Characterization of the Running-in Period in Total Hip Resurfacing Arthroplasty: An in Vivo and in Vitro Metal Ion Analysis

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Characterization of the Running-in Period in Total Hip Resurfacing Arthroplasty: An in Vivo and in Vitro Metal Ion Analysis

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Background: Metal-on-metal total hip resurfacing arthroplasty is increasingly being performed in young and active patients. Preclinical in vitro testing of implants is usually performed with use of hip simulators, and the serum metal ion concentration is determined for the purpose of monitoring the patients. The goal of this study was to characterize the early running-in period in vivo and in vitro by characterizing metal ion levels.

Methods: A well-functioning total hip resurfacing prosthesis was implanted in fifteen consecutive patients, and the serum metal ion concentrations in these patients were then determined preoperatively and at intervals during the first postoperative year (at one, six, twelve, twenty-four, and fifty-two weeks). The number of walking cycles was measured with use of a computerized accelerometer in order to compare walking cycles to hip simulator cycles. In vitro, five similar components were investigated for 3 million cycles with use of a hip simulator. Serum samples were obtained at different time points, and wear was measured by quantifying wear particles and ions in the samples. All patient and simulation serum samples were analyzed with use of inductively coupled plasma-mass spectrometry. One simulator implant was investigated with use of scanning electron microscopy.

Results: The serum chromium and cobalt levels of the patients continuously increased during the first six months and showed an insignificant decrease thereafter. The molybdenum concentration was unchanged compared with preoperative values. In contrast, the simulator measurements showed a different wear pattern with a high-wear running-in period and a low-wear steady-state phase. The running-in period was delayed by 300,000 cycles and lasted up to 1 million cycles. Scanning electron microscopic analysis showed a carbon-rich protein film predominantly in the early phases of simulation. Scratches were detected originating from pits filled with aluminum oxide and silicon oxide and from pulled-out carbides that were causing third-body wear.

Conclusions: The simulator study allowed an exact characterization of the running-in period and showed a delayed onset of running-in wear. In contrast, the clinical data showed a slow increase in measured ion concentrations. These different wear patterns are probably due to the effects of distribution, accumulation, and excretion of particles and ions in vivo.

Level of Evidence: Therapeutic Level IV. See Instructions to Authors for a complete description of levels of evidence.

Metal-on-metal articulations have been in clinical use for more than fifty years. High failure rates of historical designs occurred because of metallurgy and imprecise manufacturing technology[1,2]. Modern metal-on-metal components have been in use since the late 1980s and have been associated with good clinical success[3,4]. Current total hip resurfacing implants are made of two articulating metal components. Friction between bearing surfaces leads to the release of metal particles into the body. The biological interactions caused by the released metal ions are still a cause for concern, and much research is being performed in this area[5,6].

Metal-on-metal bearings generally show relatively low surface wear compared with conventional metal-on-polyethylene total hip replacements and are commonly used in modern joint

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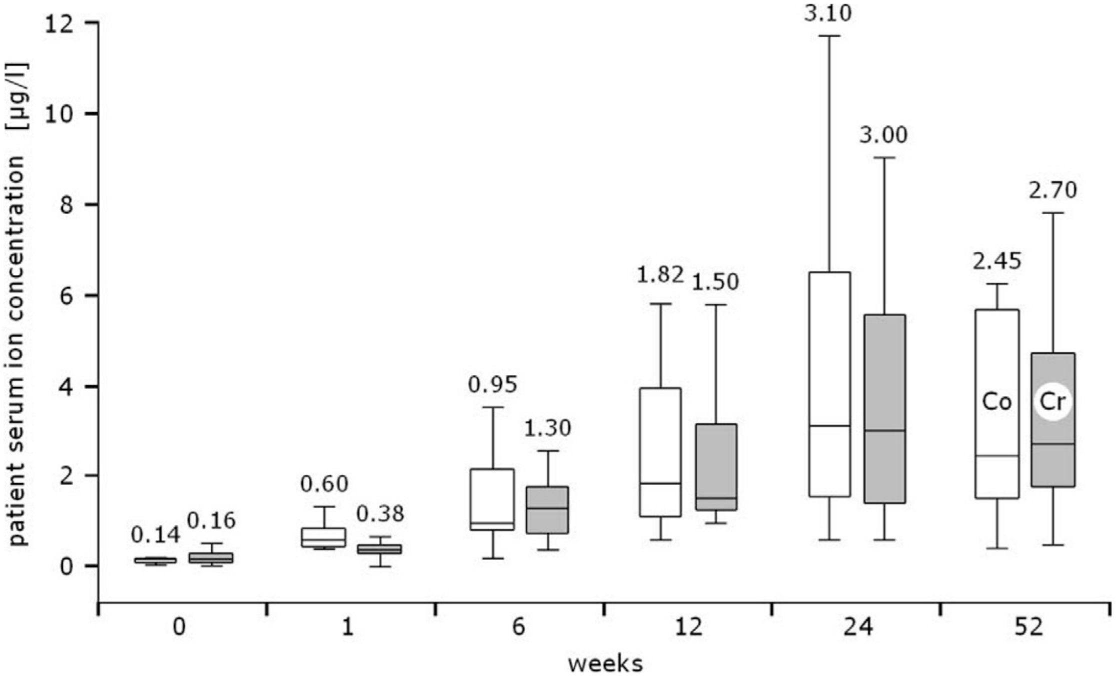

Fig. 1

The median patient chromium (Cr) and cobalt (Co) concentrations (n = 15).

arthroplasty, especially in total hip resurfacing[1,7]. The total wear volume in metal-on-metal bearings is much smaller than that in metal-on-polyethylene bearings, but, because metal particles are much smaller than polyethylene particles, the number of particles produced by metal-on-metal bearings can be higher[8]. The surface-to-volume ratio and total surface area of metal-on-metal particles may be higher than those of metal-on-polyethylene particles, and the ions released from these particles may have both local and systemic effects.

