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Wear in Total Joint Replacements

Characteristics and biological activity of wear debris from different materials

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Linda Keijzer

Abstract: In all total joint replacements, at the articulating surfaces, wear particles are generated. Prostheses can be made from different materials, resulting in wear debris with distinctive characteristics. In comparison to metal or ceramic prostheses, polyethylene (UHMWPE) artificial joints produce a huge amount of wear debris (40-90 mm3 per year compared to 0.1-3 mm3 per year). Cross-linking the polyethylene acetabular cups reduces this amount to almost a fifth (7-20 mm3 per year) but still too much wear debris is generated. The body responses to these wear particles by inducing a chronic foreign body reaction. After macrophages phagocytose polyethylene particles, they become activated and start releasing chemokines. As a result, osteoclasts become more active, reabsorp more bone and the prosthesis fails due to aseptic loosening. Metal wear particles are nanometer sized (1-40 nm) and much smaller than polyethylene particles (0.1-1 µm). Ceramic particles are also nanometer sized but a small part of the particles is larger. Because their small sizes metal and ceramic particles can easily penetrate and harm cells. They can even enter the nucleus and damage DNA. Hypersensitivity and corrosion are other problems of metal joint prostheses. The distinct characteristics of the wear particles from different materials evoke unique responses from the body. Knowing these characteristics and the biological activity they induce is thus essential.

Total joint replacements with prosthetic components are one of the major successes of modern surgery. They relieve pain and correct deformities in patients with arthritis or otherwise damaged joints. A broad view from the literature shows that 90-95 percent of hip arthroplasties are successful for 10-15 years and knee replacements are only slightly less successful long term [1].

Prosthesis fail due to a variety of reasons with most of the time both mechanical and biological causes. Mechanical reasons are excessive wear at the bearing surfaces, recurrent dislocation, malalignment, stress shielding and bone fractures. Biological reasons consist of local osteoporosis, a form of disuse atrophy caused by an altered loading and septic or aseptic inflammation which also leads to bone loss and loosening of the prosthesis. [2]

This review concentrates on late aseptic loosening caused by adverse cellular reactions to debris generated by wear. Wear debris generated at the articulating surfaces are released in the synovial fluid. There they can come in contact with macrophages from the capsule around the joint. After the particles are phagocytozed, the macrophages release pro-inflammatory cytokines and other inflammatory mediators that stimulate orthoclastic bone resorption. This leads to osteolysis and eventual loosening and failure of the prosthesis. [1;3]

In order to reduce the forming of wear debris and thus extending the lifetime of the prosthesis, in the last 30 years research in new and old materials has led to many different designs for total joint replacements. The different prostheses all produce various amounts of wear debris with different characteristics, which has a direct influence on the successes of the

prostheses. The most common materials currently used for total joint replacements are polymers, Ultra High Molecular Weight Polyethylene (UHMWPE) and Highly Cross linked Polyethylene, metal, Cobalt-Chromium alloy's and ceramic, Alumina and Zirconium.

The biological response to wear particles depends on their characteristics, the amount of wear debris and the size and shape of the particles. This means that these characteristics play an important role in the success or failure of total joint replacements. The aim of this review is to compare the characteristics of wear debris generated from different materials and their biological activity.

Are the characteristics of the wear particles really so important? A. Kobayashi *et al.* [4] showed that the concentration of wear particles accumulated in the tissue surrounding the joint was the most critical factor in the pathogenesis of osteolysis. The size and shape of particles play an important role in the sort of biological response that will be evoked. Small nano-sized particles can enter cells and can damage them from within, while slightly larger particles activate macrophages and are phagocytozed. Particles larger than 5 μm cannot be taken up by macrophages and induce the formation of multi-nucleated giant cells [1;3;5]. Fibril shaped particles are more biological active than round particles with the same size [6].

The size and shape are also determine, in combination with the volume, the number and concentration of wear particles released in joint replacements. J. Gallo *et al.* [7] calculated that the changes of average size of wear particles in the interval (0-1 μm) can change the final number of wear particles by as much as five orders of magnitude when the volume of the wear debris is constant.

How are all these characteristics determined? There are several *in vivo* and *in vitro* methods to determine the amount, size, shape and biological activity of wear debris. For different materials, different methods are used for the characterization of the wear debris. Larger particles and the cellular responses can be seen in histological sections with light microscopy. Tissue digestion techniques can be used to isolate wear debris from retrieved tissue on micropore filters and scanning electron microscopy is used to determine the size distribution and the shape of wear debris. The amount of wear can sometimes be estimated from radiographic images, or measurements on retrieved prostheses. Another way to collect wear debris is from joint simulators. Since no digestion technique is necessary to remove the tissue, the characteristics of particles generated by joint simulators can more easily be determined with electron microscopy. Particles produced by a hip simulator in a sterile surrounding can also be used in *in vitro* studies to determine the biological activity.

