

THE CLINICAL PERFORMANCE OF METAL-ON-METAL AS AN ARTICULATION SURFACE IN TOTAL HIP REPLACEMENT

William T. Long, M.D.*

ABSTRACT

The metal-on-metal articulations in total hip arthroplasty (THA) were widely used between 1960 and 1975. The McKee-Farrar and other first-generation prostheses failed at a high rate because impingement caused early component loosening. The problem of early component loosening was corrected by improved component design and better manufacturing quality. Second-generation metal-on-metal total hip replacements have experienced short and medium-term success as assessed by Harris Hip Scores and patient self-assessment. The combined annual linear wear of the metal-on-metal femoral head and acetabular insert is less than 10 mm and osteolysis has only rarely been observed in association with well-fixed metal-on-metal total hip replacements. Hypersensitivity is not a common cause of loosening with second-generation hip replacements and remains to be proven as a definitive diagnosis in unusual cases of unexplained pain. More than 40 years of use has demonstrated no increase in the incidence of renal failure or cancer in patients with metal-on-metal total hip replacements. The scientific evidence of the results using the metal-on-metal articulations would recommend its continued use in any patient who does not have compromised renal function.

INTRODUCTION

A high rate of early component loosening with metal-on-metal total hip replacements and the superior clinical results of the Charnley prosthesis during the 1970s discouraged the continued use of the metal-on-metal articulation. August¹ reported a high loosening rate in patients with the McKee-Farrar total hip arthroplasty and concluded that equatorial bearing and high friction moments contributed to failure at the bone-cement in-

terface. Evans et al.² suggested that metal sensitivity caused obliteration of the blood flow to bone and bone necrosis was responsible for aseptic loosening. Walker et al.³ demonstrated that mechanical failure caused loosening when impingement of McKee-Farrar femoral neck against the rim of the acetabular component compromised component fixation. Retrieved total hip replacement components and periprosthetic tissue provided important information to determine what caused the high rate of aseptic loosening observed with the use of first-generation metal-on-metal hips. Equatorial bearing and jamming was suspected but the study of retrieved implants never demonstrated this mechanism of failure. All of the retrieved total hip prostheses had polar bearing and a diametral clearance of 120 mm or greater between the ball and socket.^{4,5} Low wear has been a consistent finding with cobalt-chrome on cobalt-chrome total hip articulations. Anissian et al.⁶ found that the metal-on-metal hip prosthesis generates 100-fold less wear debris than metal-on-polyethylene in hip simulator studies. The combined annual linear wear rate for both first and second generation metal-on-metal articulations is reported to be from 1 to 6 mm according to implant retrieval studies.^{7,8,9,10} Low in vivo wear rates were measured in both the McKee-Farrar and Metasul retrievals and durability of the bearing surface was established by the study of implants retrieved from patients more than 20 years after the index operation.¹¹ The histological response of tissues around metal-on-metal hips is different than the response of periprosthetic tissues to polyethylene wear debris.^{11,12} Macrophages and giant cells that are associated with osteolysis are not prevalent around retrieved metal-on-metal components.

Periprosthetic tissue specimens around revised metal-on-metal hips demonstrated fibrous tissue and little inflammation in some hips and perivascular lymphocytic infiltrates with plasma cells in others. Hypersensitivity reaction has not caused a high rate of component loosening or a high incidence of unexplained pain with the use of second-generation metal-on-metal total hip replacements.^{13,14,15,16} There is growing evidence that the smaller volume of wear debris generated by metal-on-metal bearing couples results in a lower incidence of osteolysis.¹⁷ Bone loss observed in association with well-fixed metal-on-metal hips has been limited to

Correspondence:

*William T. Long, M.D.
The Arthritis Institute
501 E. Hardy Street, 3rd Floor
Los Angeles, CA 90301
Telephone: 310-695-4800
FAX: 310-695-4802
EMAIL: patriciajppaul@yahoo.com

calcar resorption from stress shielding. The radiographic findings with metal-on-metal bearings do not resemble those seen in patients with osteolysis from polyethylene debris.¹³ There is one published case report of osteolysis in a patient with a well-fixed metal-on-metal hip.¹⁸

Zimmer reports that more than 250,000 of the Metasul articulations have been sold worldwide since November 1988 and eight manufacturers currently offer metal-on-metal articulations for hip replacement and surface replacement arthroplasty.^{16,17}

The purpose of this review is to describe causes of component loosening and describe the improvements that corrected the problem, review current *in vivo* wear data, provide evidence that the incidence of overall osteolysis has decreased with the use of metal-on-metal articulations, and show that hypersensitivity is not proven to be a definitive diagnosis in unusual cases of unexplained pain.