In order to study wear resistance in metal-on-metal bearings, tribological experiments have been performed with use of wear simulators. Nearly all previously conducted simulator tests have described a characteristic wear pattern that is initially marked by a running-in period, after which the wear pattern decreases to a lower-wear steady-state phase during the course of the simulation. Because wear is highest during the running-in phase, it is imperative to precisely describe this wear period. However, little is known about the duration of the running-in period. Most studies have indicated a duration of approximately 500,000[9,10] to 1 million cycles[11-13]. The reasons for this range with metal-on-metal bearings may be the inaccuracy of the gravimetric method of measurement and the large measurement intervals. For example, in numerous reports, high weight fluctuations have been observed, in part accompanied by increases in weight[10,12,14]. In other simulator studies, no wear was detected[15,16].

The goals of this study were to perform in vivo and in vitro investigations of the running-in period with use of high-resolution inductively coupled plasma-mass spectrometry. This method is currently used in an attempt to more accurately analyze blood samples of patients with metal-on-metal joints and was adopted for wear analysis in a hip simulator. The use of the same measurement technique allows a comparison of the in vivo and in vitro results.

Materials and Methods

Patients

Fifteen consecutive patients with a well-functioning metal-on-metal total hip resurfacing prosthesis were prospectively enrolled into this study after approval by the institutional review board at our university. All participants had normal renal function as determined by measurement of serum creatinine levels and creatinine clearance. Eight women and seven men with a mean age of fifty-one years (range, thirty-one to sixty-one years) and a mean body mass index of 28 (range, 24 to 35) participated. The preoperative diagnoses were primary osteoarthritis in thirteen hips and osteonecrosis in two hips. Thirteen hips were classified as having Charnley class-A disease, and two hips were classified as having Charnley class-B disease[17].

All patients had a unilateral total hip resurfacing system implanted with use of articular surface replacement components (ASR; DePuy, Warsaw, Indiana). All operations were performed through a posterior approach and with the patient placed in the lateral decubitus position. The mean size of the acetabular component was 54 mm (range, 46 to 62 mm), and the mean corresponding cemented femoral component was 48 mm in diameter. Implants made of a high carbon-content cobalt-chromium-molybdenum casting alloy with a non-heat-treated femoral component and a heat-treated acetabular component were used.

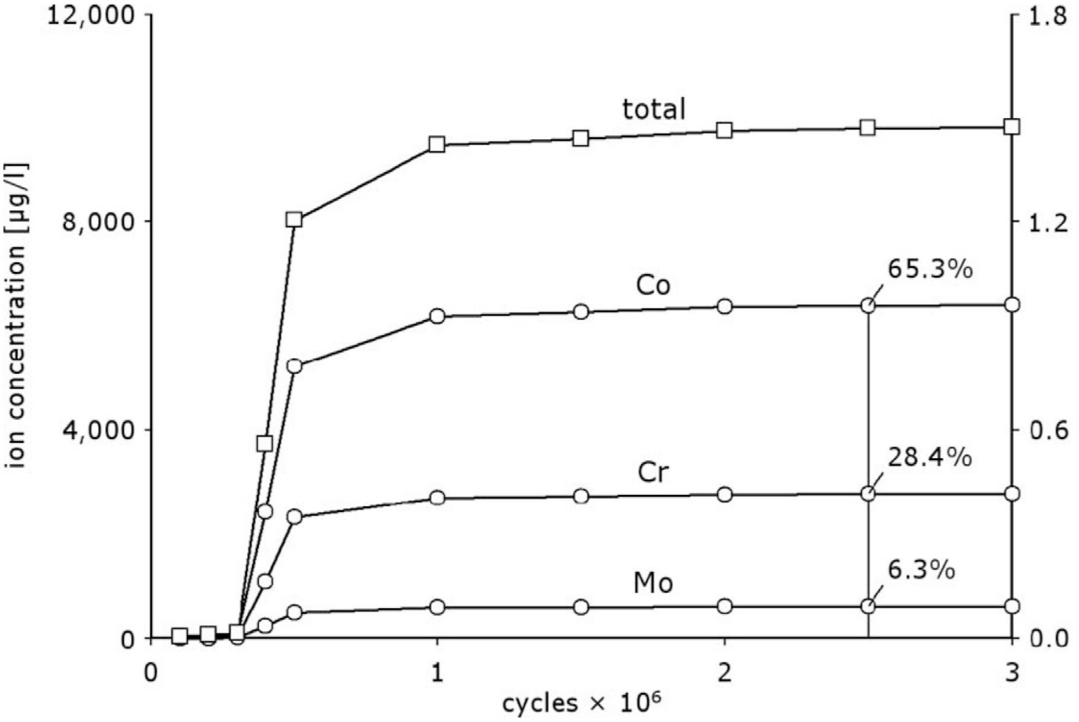

Fig. 2

Median cumulative wear progression in the hip simulator. The measured median element percentage in the samples corresponds to the element ratio of cobalt-chromium-molybdenum alloy. Co = cobalt, Cr = chromium, and Mo = molybdenum.

