LOW IN VITRO THIRD-BODY WEAR ON TOTAL HIP PROSTHESSES INDUCED BY CALCIUM SULPHATE USED FOR LOCAL ANTIBIOTIC THERAPY

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Abstract

In case of implant associated infection, implant preservation is associated with high failure rates. Therefore, a removal or exchange of the implant is most often mandatory for treatment success. Alternatively, under certain conditions, local antibiotic delivery can be applied – preserving the implant, using for example calcium sulphate as a resorbable carrier. In this work, third-body wear on total hip prostheses caused by calcium sulphate particles was tested in a hip simulator. Inlays made of ultra-high-molecular-weight polyethylene (UHMWPE) and cross-linked polyethylene (XLPE) against 28 mm CoCrMo heads and 36 mm alumina pairings were tested in triplicate, both with and without calcium sulphate particles in the test liquid.

Neither the alumina articulations nor the CoCrMo heads were affected by the calcium sulphate particles since calcium sulphate is a relatively soft material. The polyethylene inlays showed 39-89% higher wear during exposure compared to references, but wear returned to normal when no more particles were added. Thus, calcium sulphate might be used as antibiotic carrier even in the presence of total hip prostheses without fearing excessive third-body wear.

Keywords: Third-body wear, total hip prosthesis, calcium sulphate, gypsum, plaster of Paris, antibiotic carrier, ultra-high-molecular-weight polyethylene, cross-linked polyethylene, vitamin E.

Introduction

Medical implants are increasingly used in various domains. While standard surgical techniques and prophylactic antibiotics allow keeping overall infection rates relatively low, implants remain very susceptible to bacterial colonisation (Elek and Conen, 1957; Zimmerli et al., 1982; Darouiche, 2001). Contamination with a very low number of bacteria, some hundred colony forming units, is enough to develop infection (Elek and Conen, 1957; Zimmerli et al., 1982; Darouiche, 2001). Most often, infection cannot be eradicated without removal of the implant, because of biofilm formation at the device’s surface and other particularities of implant-related infections, such as poor local antibiotic penetration and leucocyte function impairment (Zimmerli et al., 1982, 1984; Widmer et al., 1990; Darouiche, 2004; Zimmerli et al., 2004; Osmon et al., 2013). Considering reoperation, functional losses and risks, this leads to high costs, not only for the patient’s health, but also for the entire health system (Wolf et al., 2011; Kurtz et al., 2012; Vanhegan et al., 2012).

Removal might be particularly problematic for permanent implants such as joint replacements. Under certain circumstances, the infection might reasonably be treated while preserving the implant (Zimmerli et al., 2004; Marculescu et al., 2006; Koyonos et al., 2011; Lora-Tamayo et al., 2013; Osmon et al., 2013). The criteria leading to the recommendations for removal or attempt of implant preservation are listed and discussed elsewhere (Zimmerli et al., 2004; Osmon et al., 2013). However, success rates are only around 50-60% in large series, failures requiring later removal, exchange, fusions or amputations (Zimmerli et al., 2004; Marculescu et al., 2006; Koyonos et al., 2011; Lora-Tamayo et al., 2013; Osmon et al., 2013).

In order to improve antibiotic treatment efficacy, local application has become common practice in orthopaedic surgery (Buchholz and Engelbrecht, 1970; Iarikov et al., 2012; Kluin et al., 2013). There is a large variety of antibiotic carrier materials ranging from non-biodegradable bone cement, which is made of polymethyl methacrylate (PMMA), to biodegradable materials such as hydroxyapatite, calcium phosphate and calcium sulphate, collagen, fibrin, or polymers such as polyactides, polyglycose or polyurethanes (Kanellakopoulou and Giamarellos-Bourboulis, 2000; Kelly et al., 2001, Kluin et al., 2013). Gross functional impairment of a joint might be avoided using soft and biodegradable carrier materials.