We have experience with 582 patients (619 Metasul articulations), and the majority of published data of four years or more are on this articulation couple, so the results of Metasul will be the focus of this review.

LOOSENING

First generation metal-on-metal THAs failed due to acetabular and femoral component loosening at a higher rate than Charnley's prosthesis. Dandy and Theodorou¹⁹ reported the loosening rate in 739 McKee-Farrar THRs with 3.1% for the femoral component and 4.4% for the acetabular component at 2 to 7 year follow-up. In a study of 230 McKee-Farrar prostheses, August¹ reported 50% femoral component loosening, 51% acetabular component loosening, and 67.7% overall loosening at an average follow-up of 13.9 years. Dobbs²⁰ introduced survivorship to the orthopaedic literature with a study of 273 Stanmore THRs. The Stanmore femoral component had a similar design to the McKee-Farrar and a similar poor survival rate of 53% at 11 years. Despite the similar pattern of early failure reported by each of these investigators, the cause of loosening was poorly understood.

In 1974, Peter Walker³ suggested that impingement was a reason for loosening and demonstrated that the neck of the femoral component made repeated contact against rim of the acetabular component. The design flaw was the large diameter femoral neck and unfavorable head/neck ratio of the McKee Farrar, Stanmore, and similarly designed total hip prostheses. Szuszczewicz²¹ observed that metallosis, component loosening, and progressive bilateral pelvic osteolysis was caused by impingement in one patient with failed bilateral McKee-Farrar hips. During the past two decades, designers of total hip prostheses have come to under-

stand that bearing surface damage, component loosening, and hip dislocation are all potential consequences of hip component impingement.

Second generation metal-on-metal THAs were introduced with more favorable head-neck ratios and the incidence of impingement and aseptic loosening has decreased. Second-generation metal-on-metal hips do not have a high failure rate due to aseptic loosening.¹⁷ Recent studies with second-generation metal-on-metal prostheses show a low rate of aseptic loosening that is not higher than the rate reported with metal-on-polyethylene.^{22,23} Improved component design has diminished, but not eliminated impingement as a contributing factor in cases of aseptic loosening.

Inadequate diametric clearance can contribute to loosening by causing equatorial contact, high torque, and jamming. In a hip simulator wear test, Farrar et al.²⁴ demonstrated that a complete seizure was observed after 20,000 cycles for the samples having a negative diametral clearance (-40 and -74 μm). Semlitsch²⁵ reported the analysis of six retrieved Huggler and 11 Muller prosthesis and demonstrated diametral clearance in the range 120-200 μm , with one bearing couple having a diametral clearance of 500 μm . McKellop et al.⁸ retrieved McKee-Farrar hips and reported a diametral clearance of 127-386 μm , with one outlier with an extreme clearance of 1.75 mm. None of these specimens had equatorial contact and the author is not aware of any report of retrievals with inadequate diametral clearance that caused jamming and loosening.

Jones et al.²⁶ believed that cobalt toxicity was responsible for component loosening in a series of loose McKee hip arthroplasties. Willert²⁷ continues to support the possibility of a lymphocyte-dominated immunological response as an uncommon cause of loosening. The experience with second-generation metal-on-metal hip prostheses suggests that if hypersensitivity is a cause of loosening, then its prevalence is low.^{17,27} Both first and second-generation metal-on-metal total hip replacements generate a similar volume of wear debris, but the high loosening rate that was observed with first-generation metal-on-metal hips was not been observed with the use of second-generation hips.^{7,17} The low loosening rates observed with second-generation metal-on-metal hips suggest that it is unlikely that the high rate of loosening with the use of first-generation implants was caused by an allergic reaction to metal debris. Better component design, including a more favorable head-neck ratio, and a decreased incidence of impingement probably contributed most to the improved loosening rates, and components designed with an unfavorable head/neck ratio are no longer used.