Clinical Study Protocol

Blood samples were taken preoperatively and at one, six, twelve, twenty-four, and fifty-two weeks postoperatively. The sampling protocol was described previously and patient data were included in the study if at least five of the six blood samples were obtained[18]. At the time of the one-year follow-up, patient activity was assessed with use of a computerized, two-dimensional accelerometer worn at the ankle for a mean of twelve days (range, ten to fourteen days) in order to calculate the number of walking cycles per year. During clinical evaluation, the Harris hip score[19], range of motion, and Devane activity score[20] were documented. Pelvic radiographs were obtained postoperatively at six weeks and at six and twelve months.

Simulator Study

Five similar total hip resurfacing implants (ASR; DePuy) with a nominal diameter of 47 mm were tested in a hip simulator. The single-station hip joint simulator (858 Mini Bionix II system; MTS Systems, Eden Prairie, Minnesota) was altered to run completely free of metal ions, especially with regard to cobalt, chromium, and molybdenum. Wear was measured by identifying the particles and trace elements that were released into the serum test media. The simulation was performed to a total of 3 million cycles. The serum protein concentration was 30 g/L. Serum samples were obtained every 100,000 cycles. After 500,000 cycles, the sampling interval was increased to 500,000 cycles, with serum changed every 500,000 cycles.

Linear regression was performed to identify the running-in and steady-state wear phases. The implants were kept within the simulator for the whole simulation to avoid any negative influence of the demounting and remounting procedure on the wear behavior, such as material transfer from the implant fixation or destruction of surface layers. After each serum exchange, the implant chamber was flushed with ultra-pure water to remove any serum and wear residua. One of the implants was removed from the simulator every 500,000 cycles for the purpose of investigating the worn contact area with use of a scanning electron microscope (Type 440; Carl Zeiss, Cambridge, United Kingdom). The elemental composition of the implants and surface layers in different areas was analyzed with use of energy dispersive x-ray analysis (Link-ISIS; Oxford Instruments, Oxfordshire, United Kingdom). Wear data of this implant were not included in the analysis.

Trace Metal Analysis

The concentrations of the main elements of the implants (cobalt, chromium, and molybdenum) were analyzed with use of high-resolution inductively coupled plasma-mass spectrometry (Element2; Thermo Fisher Scientific, Bremen, Germany). In order to detect not only the ions but also the metal particles in the serum, the samples were first digested with high-purity nitric acid (HNO_3) and hydrogen peroxide (H_2O_2) in Teflon containers under clean-room conditions in a microwave high-pressure autoclave (UltraClave II; Milestone,

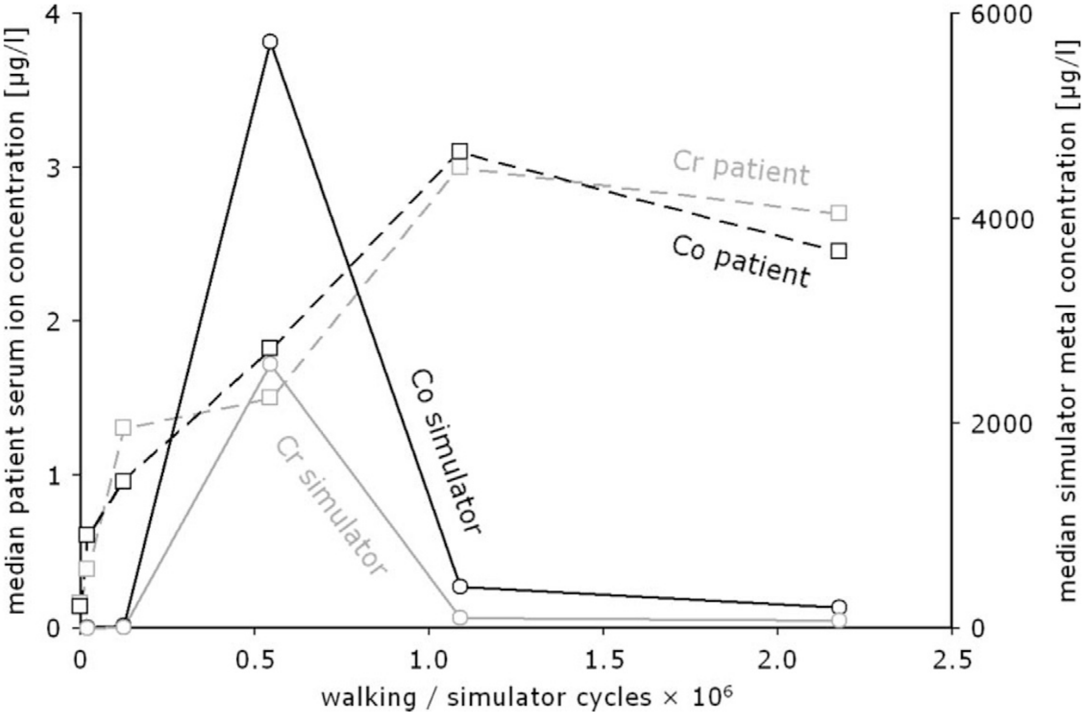

Fig. 3

Comparison between clinical and simulator data (patient data dashed). Cr = chromium, and Co = cobalt.