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The clinical problem of infection treatment using calcium sulphate pellets is illustrated by a case in the appendix. Calcium sulphate had been chosen as drug carrier material because it is a resorbable material benefiting from a long lasting and broad medical experience, that appears to be very suitable for local delivery of antibiotics (Kelly et al., 2001; Rauschmann et al., 2005; Bibbo and Patel, 2006; Wahl et al., 2011a). The fact that it is resorbable renders it ideal for the delivery of antibiotics: together with drug release, the surface of the calcium sulphate pellets is dissolved, making biofilm formation impossible contrary to what is observed on antibiotic loaded PMMA (Neut et al., 2001; Van De Belt et al., 2001; Anagnostakos et al., 2008). Antibiotics are released over a time period of more than 10 days (Wichellhaus et al., 2001; Rauschmann et al., 2005; Wahl et al., 2011b; Wang et al., 2011) up to 4 or even 6 weeks, depending on the antibiotic used (Rönn et al., 2014). This corresponds approximately to the duration of antibiotic treatment usually recommended for bone and joint infections (Lew and Waldvogel, 2004; Zimmerli et al., 2004; Osmon et al., 2013). Heat production at rehydration of calcium sulphate hemihydrate is much lower than during PMMA polymerisation, which is beneficial as most antibiotics have low heat resistance (Doadrio et al., 2004). Another advantage of calcium sulphate is that this material is relatively soft. With a Mohs hardness of 2, it can be scratched with a finger nail.

However, third body wear of the prostheses caused by particles freed during dissolution remains an issue. For example, particles originating from the bone cement do induce excessive wear (Hauptmann et al., 2008). Worst case scenarios are well illustrated in clinical reports of failures due to ceramic particles from fractured components (Kohn and Pape, 2007; Pazzaglia et al., 2011), hydroxyapatite particles originating from the coating of the cup or the stem (Morscher et al., 1998; Rokkum et al., 2002) or metal particles (Scott et al., 2000), found embedded in polymer liners. In vitro third-body wear tests showed that both the polymer liners (Oral et al., 2006; Kubo et al., 2009) and the metallic heads are scratched by PMMA particles (Bragdon et al., 2003, 2005). Tests performed with large particles (Ø 160-500 µm, Wang and Essner, 2001; Affatato et al., 2002; Wang et al., 2002; Wang and Schmidig, 2003) lead to higher wear of the polymer components than smaller particles of about Ø 30 µm (Bragdon et al., 2003, 2005). PMMA patches were found on the head leading to abrasion of the polymeric counterpart (Kubo et al., 2009; Sorimachi et al., 2009). Ceramic heads are not affected by PMMA third-bodies (Wang and Essner, 2001; Wang et al., 2002; Grupp et al., 2014). Hip simulator tests performed with ceramic particles lead not only to higher polymer wear (Bragdon et al., 2003; Oberbach et al., 2009b; Hintner et al., 2012) but also to more scratches on metallic heads (Bragdon et al., 2003; Hintner et al., 2012) or to scratches and grain breakouts on ceramic heads (Oberbach et al., 2005, 2009a, 2009b; Hintner et al., 2012). Ceramic-on-ceramic articulations are not affected by small ceramic particles (Oberbach et al., 2009b). This study aimed at quantifying wear induced in vitro by calcium sulphate particles on total hip prostheses.

### Materials and Methods

#### Hip simulator tests

In vitro hip simulator tests were conducted according to ISO 14242-1:2012 and ISO 14242-2:2000. Inlays made of ultra-high-molecular-weight polyethylene (UHMWPE) (sterilised with 30 ± 5 kGy γ-irradiation, # 55.43.2805) and cross-linked polyethylene containing vitamin E (XLPE, cross-linked with 100 ± 5 kGy γ-irradiation, trade name Vitamys®, # 52.34.0134) were in articulation against Ø 28 mm CoCrMo heads (± 2.30.011). Additionally, alumina pairings (Ø 36 mm, Bionit®2, inlays 36 GG, heads 36 M 12/14) were investigated. The tests were performed with at least three pairings each. All prosthesis components were of the seleXys® line and were provided by Mathys, Bettlach, Switzerland.

