm [range 0–1.8 mm]) at 1 year; this change was maintained at 2 years (mean 0.6 mm [SD 0.35 mm]; median 0.3 mm [range 0–3.75 mm]).

The mean changes in each value between the postoperative radiograph and the 1-year radiograph, and between the postoperative radiograph and the 2-year radiograph for the 2 cohorts are presented in Table 3. At 1 year, the stems in the anterior approach cohort had subsided by 1.88 mm on average, compared to 0.47 mm in the lateral approach cohort. The amount of varus tilt was slightly greater in the lateral approach group than in the anterior approach group (0.418° v. 0.176°). There was minimal difference in the measurements of distance to the medial and lateral cortices between the cohorts. No statistically significant differences were observed between the cohorts for any of the measurements described at either follow-up time.

At the time of writing, 19 patients (2.5%) had undergone revision surgery (Table 4). There was no statistically significant difference in the revision rate between the anterior approach and the lateral approach cohorts (2.5% v. 2.4%, *p* = 0.95). The most common reason for revision in both cohorts was periprosthetic infection (7 patients [37%]), followed by aseptic loosening (6 [32%]), periprosthetic fracture (4 [21%]) and recurrent instability (2 [10%]).

**DISCUSSION**

Our radiographic analysis confirmed that there is subsidence of the implant over the first 2 years after THA with both the direct anterior and the direct lateral approach. A small amount of shift in alignment toward the varus direction was also observed over this time. This has been theo-

**Table 4. Indications for revision surgery**

Indication	Approach; no. (%) of hips		<i>p</i> value*
	Direct anterior <i>n</i> = 281	Direct lateral <i>n</i> = 497	
Aseptic loosening	4 (1.4)	2 (0.4)	0.1
Periprosthetic infection	2 (0.7)	5 (1.0)	0.7
Periprosthetic fracture	1 (0.4)	3 (0.6)	0.6
Instability	0 (0.0)	2 (0.4)	0.9

\* $\chi^2$  test.

riized to occur in collared femoral components like the one investigated in our study owing to the weight-bearing force vectors acting on the component, with the collar contacting the calcar bone and subsequently acting as a fulcrum around which the component can tilt into varus.<sup>16</sup>

Our mean value for the extent of subsidence of the fully hydroxyapatite-coated collarless stem postoperatively was significantly lower than that previously reported,<sup>15</sup> which supports the hypothesis that having a collared femoral implant reduces overall subsidence.<sup>17</sup> This finding, however, is mitigated by the SD values for our subsidence measurements 1 and 2 years postoperatively (11.7 mm and 8.1 mm, respectively), which indicate a broad range of values for subsidence, more in keeping with the published literature.

The only statistically significant difference in demographic characteristics between our 2 cohorts was in body mass index, which was 2 points higher for patients who underwent THA with the direct lateral approach than for those who had surgery via the direct anterior approach.

We observed large SD values for each radiographic measurement, which indicates the limited accuracy of the radiographic analysis method described. However, there were no statistically significant differences between the anterior and lateral approaches for any of the measurements. We infer from this finding that surgical approach does not significantly influence postoperative migration of the femoral stem.

Although the findings of De Geest and colleagues<sup>7</sup> suggest that the anterior approach carries a higher risk of femoral fracture than other approaches, we did not observe this in our cohort. The periprosthetic infection rate was higher in the lateral approach cohort than in the anterior approach cohort; however, the difference was not statistically significant. Similarly, although twice as many patients in the anterior cohort than in the lateral cohort underwent revision surgery for aseptic loosening, the difference was not statistically significant.

Our revision rates, both overall and for the approach-specific cohorts, are comparable to those reported in the literature<sup>18</sup> and in recent registry data reports<sup>19</sup> with the use of a fully hydroxyapatite-coated femoral stem, as well as other femoral stem systems.<sup>20,21</sup> We found no statistically significant difference in early revision rates between the direct anterior approach and the direct lateral approach when using this stem. This is in contrast to the report by Panichkul and colleagues,<sup>8</sup> whose findings suggest that the direct anterior approach is associated with higher early revision rates than the direct lateral approach. In our study, most of the revision procedures were performed for indications that were unrelated to component position or subsidence. In the cases in which revision surgery was performed for indications that may be related to these factors, they were not considered outliers within our cohort, and change in femoral component position is unlikely to have contributed to the indication for revision surgery.