Bergamo, Italy). The solutions were diluted with ultra-pure water and examined with the high-resolution inductively coupled plasma-mass spectrometry system, which was operated under clean-room conditions. The detection limits were 0.03 µg/L for cobalt, 0.01 µg/L for chromium, and 0.02 µg/L for molybdenum.

Statistics

To compare simulator data and patient data with regard to ion concentration levels, we calculated the simulator concentrations on the basis of the running-in and steady-state wear rates and the step rate of an average patient. Because of the small sample size of simulator data and the presence of outliers in the patient ion concentrations, it must be assumed that data distribution is asymmetric. Therefore, such data have to be presented as median values, as previously described for patient ion concentrations by MacDonald et al.[21]. To clarify differences within ion concentrations of patients between measuring intervals, the Wilcoxon signed-rank test was applied. The Pearson parametric correlation test was used to correlate patient parameters and measured ion concentrations. The significance level was fixed at $\alpha = 0.05$.

Results

Clinical Study

At the time of the one-year follow-up, all joints were well functioning and all patients were satisfied with their respective result. There were no signs of component loosening or periprosthetic osteolysis on the follow-up radiographs. The mean cup inclination was 43° (range, 29° to 60°; standard deviation, ± 8.6°), and the mean angle between the femoral component and the femoral axis was 135° (range, 117° to 146°; standard deviation, ± 7.4°). The Harris hip score increased from a preoperative mean value of 49 points (range, 25 to 79; standard deviation, ± 15.7 points) to a mean of 98 points (range, 93 to 100; standard deviation, ± 2.5 points). On the average, the patients walked 2.18 million cycles per year (range, 1.01 to 3.21 million cycles per year; standard deviation, 722,000 cycles per year).

During the first six months postoperatively, a steady increase in the median chromium concentration was detected (0.16, 0.38, 1.30, 1.50, and 3.00 µg/L) (Fig. 1). In contrast, a decrease in the chromium concentration was seen at the time of the twelve-month measurement in comparison to that seen at the time of the six-month measurement (from 3.00 µg/L to 2.70 µg/L), but this decrease was not significant ($p = 0.774$). After twelve months, the individual concentrations varied from 0.5 to 19.8 µg/L. Two chromium values were excluded from the analysis due to contamination. In one patient, the preoperative value of 2.43 µg/L was 150% higher than the measurements at the next three time points. In another patient, the postoperative value (7 µg/L) was 300% higher than the preoperative and the six-week measurement.

The median cobalt concentration also continuously increased during the first six months and had an insignificant decrease ($p = 0.581$) at twelve months (0.14, 0.60, 0.95, 1.82, 3.10, and 2.45 µg/L) (Fig. 1). After twelve months, the individual concentrations varied from 0.4 to 14.6 µg/L. The me-

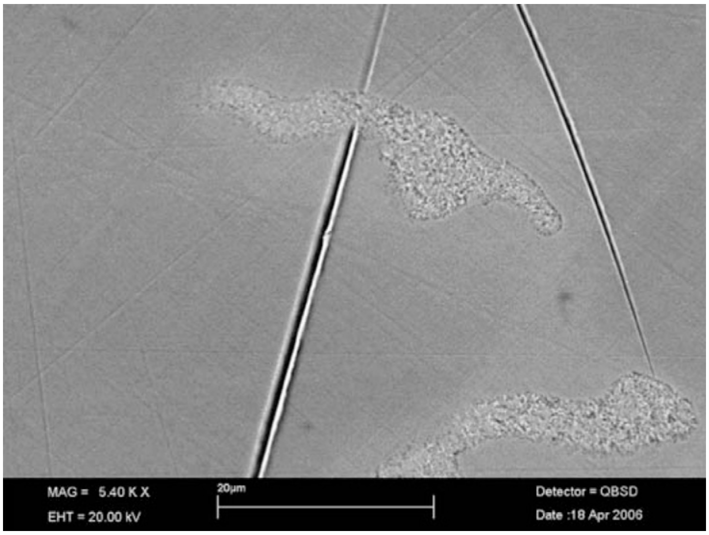

Fig. 4

Scanning electron micrograph of two blocky carbides. Scratches run through, but do not affect, the very hard carbide structure.

dian molybdenum concentration did not change significantly between preoperative and postoperative measurements (0.90, 0.87, 0.90, 0.91, 0.90, and 0.80 µg/L). With the small number studied, statistical evaluation did not reveal a significant correlation of the twelve-month values of chromium or cobalt to age ($p = 0.23$, $p = 0.19$, respectively), body mass index ($p = 0.5$, $p = 0.38$), steps per year ($p = 0.64$, $p = 0.85$), cup inclination ($p = 0.99$, $p = 0.99$), femoral implant size ($p = 0.10$, $p = 0.07$), or any other evaluated factor.