Prior to the test, the polymer inlays were pre-soaked in the test liquid in order to reduce the amount of soaking during the simulator test. The tests were conducted on a servo hydraulic hip- and spine simulator (Endolab, Thansau/Rosenheim, Germany, type C6/2-07). It offers six wear stations and two soaking stations. The inlays were fixed in titanium cups (selExys® uncemented press-fit cups, for polymer inlays: unicup UC 56) positioned with 30° inclination and the load was introduced through the cup onto the inlay and the head. Considering 10° inclination of the femoral component, total inclination was 40°. The soaking samples (only for polymer inlays) were positioned upside down (inlay beyond the head). The same load profile was applied onto the soaking samples, but without motion.

The test chambers were covered with polymer bellows. Each test chamber was equipped with a heater and a temperature sensor, controlling that the test liquid remained at 37 ± 1 °C. A fill-level sensor controlled that the articulation partners could not run dry. The test liquid was produced by dilution with deionised water of new-born calf serum from New Zealand (Thermo Fisher Scientific, Waltham, MA, USA, lot 8097790) to a protein concentration of 30 g/L, according to the ISO 14242-1:2012 standard. Sodium azide and ethylenediaminetetraacetic acid disodium salt dihydrate (both p.a., Sigma-Aldrich Chemie, Steinheim, Germany, sodium azide: # 71290, ethylenediaminetetraacetic acid disodium salt dihydrate: # 34549) were added at 2 g/L and 3 g/L respectively, to inhibit bacterial growth and to bind metallic ions. To remove bacteria and other possible contaminants from the test liquid, it was filtered through 0.2 µm filters (Nalgene® from Thermo Fisher Scientific, # 567-0020). The test liquid was either freshly prepared prior to the test or stored at -20 °C and thawed before its use. For the tests performed in the presence of calcium sulphate particles, 10 g/L calcium sulphate hemihydrate (Fig. 1, Ø 6.5-100 µm, trivial name: plaster of Paris, VWR, Radnor, PA, USA, # 22441.296) was added to the standard test liquid immediately before the start-up of the experiment. This concentration was chosen to clearly exceed the solubility of 2 g/L in water (Lide, 2004). In contact with water, calcium sulphate hemihydrate immediately forms the more stable calcium sulphate dihydrate, i.e. gypsum. If not specified otherwise,
the term “calcium sulphate” refers in this work to the calcium sulphate dihydrate.

For the hip simulation, the load-motion cycle according to ISO 14242-1 lasted one second and was repeated continually, simulating the conditions while walking. The load and motions were measured and adjusted digitally. Every 500,000 cycles, the testing chambers were taken apart, cleaned and the inlays were weighed according to ISO 14242-2. Before weighing, the samples were cleaned in an ultrasonic bath first immersed in deionised water, then in water with cleaning detergent (Borer Chemie, Zuchwil, Switzerland, deconex 12 PA) followed by two washes with deionised water. After 5 min immersion in isopropanol (99%, Thommen-Furler, Rüti b. Bühren, Switzerland, #172-VL50TN) they were dried in vacuum (pressure < 10 Pa). The weighing was performed on a balance with an accuracy of 0.01 mg (Mettler Toledo Intl., Columbus, OH, USA, AX205). Each sample was weighed twice and the measurement was repeated if the difference between the two values was larger than 0.1 mg. After weighing, the test chambers were cleaned, reassembled, filled with fresh test liquid and switched to another measuring station of the simulator. The test was finished after 5 million cycles (MC). Polymer inlays tested with calcium sulphate were then subject to 1 million additional cycles without calcium sulphate particles. The wear rate of each sample was determined with linear fits of the weights (without taking the starting point into account) according to ISO 14242-2. It was corrected for the mass gain of the soaking sample.

**Powder examination**

Images of the calcium sulphate hemihydrate particles were taken using scanning electron microscopy (SEM; Carl Zeiss, Jena, Germany, EVO MA25). The size distribution was analysed with a laser diffractometer (Beckman Coulter, Krefeld, Germany, LS 13320, measured with dry powder system).