### Limitations

Limitations of this study include considerable loss to follow-up at 2 years. However, it is our institutional policy to see patients 1 year postoperatively and every 2 years thereafter; thus, most patients are not routinely seen in clinic at 2 years. The limitations of the radiographic analysis technique used to assess change in component position over time<sup>15</sup> must also be acknowledged. The chief drawback of this technique is that measurements (particularly angle and cortex distance measurements) are highly susceptible to error when the radiographs are obtained with the limb in differing degrees of rotation. In addition, although our cohort was large enough to permit statistical analysis, our study remained underpowered to detect statistically significant differences in infrequent events such as revision surgery. This is an important factor to consider when comparing our revision rates between approaches, particularly with respect to revision for aseptic loosening (a higher-powered study may conceivably show statistically significant differences in revision rates for this diagnosis). Finally, although having 3 different surgeons perform the procedures introduced heterogeneity and bias into our study, it enhances the generalizability of our results and eliminates single-surgeon bias.

### CONCLUSION

In our patient population, who received fully hydroxyapatite-coated collared femoral stems as part of THA, we observed a mean amount of femoral stem subsidence of about 2 mm during the first 2 postoperative years. The stems also appear to have shifted in the varus direction by 0.4° during this time. Surgical approach does not appear to have affected femoral stem migration patterns significantly. Further study with RSA in a prospective randomized trial is needed to obtain more accurate values for changes in femoral component position. Our revision rates for patients in both the direct anterior and direct lateral cohort were comparable to those in prior studies, and the early revision rate in the anterior approach cohort was not higher than that in the lateral approach cohort.

**Affiliations:** From the Department of Orthopaedics, London Health Sciences Centre, London, Ont. (Heaven, Vasarhelyi, Howard, Lanting); the School of Biomedical Engineering, Western University, London, Ont. (Perelgut); and the Department of Medical Biophysics, Schulich School of Medicine and Dentistry, Western University, London, Ont. (Teeter).

**Competing interests:** Edward Vasarhelyi reports consultant fees from DePuy Synthes, Zimmer Biomet and Hip Innovation Technology, and institutional research support from DePuy Synthes, Smith & Nephew, Stryker and Zimmer Biomet. James Howard reports grants from Stryker and DePuy Synthes, personal fees from Stryker, DePuy Synthes, Smith & Nephew and Intellijoint Surgical, and institutional research support from Stryker, DePuy Synthes, Smith & Nephew, Zimmer Biomet, and Microport. He holds stock in PersaFix Technologies. Matthew Teeter is on the boards of the International Society for Technology in Arthroplasty and the Canadian RSA Network, and holds stock in IdealFit Spacer Technologies and Solo Spine. Brent Lanting reports consultant, principal investigator and institutional support from DePuy Synthes, Stryker and Smith & Nephew, and institutional support from Zimmer Biomet. No other competing interests were declared.

**Contributors:** S. Heaven, E. Vasarhelyi, J. Howard, M. Teeter and B. Lanting designed the study. S. Heaven, M. Perelgut and E. Vasarhelyi acquired the data, which S. Heaven, M. Perelgut, E. Vasarhelyi, J. Howard and B. Lanting analyzed. S. Heaven wrote the manuscript, which M. Perelgut, E. Vasarhelyi, J. Howard, M. Teeter and B. Lanting critically revised. All authors gave final approval of the article to be published.