Simulator Wear Measurement

The bearings initially showed a very low wear rate, which was maintained up to approximately 300,000 cycles. The median volumetric wear rate during this period was 0.04 mm^3 per million cycles. A second more intense running-in wear phase followed, which lasted up to approximately 1 million cycles. During this period, the wear rate increased to 1.69 mm^3 per million cycles. At 1 million cycles, a median total wear volume of 1.42 mm^3 was detected. Subsequently, the wear rate decreased and the steady-state wear phase began, with a median wear rate of 0.03 mm^3 per million cycles. At the end of the simulation, the total wear volume had reached 1.47 mm^3. Figure 2 shows the median cumulative wear progression as measured in the simulator. The detected mean element percentage in the samples corresponds to the element ratio in the cobalt-chromium-molybdenum alloy (chromium: 26% to 30%, molybdenum: 4.5% to 7%, cobalt: balance; according to ISO [International Organization for Standardization] 5832-4).

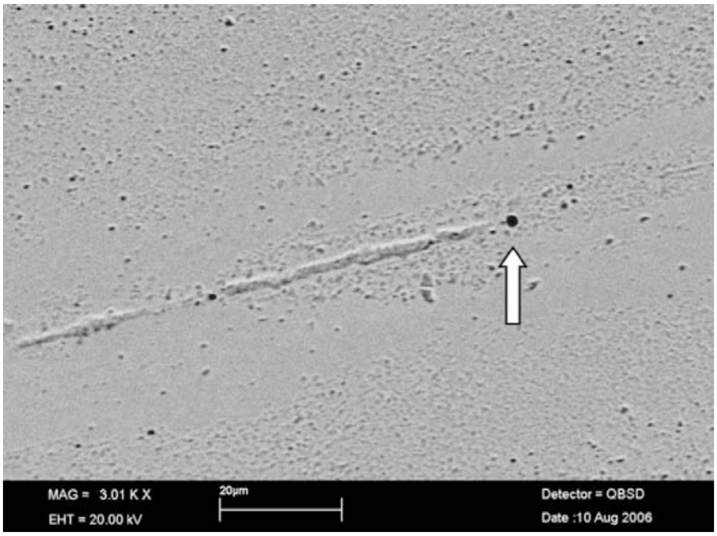

Fig. 5

Scratch originating from an alumina-filled pit (arrow).

Fig. 6

Partially pulled-out carbide with a scratch (arrow) originating from the defect.

Comparison of Clinical Wear Data and Simulator Wear

In Figure 3, patient data and simulator metal ion concentrations are plotted for cobalt and chromium on the basis of the same measurement intervals in cycles (walking or simulator cycles). The patients, on the average, walked 125,300 cycles during the first six weeks, 544,500 cycles after three months, 1.09 million cycles after six months, and 2.18 million cycles after the first year.

For the simulator, the median absolute ion concentration plot indicates that ion release was highest during the running-in wear phase (between 300,000 and 1 million cycles). The highest levels were found to be 5724 µg/L for cobalt and 2579 µg/L for chromium at 544,000 cycles. The ion concentration then continuously decreased to 204 µg/L for cobalt and 78 µg/L for chromium at the end of the simulation after 2.18 million cycles.

In contrast, the patients' median ion concentrations continuously increased over the first six months (1.09 million cycles) to 3.1 µg/L for cobalt and 3.0 µg/L for chromium. Subsequently, the cobalt and chromium concentrations decreased slightly.

Scanning Electron Microscopy

The microstructure of the femoral component showed a network of blocky eutectic carbides within the cobalt-rich matrix of the cast material. These carbides have a very high hardness and cannot be damaged structurally by scratches (Fig. 4). In the acetabular component, the carbide content was lower com-

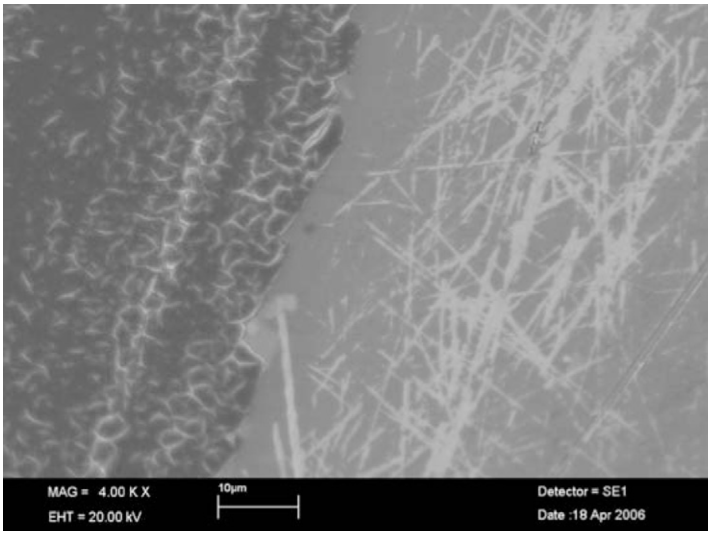

Fig. 7

Carbon-rich protein film on the surface (dark area, left) and scratched metal surface (right).

pared with that of the femoral head and the carbides were not linked in a network. This indicates heat treatment of the material after the casting process, which reduces the size and amount of carbides.