**Sample examination**

The dimension of the ceramic heads and inlays was measured with a coordinate measuring machine (Hexagon, Stockholm, Sweden, Etalon-Derby, measured at Mathys, Mörsdorf, Germany). The articulating surfaces of the heads and inlays were examined qualitatively with a binocular microscope (Leica Microsystems, Wetzlar, Germany, M205A) equipped with multifocus to increase the depth of field. Selected samples were additionally investigated using SEM equipped with energy-dispersive X-ray spectroscopy (EDX; Oxford Instruments, Abingdon, UK, INCA Energy 350 with x-Max 50 Silicon Drift Detector). The roughness and the topography of the metallic heads and of several polymer inlays were investigated using confocal microscopy (NanoFocus, Oberhausen, Germany, µSurf, data processing with µSoft analysis XT, V6.2.6122). The roughness of the ceramic surfaces was determined with contact profilometry (Jenoptik, Jena, Germany, hommel etamic T8000, tip TK50, measured at Mathys, Mörsdorf, Germany). The roughness parameters were determined according to ISO 4287, 4288 and 13565-2. Selected polymer inlays were investigated using a Fourier transform infrared microscope (FT-IR; Bruker, Billerica, MA, USA, LUMOS).

**Statistical analysis**

Results are represented as average ± standard deviation. Statistical testing was carried out using an independent two-sided Student’s t-test with unequal variances.

**Results**

**Wear**

In the presence of calcium sulphate particles in the test liquid, the wear rate of the UHMWPE inlays was slightly higher in the first half of the experiment with $41 \pm 4$ mg/MC than during the second half, were it reduced to $31 \pm 5$ mg/MC (Fig. 2a, $p = 0.05$). Mean overall wear rate was $36 \pm 5$ mg/MC (Fig. 3). The wear rate of the XLPE inlays remained constant with $9 \pm 2$ mg/MC over the whole 5 MC. The amount of the soaking was with $0.7$ mg/MC and $0.2$ mg/MC relatively small for both the UHMWPE and the XLPE respectively. Wear was 39-89% higher in the presence of calcium sulphate particles compared to
the references tested without particles in the test liquid (Fig. 3). The wear rates decreased when no more particles were added. For the UHWMPE it was in the range of the reference samples, while for the XLPE inlays it remained slightly higher than the references.

The measured weight of the ceramic inlays did highly scatter (Fig. 2b). Most likely this was because of protein remnants on the sample surface persisting despite the cleaning procedure. Additionally, there were metallic traces on the inlay’s backside from the cup. Unfortunately, one inlay was damaged on the rim during the cleaning/weighing procedure. Therefore, the results of one inlay could only be used until 2.5 MC. The wear rates were $0.19 \pm 0.05$ mg/MC with calcium sulphate particles and $0.22 \pm 0.04$ mg/MC without. The weight of the ceramic heads increased continually, which went together with the observation of corrosion products from the metallic cone deposited on the inner cone of the heads. Thus, no reliable wear rate could be determined for the heads. No significant difference was obtained for the measured dimensions of the inlays and heads determined before and after the simulator test.

**Examination of the articulating surfaces**

The metallic heads and the polymer inlays exhibited few scratches (Fig. 4), but there was no obvious difference between the articulations tested with and without calcium sulphate particles. In agreement, the mean arithmetic roughness $R_a$ determined on the CoCrMo heads after the test revealed values between 1 and 3 nm for both with and without calcium sulphate particles in the test liquid.
Fig. 4. Images of the CoCrMo heads (a-d) and the polymer inlays (e-h) after the hip simulator test with calcium sulphate particles in the test liquid (a, b, e-h: microscopy; c and d: SEM-images).
Before the test, the heads were slightly rougher with $R_a$ of 2-5 nm. The roughness parameter “reduced peak height” $R_{pk}$ was reduced during the test, indicating that some of the peaks were removed by abrasion. Additionally, zones with pitting-like irregularities were observed on the anterior-superior wall of the inlays. Topography measurements using confocal microscopy showed that these irregularities were actually elevations with a height of 5 to 15 µm on the UHMWPE inlays (Fig. 5a-c). More elevations with a height of only about 2 µm were present on the XLPE inlays. SEM showed that these elevations were composed of small wear particles, pressed together under the high contact pressure (Fig. 5d). The FT-IR spectra of both the elevations and the worn surface showed the typical spectrum of polyethylene, but with an additional absorption at 1050 and 1110 cm$^{-1}$, which can be attributed to the C-O binding from oxidised polyethylene. This signal was absent in the spectrum of the bulk material. This transferred material was observed independent on the test liquid containing calcium sulphate particles or not. On the metallic heads, few agglomerations of particles were found (Fig. 5e). EDX-Spectra confirmed that these were made of carbon.