WEAR

Cobalt-chrome bearings demonstrate wear well below the annual linear wear of 100 μm per year that is considered to be the threshold for osteolysis.^{16,27,28,29} A combined annual linear wear below 10 μm has been observed in hip simulator wear tests and substantiated by analysis of retrieved first and second-generation hip replacement articulations.^{9,31,33} Wear of this magnitude cannot be measured radiographically, so assessment of wear in vivo has been done on implants obtained during revision hip surgery and on autopsy retrievals. The earliest reports of wear from metal-on-metal retrievals were anecdotal in character and based on small numbers of failed implants. Smith³⁷ described eight patients revised for loosening of Gaenslen cups mated to Austin-Moore femoral prostheses. The retrieved prostheses showed virtually no visible signs of wear and the tissues involved about the metal showed little staining, discoloration, or pathologic changes to indicate wear. Walker et al.³ analyzed wear of 12 retrieved McKee-Farrar prosthesis using low power microscopy, scanning electron microscopy, and surface profilometry. Three types of wear were described: type 1, a surface with initial scratching, type 2, a surface in which the scratches had been smoothed or polished, and type 3, a smoothed surface (after scratching) showing signs of deterioration. The depth of wear estimated by stylus profilometry was estimated to be 1 μm . When modern techniques to analyze wear were applied to retrieved first-generation implants similar low wear measurements were obtained. Jantsch et al.³¹ reported an annual linear wear of 1 μm for three McKee-Farrar hips retrieved 14 years after implantation. Using a coordinate measuring machine Schmalzreid et al.³³ found a combined annual linear wear of 4.2 μm more than 20 years after implantation of five McKee-Farrar hips. The annual linear wear rate was below 5 μm for 11 Mueller, and for six Huggler prostheses that were implanted for an average of 11 years (range 3-20).²⁵ The consistently low in vivo wear rates established by retrieval studies of first-generation metal-on-metal total hip replacements stimulated interest in reintroducing metal-on-metal as wear resistant articulation.

Second-generation metal-on-metal hip prostheses were manufactured using modern techniques in order to promote lubrication and further decrease wear.⁷ The Metasul bearing surface was manufactured as a wrought-forged, high-carbon cobalt-chrome, and the diametral clearance was approximately 100 μm .^{7,17} Wrought-forged cobalt chrome alloys are harder, and have better abrasive and adhesive wear characteristics than cast alloys.⁷ High-carbon cobalt-chrome (0.20-0.25% C) alloys were developed to induce a lower wear rate

than a low-carbon cobalt-chrome (0.05-0.08% C) alloys.⁷ Hip simulator studies have shown that a small clearance decreases the wear of metal-on-metal bearings, but clearance must be sufficient to prevent jamming. Seiber et al.⁹ reported the wear of 118 retrievals with the Metasul articulation couple as 5 μm 3 to 8 years after implantation. Rieker et al.^{7,34} reported the results of 172 Metasul couples with an annual linear wear rate of 6.2 μm . Recent published reports have all shown that the annual linear wear is below 10 μm with the use of second-generation implants. Although laboratory studies indicated that the wear of second-generation metal-on-metal THRs should be lower than that of first-generation devices, retrieval analyses do not indicate superiority in this regard.^{34,35}

OSTEOLYSIS

Metal-on-metal articulations were reintroduced to address the emerging problem of osteolysis. August¹ defined bone erosions adjacent to the components and/or a change position of the McKee-Farrar components as loosening. In that study, bone erosions were not considered to be osteolysis. Using those criteria, 67.7% of the patients had radiographic evidence of loosening and none had osteolysis. In a study by Zahiri et al.¹¹ of 15 hips with McKee-Farrar THAs still in place at 21 to 26 years postoperatively, only 4 of the 15 (25%) had some osteolysis. In that study, 10 periprosthetic tissue specimens were obtained from a group of 15 patients that had revision of a McKee-Farrar hip replacement. Chronic inflammation (lymphocytes, and plasma cells) was minimal to absent in all cases. Multinucleated histiocytes (foreign body-type giant cells) were mostly found along the edges of polymethylmethacrylate globules. These radiographic findings and the histological findings demonstrated that the response of the human body to metal debris from the McKee-Farrar total hip replacements could be distinguished from the response to polyethylene wear debris.