In addition to commonly occurring abrasive wear scars, micrometer-size pits were detected, indicating adhesive wear. Abrasive wear scratches originating from some larger pits were also found (Fig. 5). A high content of aluminum oxide and silicon oxide in these pits suggested the presence of residua from the polishing agent.

At the acetabular component, some of the carbides were fully or partially pulled out of the matrix (Fig. 6). Significant scratches originating from these areas suggest that the pulled-out carbides caused third-body wear. The size of these pits reached up to 80 µm. No pits were observed on the femoral components.

A solid carbon-rich organic film, abraded in some areas (Fig. 7), was present in the contact zone of the acetabular and femoral implant surfaces at the beginning of the simulation. With increasing simulation time, the organic protein film in the contact area wore off.

Discussion

To our knowledge, this is the first study that investigates the same total hip resurfacing implant in an experimental and clinical setting with use of the same method. The high-resolution inductively coupled plasma-mass spectrometry method was adapted to measure wear particles directly in the hip simulator. The possibility of precisely establishing the duration of the different wear phases represents a major advantage of this method in comparison with conventional methods of wear measurement. The method allows direct measurement of wear debris in the simulator without the need to use the less exact gravimetric method and without dismounting the implants from the simulation chamber. The calculated wear rates in the present study are in agreement with data from other simulator studies on similar bearings. However, the running-in wear rates in other studies have tended to be lower and the steady-state wear rates higher[10,22]. For example, according to Morlock et al., the mean in vivo wear rate for correctly implanted resurfacing hip implants is 2.3 mm^3 per year after 1.5 years in situ[23]. The results of our simulator test showed remarkably high agreement with these data.

The phenomenon of delayed running-in wear has not yet been reported. Since the measurement intervals used in most simulator tests are higher than those used in this study (mostly more than 300,000 cycles), such patterns may not have been detected. Carbon-rich organic surface layers were found on the gliding surfaces of the prostheses. This debris consisted of a carbon-rich precipitate from proteins in the test medium. The deposits presumably developed from proteins that denatured as a result of the high temperatures in the contact area of the metal-on-metal bearings[24]. Such precipitations are not restricted to simulator tests and have also been observed on the surface of explanted prostheses[25,26]. A protective protein layer may cause a delayed running-in period. Initially, the deposits may fulfill a protective function, minimizing immediate wear of the joint. The structure of these deposits possibly also promotes surface wettability. In some areas, the solid protein layer is abraded or worn down. As a result of the self-polishing effect of the alloy, the surface roughness of the exposed areas decreases and new deposits can no longer adhere. The protein concentration of the test medium may have an important effect on layer formation and characteristics and deserves further investigation.

Other possible causes for the delayed running-in period are aluminum oxide and silicon oxide-filled pits and scratches originating from these pits. These compounds are used as polishing agents during manufacturing. Residua of these very hard compounds may become incorporated into the surface and could later be released during simulation, thus causing third-body wear. This would explain the abrasive scratches originating from these pits. It is, however, questionable whether these particles are released exactly after 300,000 cycles.

Further explanations for the delayed running-in period are pulled-out carbides, which also lead to third-body wear. We found scratches originating from these carbide pits. Carbide defects were seen mainly at the acetabular component, leading to the hypothesis that heat treatment of the cups may negatively affect carbide stability on the surface. A correlation between increased wear and heat treatment is described in the literature[27], but most reports could not show a significant influence of heat treatment on wear properties[28,29]. It is difficult to characterize wear with use of scanning electron microscopy because these images only provide a selective view of a small area at a given point in time. The delayed running-in period may be a combination of the described mechanisms.

The simulator study showed that the running-in period lasted up to 1 million cycles and was followed by a very-low-wear steady-state phase. During the running-in period, a high wear rate was observed, which decreased after a peak ion release during the first 1 million cycles. A comparison with the patient data showed that a different pattern of metal ion concentrations was seen in vivo. During the running-in period, the patients started off with very low concentrations, which slowly increased over time.

If ions are produced during walking and are cleared through the kidneys, one would expect a very high initial ion concentration with a drop at the end of the running-in period. The pattern observed in this study suggests a different mechanism in vivo. Other studies investigating total hip resurfacing with longer measurement intervals report comparable results. Witzleb et al.[30] measured a steady increase in chromium and cobalt serum levels over three, twelve, and twenty-four months. Although they investigated a different high-carbon component, their results with respect to serum ion concentrations correspond to the results presented in this study. Maezawa et al.[31] also found a steady increase in ion levels between six and twenty-four months with conventional metal-on-metal articulations. Ion levels later seemed to stabilize up to the third year. Brodner et al.[32] looked at cobalt concentrations in patients with conventional 28-mm metal-on-metal articulations and reported a continuous increase during the first year, with the highest increase at the beginning (three to six weeks).

There are, however, also contrary reports in the literature that show a steady decrease in the ion levels after a peak at three months[33]. It is difficult to compare studies due to different sampling protocols (whole blood, serum, plasma) and measurement methods (high-resolution inductively coupled plasma-mass spectrometry or atomic absorption spectrophotometry). Patients are often not comparable, different implants are used, and ion levels may show a high interindividual variation.