**Content licence:** This is an Open Access article distributed in accordance with the terms of the Creative Commons Attribution (CC BY-NC-ND 4.0) licence, which permits use, distribution and reproduction in any medium, provided that the original publication is properly cited, the use is noncommercial (i.e., research or educational use), and no modifications or adaptations are made. See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

**Funding:** No funding was received for this work.

### References

1. Casper DS, Kim GK, Restrepo C, et al. Primary total hip arthroplasty with an uncemented femoral component five- to nine-year results. *J Arthroplasty* 2011;26:838-41.
2. Connolly KP, Kamath AF. Direct anterior total hip arthroplasty. *World J Orthop* 2016;7:38-43.
3. Parvizi J, Restrepo C, Mattenfort MG. Total hip arthroplasty performed through direct anterior approach provides superior early outcome: results of a randomized, prospective study. *Orthop Clin North Am* 2016;47:497-504.

4. Zhao HY, Kang PD, Xia YY, et al. Comparison of early functional recovery after total hip arthroplasty using a direct anterior or posterolateral approach: a randomized controlled trial. *J Arthroplasty* 2017;32:3421-8.
5. Meermans G, Konan S, Das R, et al. The direct anterior approach in total hip arthroplasty: a systematic review of the literature. *Bone Joint J* 2017;99-B:732-40.
6. Moskal JT. Anterior approach in THA improves outcomes: affirms. *Orthopedics* 2011;34:e456-8.
7. De Geest T, Vansintjan P, De Loore G. Direct anterior total hip arthroplasty: complications and early outcome in a series of 300 cases. *Acta Orthop Belg* 2013;79:166-73.
8. Panichkul P, Parks NL, Ho H, et al. New approach and stem increased femoral revision rate in total hip arthroplasty. *Orthopedics* 2016;39:e86-92.
9. Eto S, Hwang K, Huddleston JI, et al. The direct anterior approach is associated with early revision total hip arthroplasty. *J Arthroplasty* 2017;32:1001-5.
10. Petis SM, Howard JL, Lanting BA, et al. In-hospital cost analysis of total hip arthroplasty: Does surgical approach matter? *J Arthroplasty* 2016;31:53-8.
11. Kamath AF, Chitnis AS, Holy C, et al. Medical resource utilization and costs for total hip arthroplasty: benchmarking an anterior approach technique in the Medicare population. *J Med Econ* 2018;21:218-24.
12. Onsten I, Berzins A, Shott S, et al. Accuracy and precision of radiostereometric analysis in the measurement of THR femoral component translations: human and canine in vitro models. *J Orthop Res* 2001;19:1162-7.
13. Bottner F, Su E, Nestor B, et al. Radiostereometric analysis: the hip. *HSS J* 2005;1:94-9.
14. Ryd L, Yuan X, Lofgren H. Methods for determining the accuracy of radiostereometric analysis (RSA). *Acta Orthop Scand* 2000;71:403-8.
15. Selvaratnam V, Shetty V, Sahni V. Subsidence in collarless Corail hip replacement. *Open Orthop J* 2015;9:194-7.
16. Whiteside LA, Easley JC. The effect of collar and distal stem fixation on micromotion of the femoral stem in uncemented total hip arthroplasty. *Clin Orthop Relat Res* 1989;239:145-53.
17. Demy G, Fary C, Lustig S, et al. Does a collar improve the immediate stability of uncemented femoral hip stems in total hip arthroplasty? A bilateral comparative cadaver study. *J Arthroplasty* 2011;26:1549-55.
18. Vidalain JP. Twenty-year results of the cementless Corail stem. *Int Orthop* 2011;35:189-94.
19. *National Joint Registry for England, Wales, Northern Ireland and the Isle of Man 14th annual report 2017*. London: Healthcare Quality Improvement Project; 2017.
20. Pennington M, Grieve R, Black N, et al. Functional outcome, revision rates and mortality after primary total hip replacement — a national comparison of nine prosthesis brands in England. *PLoS One* 2013;8:e73228.
21. Danesh-Clough T, Bourne RB, Rorabeck CH, et al. The mid-term results of a dual offset uncemented stem for total hip arthroplasty. *J Arthroplasty* 2007;22:195-203.