Published reports with the use of second-generation metal-on-metal prostheses indicate that osteolysis is only rarely observed in association with well-fixed components. In our report of 156 patients (161 hips),¹³ only calcar resorption in nine hips (5.5%) (with no other osteolytic lesions) was observed at an average of seven years follow-up. Calcar resorption was a focal radiolucent area seen immediately beneath the collar of the femoral stem, identified by its location between the calcar cortical bone, and the medial stem.³⁵ The radiographs of eight of the hips showed radiolucencies that had a maximum size of 2 x 2 mm. One patient had a lesion that grew to 2 x 2 cm five years after the index hip operation. Nine other recent clinical studies with

radiographic follow-up of second-generation metal-on-metal hip replacements report no osteolysis.^{13,14,15,23,35,40,41} Beaulé¹⁸ reported one case of osteolysis in a patient with a well-fixed, cementless, Zweymuller stem coupled with a Metasul metal-on-metal bearing. In that report, localized osteolysis was identified on the plain radiographs at the tip of the Zweymuller, Ti alloy stem. At the time of revision surgery minimal bearing surface wear was visible and there was no metallic staining of the capsule or acetabular membrane. Specimens of tissue from the hip capsule and the femur in the area of osteolysis showed only small numbers of inflammatory cells, such as macrophages and no lymphocytic infiltrations or granulomas. The authors concluded that this was not a typical case of particulate-induced osteolysis as seen with polyethylene wear debris. Joint fluid pressure within the effective joint space was implicated as the cause of the osteolytic lesion. The predominantly histiocytic inflammation with abundant giant cells that is associated with metal-on-polyethylene debris is a not observed in association metal-on-metal wear debris.

HYPERSENSITIVITY

Evans et al.² were recognized as the first to draw attention to the possibility that metal toxicity occurred after total hip replacement using metal-on-metal bearings. They suggested that in certain patients, the release of metal from a prosthesis may result in tissue sensitization and that this was detected clinically by a skin patch test in which a soluble salt of the metal was used as the test object. They reported that the release of metal from prostheses in metal-sensitive patients caused obliterative changes in blood vessels supplying the bone into which the prosthesis was implanted. According to this theory, metal sensitivity caused bone necrosis and loosening of the McKee-Farrar prostheses. Jones et al.²⁶ reported cobalt toxicity in seven patients that had failure due to aseptic loosening after McKee hip arthroplasty from nine months to four years after the index total hip replacement. Six of these patients were cobalt-positive, but nickel- and chrome-negative on patch testing. In patients with McKee-Farrar or Charnley prostheses, these authors suggested that cases of aseptic loosening were caused by sensitivity of the tissues to one of the metals in the alloy of which the prosthesis is composed.

Several authors have reported on the histological appearance of periprosthetic tissues obtained from the area around early metal-on-metal joint replacements and they did not identify any lymphocytic or plasma-cell infiltration of the periprosthetic tissues.^{11,26,32} Wilert et al.³⁰ analyzed tissues that had been retrieved from fourteen hips in which a contemporary metal-on-metal joint re-

placement had failed after an average of thirty months *in vivo*. The investigators found a perivascular lymphocytic infiltrate, which they suggested was similar to that found in association with a type-IV hypersensitivity reaction. The histopathological changes in the soft tissue were characterized by few wear particles and granulomas compared to tissues obtained from patients with osteolysis from polyethylene debris. Davies et al.¹² also reported an unusual lymphocytic perivascular infiltration in tissues around contemporary metal-on-metal joint replacements. The lymphocytic infiltration was more pronounced in samples obtained at the time of revision for aseptic loosening than in samples retrieved at the time of autopsy or during arthrotomy for reasons other than aseptic failure. The authors did not know the prevalence or clinical implications of the findings, but suggested that they may represent a novel mode of failure for some metal-on-metal joint replacements.