The surface of the ceramic heads and inlays was highly polished both before and after the hip simulator test. There were only tiny scratches observed (Fig. 6) together with few pores and some residual proteins. The arithmetic roughness $R_a$ of the ceramic inlays was 8 ± 1 nm before and 7 ± 3 nm after the tests. The heads were even smoother with 4 ± 1 nm both before and after the test. There was no significant difference in the roughness between the samples before and after the test or between the articulations tested with or without calcium sulphate particles ($p = 0.16$ or higher).

**Discussion**

**Wear of reference samples**

The almost 5 times lower wear rate of the XLPE reference, compared to the UHMWPE reference, is in agreement with *in vivo* (Mutimer *et al.*, 2010; Johanson *et al.*, 2012) and *in vitro* data (McNulty *et al.*, 2006; Oral *et al.*, 2006; Bistolfi and Bellare, 2011; Affatato *et al.*, 2012). The wear rate of the ceramic references is also in agreement with the
No third-body wear was detected in the heads and inlays, which was also confirmed by coordinate measurements. The uncertainties of the volumetric wear determined with coordinate measurements were ±3.4 mm$^3$, which is 17 times larger than the obtained, gravimetric total wear of the inlays. However, the coordinate measurements confirm that the wear rates of the heads and inlays were low.

**Third-body wear**

With calcium sulphate particles in the test liquid, the wear rate of the UHMWPE inlays increased by 39% and the wear rate of the XLPE inlays by 89%, compared to references ($p = 0.07$ and 0.05 respectively). This increase was much smaller compared to third-body wear tests with PMMA particles with a 10 to 1000 fold increase (Bragdon et al., 2003; Oberbach et al., 2009b; Hintner et al., 2012). Similar wear rates were obtained only with very small PMMA particles (Bragdon et al., 2003, 2005) or with ceramic-on-polymer instead of metal-on-polymer pairings (Wang and Essner, 2001; Kubo et al., 2009; Grupp et al., 2014). Appending one million cycles without particles led to a significant reduction of the wear, as it was observed by Wang et al. after their PMMA third-body wear tests (Wang and Essner, 2001; Wang and Schmidig, 2003). In this work, the addition of calcium sulphate particles had no significant effect on the alumina articulations. However, even applying small alumina particles (Oberbach et al., 2009b: Ø 1.3-2.6 µm) or hydroxyapatite particles (Wang et al., 2002) had no significant effect on the wear of ceramic pairings. Only with larger alumina particles was an increase of wear observed in ceramic-on-ceramic pairings (Oberbach et al., 2005, 2009a).

The tests were performed with calcium sulphate without antibiotics in order to not risk the creation of antibiotic resistant bacteria. The implementation of organic material such as antibiotics in the calcium sulphate pellets will lead...
to a weakening of the hardness. Thus the tests with pure calcium sulphate represent a worst case situation.

Since the particle size of the calcium sulphate used (0.5-100 µm) was in the same range as that of particles tested in the literature, the main reason for the lower wear in this study must be the mechanical and chemical properties of the particles. The hardness of the calcium sulphate is similar to the hardness of polyethylene (Briscoe et al., 1998), but much softer than CoCrMo or alumina. In contrast, PMMA is harder than polyethylene (Briscoe et al., 1998; Zivic et al., 2012) but softer than common metals or ceramics. This explains why PMMA is able to scratch polyethylene but has little effect on metals and no effect on ceramics (Wang and Essner, 2001; Oral et al., 2006). Ceramics are among the hardest materials, thus ceramic particles can cause severe damage to polymer liners, metallic heads and ceramic counterparts. Once a particle gets into the articulation, possibly by a subluxation of the prosthesis (Heiner et al., 2008), it might become embedded in the polymer (if present) or be trapped between the two articulating surfaces. Since calcium sulphate is a soft and resorbable material, it will most likely be milled into smaller particles, which are slowly dissolved once the synovium is not saturated with calcium and sulphate anymore. Thus, in contrast to the not dissolvable and harder PMMA, metallic or ceramic particles, it does not stay in the articulation for a long time, thus limiting third-body wear. Based on these findings, it can be assumed that applying calcium sulphate particles to ceramic-on-polymer or to mixed ceramic (ATZ, ZTA) articulations will have less or even no adverse effect, compared to the tested pairings.