Limited data are available about the causation of metal ion concentrations measured in the blood. Patients with metal implants have elevated metal ion levels, with metal-on-metal bearings causing the highest elevations[34,35]. Both the ratio between production, excretion, distribution, and accumulation, and the "total body load" are still unknown. Excretion is certainly influenced by kidney function[36]. In a case report, we have shown that urinary chromium excretion was strongly correlated to urine volume but independent of patient activity or serum ion concentration[37]. Since an activity-related increase in ions could not be shown in a previous study[18], accumulation of particles and slow release of ions from deposited particles might play a key role. In a patient with total hip resurfacing, De Haan et al. did not find elevated ion levels even after completion of a triathlon[38].

The main difference between simulator studies and in vivo measurements is the accumulation and excretion of ions. In the simulator, the metal ions that are measured are ions or particles produced and released by the bearing surfaces. At a specific point in time, the serum is replaced and measurement with the high-resolution inductively coupled plasma-mass spectrometry method resumes at a level of zero. The situation in vivo is different. The metal ion concentration measured in the serum of patients is a function of ion production, distribution and accumulation in the body, and excretion by the kidneys. Therefore, it is impossible to directly compare and correlate in vivo and in vitro measurements.

The measurements presented in this study have to be viewed with different goals in mind. Ion measurements in simulators are used to obtain more accurate and specific wear data. Direct wear measurement is suitable to evaluate extremely low wear rates, which are generally seen in all hard-on-hard bearing combinations. Measurement of in vivo ion concentrations can be used to monitor individual patients. It can help to detect bearing problems or bearing failure and can be used to identify loose components[39]. The necessity of longitudinal measurement of each individual patient, combined with the high costs of analysis, limits widespread use of this technique. Today, it remains a research tool in orthopaedic centers for scientific investigations. ■

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References

1. Heisel C, Silva M, Schmalzried TP. Bearing surface options for total hip replacement in young patients. Instr Course Lect. 2004;53:49-65.

2. Schmalzried TP, Szuszczewicz ES, Akizuki KH, Petersen TD, Amstutz HC. Factors correlating with long term survival of McKee-Farrar total hip prostheses. Clin Orthop Relat Res. 1996;329 Suppl:S48-59.

3. Weber BG. Experience with the Metasul total hip bearing system. Clin Orthop Relat Res. 1996;329 Suppl:S69-77.

4. Dorr LD, Long WT. Metal-on-metal: articulations for the new millennium. Instr Course Lect. 2005;54:177-82.

5. Dumbleton JH, Manley MT. Metal-on-metal total hip replacement: what does the literature say? J Arthroplasty. 2005;20:174-88.

6. Silva M, Heisel C, Schmalzried TP. Metal-on-metal total hip replacement. Clin Orthop Relat Res. 2005;430:53-61.

7. Mont MA, Ragland PS, Marker D. Resurfacing hip arthroplasty: comparison of a minimally invasive versus standard approach. Clin Orthop Relat Res. 2005;441:125-31.

8. Doorn PF, Campbell PA, Worrall J, Benya PD, McKellop HA, Amstutz HC. Metal wear particle characterization from metal on metal total hip replacements: transmission electron microscopy study of periprosthetic tissues and isolated particles. J Biomed Mater Res. 1998;42:103-11.

9. Rieker CB, Schön R, Köttig P. Development and validation of a second-generation metal-on-metal bearing: laboratory studies and analysis of retrievals. J Arthroplasty. 2004;19(8 Suppl 3):5-11.

10. Chan FW, Bobyn JD, Medley JB, Krygier JJ, Yue S, Tanzer M. Engineering issues and wear performance of metal on metal hip implants. Clin Orthop Relat Res. 1996;333:96-107.

11. Firkins PJ, Tipper JL, Saadatzadeh MR, Ingham E, Stone MH, Farrar R, Fisher J. Quantitative analysis of wear and wear debris from metal-on-metal hip prostheses tested in a physiological hip joint simulator. Biomed Mater Eng. 2001;11:143-57.

12. Goldsmith AA, Dowson D, Isaac GH, Lancaster JG. A comparative joint simulator study of the wear of metal-on-metal and alternative material combinations in hip replacements. Proc Inst Mech Eng [H]. 2000;214:39-47.

13. Chan FW, Bobyn JD, Medley JB, Krygier JJ, Tanzer M. Wear and lubrication of metal-on-metal hip implants. Clin Orthop Relat Res. 1999;369:10-24.

14. Clarke IC, Good V, Williams P, Schroeder D, Anissian L, Stark A, Oonishi H, Schuldies J, Gustafson G. Ultra-low wear rates for rigid-on-rigid bearings in total hip replacements. Proc Inst Mech Eng [H]. 2000;214:331-47.

15. Saikko V, Pfaff HG. Low wear and friction in alumina/alumina total hip joints: a hip simulator study. Acta Orthop Scand. 1998;69:443-8.

16. Firkins PJ, Tipper JL, Ingham E, Stone MH, Farrar R, Fisher J. A novel low wearing differential hardness, ceramic-on-metal hip joint prosthesis. J Biomech. 2001;34:1291-8.

17. Charnley J. The long-term results of low-friction arthroplasty of the hip performed as a primary intervention. J Bone Joint Surg Br. 1972;54:61-76.

18. Heisel C, Silva M, Skipor AK, Jacobs JJ, Schmalzried TP. The relationship between activity and ions in patients with metal-on-metal bearing hip prostheses. J Bone Joint Surg Am. 2005;87:781-7.