The diagnosis of hypersensitivity was considered as a possible explanation for the high rate of failure of first-generation metal-on-metal total hip replacements. The low incidence of loosening or clinical symptoms reported with the use of second-generation metal-on-metal prostheses suggests that hypersensitivity is not a common problem that leads to failure and that it should only be considered a diagnosis of exclusion in a small number of patients with unexplained pain. In a study by Dorr et al.¹⁶ of 213 hips with a Metasul articulation, two patients (1%) were explored and had exchange of a metal-on-metal bearing surface with a preoperative diagnosis of hypersensitivity. Tissue and serum samples were sent to the laboratory for examination and neither patient had positive serum levels that indicated allergy to the implant. One patient had perivascular lymphocytes in only one of seven tissue samples, and the other patient had lymphocytes in four of five specimens. Neither patient had relief of pain more than one year after exchange of the metal-on-metal bearing surface for a metal-on-ceramic bearing. Pain was completely relieved in one patient two years the index hip operation following an operation for degenerative disease of the lumbar spine. The authors concluded that neither case qualified as a definitive diagnosis of hypersensitivity. There have never yet been reported cases of hypersensitivity that included a symptomatic patient, positive serologic testing for hypersensitivity, and tissue specimens that substantiated the diagnosis of a hypersensitivity reaction.

DISCUSSION

The clinical results of metal-on-metal have been studied for more than 40 years, including second-generation metal-on-metal results that are approaching 20 years

in Europe and 10 years in the United States. We here review the status of metal-on-metal total hip articulations based primarily on the clinical performance reported in human subjects. It is now generally accepted that the early loss of fixation observed with first-generation metal-on-metal hips was due primarily to poor component design, and this problem was corrected by improved second-generation implants designs. The combined annual linear wear rate for metal-on-metal hip replacements in vivo is well established and it has been consistently reported to be below 10 μm . Osteolysis has been a rare radiographic finding during the first 10 years of reports with the use of second-generation metal-on-metal hips. Tissue specimens demonstrate that the histological response that defines polyethylene induced osteolysis is not found in association with well-fixed metal-on-metal total hip replacements. Hypersensitivity is currently a diagnosis based on pathological findings of lymphocytes adjacent to blood vessels in capsules of retrievals and it is not a common cause of hip pain or component loosening.

For more than three decades, the problem of aseptic component loosening was poorly understood and several theories were proposed. The Charnley prosthesis was referred to as a low friction arthroplasty and the relatively higher friction of metal-on-metal articulations demonstrated by the pendulum that lead some investigators to suspect that high friction was the cause of early loosening.⁷ Retrieval studies that examined both first and second-generation metal-on-metal hips did not identify increased friction as a cause of failure. All metal-on-metal specimens retrieved during the past 40 years have demonstrated polar bearing.⁷ Polar bearing and increased diametral clearance have been shown in simulator studies and by retrievals to cause higher bearing surface wear rates, however, none of the retrieved couples that had a wide diametral clearance failed as a direct result of excessive wear. The optimal diametral clearance for total hip replacement articulations is reported to be between 50 and 100 μm .⁷ Retrieved specimens with diametral clearances greater than 100 μm demonstrated more wear than couples with smaller clearance, however, combined annual linear wear was still below 10 μm . It is now generally accepted that the high rate of early loosening observed with first-generation total hip replacements was not due to clamping or jamming of the articulation couple. The problem of early metal-on-metal component loosening was corrected when implants were redesigned.

The low wear of metal-on-metal articulations was established both in vitro and in vivo. There are no reports of catastrophic failure or wear-through. Based on the published annual linear wear rates established for metal-on-metal, a well-fixed hip replacement could func-

tion in an active patient for more than thirty years without wearing out. Attention has turned away from the problems of early failure due to loosening or late failure due to wear. The focus today is on evaluating potential problems that might occur as the result of metal-on-metal wear debris and metal ions. It is well established that small cobalt and chromium particles and ions are generated by the metal-on-metal bearing surface, widely distributed throughout the body through the bloodstream and the lymphatics, and excreted in the urine. Serum, blood, and urine samples consistently demonstrate elevated levels of chromium and cobalt compared to the levels measured in patients with metal-on-polyethylene implants. The clinical significance of these elevated ion levels is unknown. Long-term follow-up of patients with first generation metal-on-metal total hip replacements, and short-term follow-up of patients with second-generation metal-on-metal implants have not demonstrated any unique complications. In spite of the concerns of some authors that complications such as cancer or hypersensitivity would occur, currently none have been reported clinically. It is likely that large, long-term, multi-center studies will be necessary to identify any increased risk of local or systemic disease caused by the use of metal-on-metal bearing surfaces for total hip replacement.