Transfer film
Patchy transfer films with elevations of 2 µm height on the XLPE and up to 15 µm height on the UHMWPE were found on the anterior-superior wall of the inlays, which is the inlay with the highest contact pressure. They are like transfer films, but were not deposited on the counterpart as usual (Walker et al., 1996; Cho et al., 2004) but on the polymer itself. Kaddick and Wimmer (2001) described similar features. These elevations were made of polyethylene particles. Pressing the tip of the FT-IR microscope into the elevations led to similar indents to those on the reference spots nearby. This indicates that these elevations were not only loosely bound on the surface, but mechanically stable elevations on the surface. A possible mechanism is that agglomerates of particles as found on the head were continuously sheared off at the zone with the highest contact pressure, building-up the elevations.

“Toxic” microparticles
With the use of calcium sulphate as antibiotic carrier material, neither the alumina articulations nor the CoCrMo heads were affected. Only the wear of the polymer inlays was increased by 39-89 %. Thus, a larger amount of polyethylene particles is released when calcium sulphate pellets are implanted. Calcium sulphate, however, dissolves within weeks to months (Kelly et al., 2001, Fig. 7c). During this first period, the patient is probably still recovering from the infection and thus presumably less active. Since the heads were not scratched to a greater extent than the reference heads, and since it was shown that the wear rates were reduced to normal values after no more particles were added, no long term damage is likely to occur. The additional particle load that the patient has to deal with is thus limited. The calcium sulphate itself is dissolved into Ca\(^{2+}\) cations, SO\(_4\)^{2-} anions and water. These chemicals are present in the body in relatively high concentrations, thus no adverse effect is expected.

Conclusions
The third-body wear on total hip prostheses was tested in a hip simulator using calcium sulphate particles. Results show that, without particles, the wear rate of XLPE was almost 5 times lower compared to the conventional UHMWPE. Adding calcium sulphate particles led to an increased wear by 39 % for the UHMWPE and by 89 % for the XLPE. The articulations recovered, at least partially, when no more particles were added. Considering the dissolution time of calcium sulphate pellets in vivo of weeks to months, potential wear increase caused by such application is not clinically relevant. The wear of the alumina pairing was not influenced by the presence of calcium sulphate.

All surfaces were slightly scratched, but not more than when compared to tests performed without calcium sulphate particles. Additionally, a patchy transfer film made of small polyethylene particles was found on the superior-anterior wall of the polymer inlays. The metallic heads became smoother during the testing, independent of whether the test was performed with or without particles. The reason for the limited third-body wear is that calcium sulphate is a resorbable and relatively soft material. Thus, if a calcium sulphate particle gets in-between the articulating surfaces, it is probably milled into smaller pieces, which cause less damage. The fact that calcium sulphate is resorbable warrants that trapped or embedded particles cannot remain in the articulation for long.

For ceramic-on-polyethylene articulations and mixed ceramics even less effects by the calcium sulphate are expected, since these heads/materials are more scratch resistant. Thus, calcium sulphate might be used as an antibiotic carrier, even in the presence of total hip prostheses, without fearing excessive third-body wear. While it cannot be claimed from this study that the application of such a local antibiotic carrier has clinically relevant advantages over a classical therapy, it does at least provide essential evidence that doing so would not harm the prosthesis significantly.

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Appendix

Case description

A 63-year-old male patient, otherwise healthy and active, had a total hip replacement on the left side through a lateral, transgluteal approach, for symptomatic primary osteoarthritis. A hybrid prosthesis with an uncemented press-fit titanium cup with an UHMWPE inlay and a cemented double-conical straight stem with a metallic head (CoCrMo) had been implanted, a combination with one of the lowest long term revision rates (AOANJRR 2013). Follow-up consultation at 6 weeks and 3 months documented a good recovery with no more pain, an excellent range-of-motion and nearly no limping.