19. Harris WH. 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 Am. 1969;51:737-55.

20. Devane PA, Horne JG, Martin K, Coldham G, Krause B. Three-dimensional polyethylene wear of a press-fit titanium prosthesis. Factors influencing generation of polyethylene debris. J Arthroplasty. 1997;12:256-66.

21. MacDonald SJ, Brodner W, Jacobs JJ. A consensus paper on metal ions in metal-on-metal hip arthroplasties. J Arthroplasty. 2004;19(8 Suppl 3):12-6.

22. Dowson D, Hardaker C, Flett M, Isaac GH. A hip joint simulator study of the performance of metal-on-metal joints: part II: design. J Arthroplasty. 2004;19(8 Suppl 3):124-30.

23. Morlock M, Bishop N, Delling G, Hahn M, Ruether W. In-vivo wear of metal-on-metal hip resurfacing implants depends strongly on cup alignment. Trans Orthop Res Soc. 2007;32:Poster no. 1663.

24. Lu Z, McKellop H, Liao P, Benya P. Potential thermal artifacts in hip joint wear simulators. J Biomed Mater Res. 1999;48:458-64.

25. Kothari M, Bartel DL, Booker JF. Surface geometry of retrieved McKee-Farrar total hip replacements. Clin Orthop Relat Res. 1996;329 Suppl:S141-7.

26. McKellop H, Park SH, Chiesa R, Doorn P, Lu B, Normand P, Grigoris P, Amstutz H. In vivo wear of three types of metal on metal hip prostheses during two decades of use. Clin Orthop Relat Res. 1996;329 Suppl:S128-40.

27. Wang KK, Wang A, Gustavson LJ. Metal-on-metal wear testing of Co-Cr alloys. In: Disegi JA, Kennedy RL, Pilliar R, editors. Cobalt-base alloys for biomedical applications. West Conshohocken, PA: ASTM; 1999. p 136-44.

28. Dowson D, Hardaker C, Flett M, Isaac GH. A hip joint simulator study of the performance of metal-on-metal joints: part I: the role of materials. J Arthroplasty. 2004;19(8 Suppl 3):118-23.

29. Bowsher JG, Nevelos J, Williams PA, Shelton JC. ‘Severe’ wear challenge to ‘as-cast’ and ‘double heat-treated’ large-diameter metal-on-metal hip bearings. Proc Inst Mech Eng [H]. 2006;220:135-43.

30. Witzleb WC, Ziegler J, Krummenauer F, Neumeister V, Guenther KP. Exposure to chromium, cobalt and molybdenum from metal-on-metal total hip replacement and hip resurfacing arthroplasty. Acta Orthop. 2006;77:697-705.

31. Maezawa K, Nozawa M, Matsuda K, Yasuma M, Mori K, Enomoto F, Ogawa S, Shitoto K, Kurosawa H. Chronological changes of serum chromium levels after modern metal-on-metal total hip arthroplasty. Acta Orthop Scand. 2004;75: 422-26.

32. Brodner W, Bitzan P, Meisinger V, Kaider A, Gottsauner-Wolf F, Kotz R. Elevated serum cobalt with metal-on-metal articulating surfaces. J Bone Joint Surg Br. 1997;79:316-21. Erratum in: J Bone Joint Surg Br. 1997;79:885.

33. Vendittoli PA, Mottard S, Roy AG, Dupont C, Lavigne M. Chromium and cobalt ion release following the Durom high carbon content, forged metal-on-metal surface replacement of the hip. J Bone Joint Surg Br. 2007;89:441-8.

34. Jacobs JJ, Skipor AK, Doorn PF, Campbell P, Schmalzried TP, Black J, Amstutz HC. Cobalt and chromium concentrations in patients with metal on metal total hip replacements. Clin Orthop Relat Res. 1996;329 Suppl:S256-63.

35. MacDonald SJ, McCalden RW, Chess DG, Bourne RB, Rorabeck CH, Cleland D, Leung F. Metal-on-metal versus polyethylene in hip arthroplasty: a randomized clinical trial. Clin Orthop Relat Res. 2003;406:282-96.

36. Brodner W, Grohs JG, Bitzan P, Meisinger V, Kovarik J, Kotz R. [Serum cobalt and serum chromium level in 2 patients with chronic renal failure after total hip prosthesis implantation with metal-metal gliding contact]. Z Orthop Ihre Grenzgeb. 2000;138:425-9. German.

37. Bitsch RG, Zamorano M, Loidolt T, Heisel C, Jacobs JJ, Schmalzried TP. Ion production and excretion in a patient with a metal-on-metal bearing hip prosthesis. A case report. J Bone Joint Surg Am. 2007;89:2758-63.

38. De Haan R, Campbell P, Reid S, Skipor AK, De Smet K. Metal ion levels in a triathlete with a metal-on-metal resurfacing arthroplasty of the hip. J Bone Joint Surg Br. 2007;89:538-41.

39. Jacobs JJ, Skipor AK, Campbell PA, Hallab NJ, Urban RM, Amstutz HC. Can metal levels be used to monitor metal-on-metal hip arthroplasties? J Arthroplasty. 2004;19(8 Suppl 3):59-65.