There is no radiographic evidence the wear debris being produced at the metal-on-metal interface leads to the occurrence of osteolysis. In the author's study of 161 total hip arthroplasties (154 patients), the only bone erosion that was measured was calcar resorption.¹³ It was not possible to determine whether this calcar resorption was from stress shielding or particulate debris. Other authors have not classified calcar resorption as osteolysis.⁴² Small focal radiolucent areas that were seen under the collar of 9 out of 161 hips were not considered in the definition of osteolysis. Maloney et al.⁴³ defined relatively small punched-out areas of bone loss under the collar as typical zone 7 osteolytic lesions. Goetz's description of osteolysis included only those lesions that caused scalloping of the endosteal cortex. These findings are in agreement with other authors who have reported cementless metal-on-metal hip arthroplasty without any osteolysis at five and six year follow-up. Longer follow-up is necessary to determine if the low incidence of osteolysis will continue beyond the first decade. The Metasul articulation has been implanted in patients in Europe since 1988. The author is not aware of any reports of the incidence osteolysis.

Hypersensitivity has been suggested as a possible unique complication and cause of failure for metal-on-metal hip arthroplasties. Hypersensitivity is a diagnosis described by Willert, based on the occurrence of lymphocytes adjacent to blood vessels in capsules of

retrievals from failed metal-on-metal hip arthroplasties.^{27,30} Hallab et al.⁴⁴ described a triple assay technique for the evaluation of metal induced, delayed type hypersensitivity responses in patients with total joint arthroplasty. The most conclusive result using this assay would be a strongly positive response to all three aspects of the triple assay technique to both cobalt and chromium ions. To our knowledge, there have been no reports of unexplained pain associated with radiographic evidence of implant loosening, supported by a positive response to the triple assay technique. Reports with the use of second-generation metal-on-metal prostheses indicate that unexplained pain occurs only rarely and loose prostheses are uncommon and therefore the diagnosis of hypersensitivity as a clinical problem remains elusive.

The potential for permanent biological fixation with noncemented components, combined with a bearing surface that does not fail due to wear or osteolysis, makes it conceivable that total hip replacements implants could survive in active patients for more than 30 years. If the clinical results are as good as metal-on-polyethylene articulations, the mechanical complications are no greater, and there is no observed increased incidence of adverse biological reactions, then continued use of metal-on-metal articulation couples is justified.