At 5 months following the operation, the patient had to be hospitalised for a periprosthetic infection of his left hip. Local symptoms had appeared suddenly 6 days before hospitalisation after some days of flu-like general symptoms. While later manifestation of a post-operative infection always has to be considered at such a short time interval, history rather indicates haematogenous seeding. Anyway, as the duration of symptoms was short and as the implant was well positioned without any signs of loosening (Fig. 7a), the option of debridement and retention of the prosthesis was chosen in agreement with current guidelines (Zimmerli et al., 2004; Haasper et al., 2014).

Debridement and drainage of the hip was performed, including an exchange of the mobile parts, followed by an empirical systemic antibiotic treatment with intra-venous amoxicillin-clavulanate. *Staphylococcus aureus*, resistant only to penicillin, was identified quickly and the antibiotic treatment could be narrowed by switching to intra-venous flucloxacillin.

After two days and despite adequate treatment, the patient remained febrile. While a second debridement could have been attempted, this situation would usually have to be considered as treatment failure, requiring removal of the implant in order to obtain control of the sepsis (Koyonos et al., 2011; Lora-Tamayo et al., 2013; Haasper et al., 2014). Removal of a well-integrated cup and of a cemented stem without any loosening however has a great risk of causing bone loss and fractures, necessitating complex reconstruction with larger implants than usually required. Considering the life-long risk of further revision in this 63 year-old patient, the option to re-debride the hip, with exchange of the mobile parts and optimisation of antibiotic treatment by implanting a local antibiotic carrier was chosen. In order to avoid major mechanical impingement and requirements for secondary operations for material removal, calcium sulphate, a resorbable rather soft material, was chosen (Kelly et al., 2001). The risk of causing minor to moderate third-body wear was accepted, considering the immediate advantages of infection control and reduced morbidity of potential later aseptic exchange. Calcium sulphate pellets (Ø 7 mm, Osteoset® Resorbable Bead Kit, Wright Medical Technology, Memphis, TN, USA) containing the antibiotic vancomycin

Fig. 7. Zone of interest from conventional anterior-posterior radiographs of the pelvis from the case described, showing his left hip. A hybrid prosthesis with uncemented press-fit cup and cemented double-conical straight stem with a metal on highly cross-linked polyethylene pairing is implanted. (a) Illustrates the situation at admission for the infection. (b) Illustrates the calcium sulphate pellets distributed in the soft tissues around the joint. (c) Is from the follow-up examination at 6 weeks, illustrating the dissolution of the calcium sulphate pellets, which are no longer visible. Note the apparent shortening of the neck due to external rotation of the leg in (b) and to a lesser extent in (c), caused by post-operative weakness of the gluteal muscles.
(about 6 wt%, Vancomycin Labatec, Labatec Pharma, Geneva, Switzerland) were prepared peroperatively. After hardening, they were placed into the soft tissue around the infected joint (Fig. 7b). This is a well-described combination, adequate for this infection, with a prolonged release at high concentrations (Wichelhaus et al., 2001; Rauschmann et al., 2005; Bibbo and Patel, 2006; Heijink et al., 2006; Wang et al., 2011).

During further evolution, symptoms regressed quickly. Following standard procedures, antibiotics were switched from intra-venous to oral after two weeks (Zimmerli et al., 2004; Osmom et al., 2013). An antibiotic combination with high bioavailability and activity against biofilm was chosen, levofloxacin with rifampin, and maintained for 3 months (Zimmerli et al., 2004; Osmom et al., 2013). Dissolution of the calcium sulphate pellets was observed during the expected period of time (Fig. 7c). Except for the persistence of a slight limp, presents only with fatigue, the patient recovered fully. More than two years after this event, there was no clinical or radiological sign of recurrence or low-grade persistence of the infection; nor could any asymmetry of the polyethylene liner be identified on the radiographs, as indication of excessive wear.

References


ISO 4287:1997 Geometrical Product Specifications (GPS) – Surface texture: Profile method – Terms,
definitions and surface texture parameters. ISO Copyright Office, Geneva, Switzerland.


Editor’s Note: All questions/comments by the reviewers were answered by text changes. There is hence no Discussion with Reviewers section.