REFERENCES

1. **August AC, Aldam CH, and Pynsent PB:** The McKee-Farrar hip arthroplasty. A Long term study. *J Bone Joint Surg* 68-B(4) 520-527, 1986.
2. **Evans EM, Swannsea, Wales, Freeman MAR, Miller AJ, Vernon-Roberts B:** Metal sensitivity as a cause of bone necrosis and loosening of the prosthesis in total joint replacement. *J Bone Joint Surg* 56B(4): 626-642, 1974.
3. **Walker PS, Salvati E, Hotzler RK:** The wear on removed McKee-Farrar total hip prostheses. *J Bone Joint Surg* 56A(1):92-100, 1974.
4. **Doerig MF, Odstrcilik E, Jovanovic M, et al:** Uncemented Alloclassic-Metasul total hip arthroplasty: early results after 2-6 years. In Rieker C, Wyndler M, Wyss U, editors. *Metasul: a metal-on-metal bearing*. Bern (Switzerland): Hans Huber:157, 1999.
5. **Doerig MF, Kratter R, Ritzler T, et al:** Ceramic-on-polyethylene versus metal-on-metal: a clinical and radiological followup study, five to ten years after implantation. In Rieker C, Oberholzer S, Wyss U, editors. *Word tribology forum in arthroplasty*. Bern (Switzerland): Hans Huber:197, 2001.
6. **Anissian HL, Stark A, Gustafson A, Good V, Clarke IC:** Metal-on-metal bearing in hip prosthesis generates 100-fold less wear debris than metal-on-polyethylene. *Acta Orthop Scand* 70(6):578-582, 1999.
7. **Rieker CB, Schon, R, Kottig, P:** Development and Validation of a second-generation metal-on-metal bearing. Laboratory studies and analysis of retrievals. *J Arthroplasty* Vol 19(Suppl 3): 5-11, 2004.
8. **McKellop H, Park SH, Chiesa R, et al:** In vivo wear of 3 types of metal on metal hip prostheses during 2 decades of use. *Clin Orthop* 329(Suppl):S128, 1996.
9. **Siber HP, Rieker CB, Kottig P:** Analysis of 118 second-generation metal-on-metal retrieved hip implants. *J Bone Joint Surg A*:810B(1): 46-50, 1999.
10. **Rieker CB, Koettig, P, Schoen R, et al:** Clinical wear performance of metal-on-metal hip arthroplasties. In Jacobs JJ, Craig TL, editors. *Alternative bearing surfaces in total joint replacement*. West Conshohocken (Pa): ASTM Spec. Tech. Publ 1346, 144, 1998.
11. **Zahiri CA, Schmalzreid TP, Embramzadeh E, et al:** Lessons learned from loosening of the McKee-Farrar metal-on-metal total hip replacement. *J Arthroplasty* 14:326, 1999.
12. **Davies AP, Willert HG, Campbell PA, Learmonth ID, Case CP:** An unusual lymphocytic perivascular infiltration in tissues around contemporary metal-on-metal joint replacements. *J Bone Joint Surg* 87A(1):18-27, 2005.
13. **Long, WT, Dorr, LD, Gendelman, V:** An American experience with metal-on-metal total hip arthroplasties. A 7 year followup study. *J Arthroplasty*. Vol 19(8), Suppl 3: 29-34, 2004.
14. **Migaud H, Jobin, A, Chantelot C, Giraud F, et al:** Cementless metal on metal hip arthroplasty in patients less than 50 years of age. Comparison with a matched control group using ceramic-on-polyethylene after a minimum 5 year followup. *J Arthroplasty* Vol 19(8), Suppl 3: 23-28, 2004.
15. **Delaunay CP:** Metal-on-metal bearings in cementless primary total hip arthroplasty. *J Arthroplasty*. Vol 19(8), Suppl 3: 35-40, 2004.
16. **Dorr LD, Long WT, Sirianni L, Campana M, Wan, Z:** The argument for the use of Metasul as an articulation surface in total hip replacement. *Clin Orthop* 429:80-85, 2004
17. **Dumbleton JH, Manley MT:** Metal-on-metal total hip replacement. What does the literature say? *J Arthroplasty*. Vol 20(2): 174-188, 2005.
18. **Beaule' PE, Campbell P, Mirra J, Hooper JC, Schmalzried TP:** Osteolysis in a cementless second generation metal-on-metal hip replacement. *Clin Orthop* 386:159-165, 2001.
19. **Dandy DJ, Theodorou BC:** The management of local complications of total hip replacement by the McKee-Farrar technique. *J Bone Joint Surg* 57B(1):30-35, 1975.

20. **Dobbs HS:** Survivorship of total hip replacements. *J Bone Joint Surg* 62-B(2): 168-173, 1980.
21. **Szuszczewicz ES, Schmalzreid TP, Petersen TD:** Progressive bilateral pelvic osteolysis in a patient with McKee-Farrar metal-metal total hip prostheses. *J Arthroplasty*, Vol 12:819, 1997.
22. **Dorr LD, Wan Z, Longjohn DB et al:** Total hip arthroplasty with the use of the Metasul metal-on-metal articulation. *J Bone Joint Surg Am* 82A:789, 2000.
23. **Dorr LD, Wan Z, Heaton K:** Modular Metasul articulation with non-cemented cups: a 2-5 year followup. In Rieker C, Oberholzer S, Wyss U, editors. *World tribology forum in arthroplasty*. Bern (Switzerland): Hans Huber, 227, 2001.
24. **Farrar R, Schmidt MB:** The effect of diametral clearance on wear between head and cup for metal on metal articulations. Presented at the 43rd Annual Meeting, Orthopedic Research Society, San Francisco, CA 1997.
25. **Semlitsch M, Streicher RM, Weber H:** Verschleissverhalten von Pfannen und Kugeln aus CoCrMo-Gusslegierung bei langzeitig implantierten Ganzmetall-Huflprothesen. *Orthopade* 18:377, 1989.
26. **Jones DA, Lucas, HK, O'Driscoll, M, Price CHG, Wibberley, B:** Cobalt toxicity after McKee hip arthroplasty. *J Bone Joint Surg* 57B(3):289-296, 1975.
27. **Willert HG, Buchhorn GH, Fayyazi A, Flury R et al:** Metal-on-metal bearings and hypersensitivity in patients with artificial hip joints. A clinical and histomorphological study. *J Bone Joint Surg* 87A(1): 28-36, 2005.
28. **Dowd JE, Sychterz CJ, Young AM, Engh CA:** Characterization of long-term femoral head penetration rates. Association with and prediction of osteolysis. *J Bone Joint Surg* 82A:1102-1107, 2000.
29. **Wan Z, Dorr LD:** Natural history of femoral focal osteolysis with proximal ingrowth smooth stem implant. *J Arthroplasty* 11:718-725, 1996.
30. **Willert HG, Buchhorn GH, Fayyazi A, Lohmann CH:** Histopathological Changes in Tissues Surrounding Metal/Metal Joints—signs of delayed type hypersensitivity? (DTH). *Word Tribology Forum in Arthroplasty*. Bern, Switzerland: Hans Huber: 147-166, 2001.
31. **Jantsch S, Schwager IW, Zenz P, Semlitsch M, Fertschak W:** Long-term results after implantation of McKee-Farrar total hip prostheses. *Arch Orthop Trauma Surg*, 110:230-237, 1991.
32. **Smith RD:** Total hip placement: Metal against metal. *Clin Orthop* 95:43-47, 1973.
33. **Schmalzried TP, Peters PC, Maurer BT, Bragdon CR, Harris WH:** Long duration metal-on-metal total hip arthroplasties with low wear of the articulating surfaces. *J. Arthroplasty* 11:322-331, 1996.
34. **Rieker CB, Kottig P:** In vivo tribological performance of 231 metal-on-metal hip articulations. *Hip International* 12:73, 2002.
35. **Rieker CB, Koettig P, Schoen R, et al:** Clinical tribological performance of 144 metal-on-metal hip articulations. In Rieker C, Wyndler M, Wyss U, editors. *Metasul: a metal-on-metal bearing*. Bern (Switzerland): Hans Huber: 83, 1999.
36. **Korovessis P, Petsinis G, Repanti M, et al:** Short-term results with the Zweymuller-SL metal-on-metal total hip arthroplasty. *Eur J Orthop Surg Traumatol* 12:81, 2002.
37. **Wagner H, Wagner M:** German clinical results with Metasul bearings. In Rieker C, Wyndler M, Wyss U, editors. *Metasul: a metal-on-metal bearing*. Bern (Switzerland): Hans Huber: 181, 1999.
38. **Delaunay C:** Metasul bearings in primary total hip arthroplasty: French experience and preliminary results. In Rieker C, Wyndler M, Wyss U, editors. *Metasul: a metal-on-metal bearing*. Bern (Switzerland) Hans Huber: 181, 1999.
39. **Delaunay C:** Metasul bearing survey in primary total hip arthroplasty consecutive series of 100 cementless Alloclassic-Metasul hips. In Rieker C, Oberholzer S, Wyss U, editors. *Word tribology forum in arthroplasty*. Bern (Switzerland): Hans Huber, 189, 2001.
40. **Lombardi AV, Mallory TH, Alexiades MM, et al:** Short-term results of the M² a-Taper metal-on-metal articulation. *J Arthroplasty*. 16, 2001.
41. **Korovessis, P, Petsinis G, Repanti M:** Zweymueller with metal-on-metal articulation: clinical, radiological and histological analysis of short-term results. *Arch Orthop Trauma Surg* 123:5-11, 2003.
42. **Goetz DD, Smith EJ, Harris WH:** The prevalence of femoral osteolysis associated with components inserted with or without cement in total hip replacements. *J Bone Joint Surg* 76A(8):1121-1129, 1994.
43. **Maloney WJ, Woolson ST:** Increasing incidence of femoral osteolysis in association with uncemented Harris-Galante Total Hip Arthroplasty. *J Arthroplasty* 11(2):130-134, 1996.
44. **Hallab NJ, Mikecz K, Jacobs JJ:** A triple assay technique for the evaluation of metal induced, delayed type hypersensitivity responses in patients with or receiving total joint arthroplasty. *J Biomed Mater Res* 53(5): 480-9, 2000.