1 ULTRA HIGH MOLECULAR WEIGHT POLYETHYLENE WEAR DEBRIS (UHMWPE)

In the 1960s UHMWPE was used in most hip and knee prosthesis for their low friction and low wear characteristics. For two decades, wear problems were considered solved for the little wear that did occur, did not impair the function of the joints. J. Charnley *et al*. [8], in 1968 are believed to be the first researchers who observed the symptoms of aseptic loosening caused by wear debris; but they associated the symptoms with infection. The harm wear debris inflicts was not realized until the late 1980s when the evidence for the role of UHMWPE wear debris was accumulated through retrieval analyses [9;10] and studies in experimental animal models [10;11]. Conventional UHMWPE prostheses are often used in comparative studies with newer or enhanced designs.

1.1 Characteristics of the debris

AMOUNT OF WEAR DEBRIS

The amount of wear debris generated by total hip prostheses with UHMWPE acetabular cups varies between different designs and materials used for the femoral head, which articulates inside the acetabular cup.

J.L. Tipper *et al.* [12] did measurements on 18 Charnley acetabular cups with an average implant life of 12.8 year. The femoral component of the Charnley hip prosthesis was manufactured from stainless steel and the acetabular cup from GUR1120 UHMWPE. All the measured prostheses were revised for loosening. The mean volume of wear debris generated was 59.6 mm^3 per year and the mean number of particles per milligram of wear debris was (1.32 ± 0.51) x 10^{10}. They estimated that the mean number of UHMPE particles released per year was (4.31 ± 1.51) x 10^{10}.

A.P. Elfick *et al*. [13] reported slightly higher numbers, they measured the penetration debt in 47 porous coated anatomic (PCA) cement less acetabular components which were also acquired at revision surgery. These components articulated against COCrMo femoral heads with a diameter of 32 mm. They calculated a mean volumetric wear rate of 96 mm^3 per year.

J.L. Tipper *et al.* [14] determined the wear rate of UHMWPE using a hip simulator. They tested moderately cross-linked GUR 1020 GVF UHMWPE (4 MRad) that articulated with ceramic (alumina) femoral heads with a diameter of 28 mm. They found an average rate of volume change of 25.6 ± 5.3 mm^3 per million cycles. Every person takes approximately 500,000-2,000,000 steps per year [15]. Assuming 1.5 million steps per year [16], a total of 38.4 mm^3 wear debris would be generated per year.

K. Iwakiri *et al.* [17] took a different approach and collected synovial fluid from three people, one year after they had undergone a total knee replacement. They measured the concentration of wear particles in synovial fluid which was (1,49 ± 0.14) x 10^6 particles/mL. It is important to note however that they used a filter with a pore size of 0.2 µm to collect the wear debris. Thus, the real concentration of particles in the synovial fluid likely was higher (see next paragraph).

SIZE DISTRIBUTION

J.L. Tipper *et al.* also determined in both studies the size distribution of the particles. 66.5% of the particles retrieved from the Charnley acetabular hip prostheses was between 0.1 and 0.5 µm; 16.8% was between 0.5 and 1.0 µm and 15,8% of particles was between 1.0 and 5.0 μm^2; 0.9% of particles was between 5.0 and 10.0 µm [12]. The particles produced by the hip simulator were smaller; 58% of the particles were smaller than 0.1µm, 41% was between 0.1 and 1 µm and 1% of the particles was between 1.0 and 10 µm (mean values). Less than 1% of the number of particles was larger than 10 µm. Volumetric this means that 4% of the particles were smaller than 0.1 µm, 66% was between 0.1 and 1 µm, 17% of the particles was between 1.0 and 10 µm and 9% of the volume consisted of particles larger than 10 µm [14]

In a more recent study in 2008, L. Richards *et al.* [18] also retrieved tissue samples from patients with failed Charnly total hip prostheses. They were able to detect more nano-sized particles with the use of a high-resolution field emission gun-scanning electron microscope. They took samples from 7 failed Charnly total hip replacements. 17% of the mean size of the particles was smaller than 0.1 µm; 68% was between 0.1 to 1 µm and only 15% of the particles were larger than 1 µm. These results are more similar to the results of from the hip simulator described in [14].

The mean particle size of the wear debris filtered out of the synovial fluid from patients with total knee replacements by K. Iwakiri *et al.* [17] was 1.21 ± 0.21 µm and 55% of the particles were submicronsized. Compared to the results described by J.L. Tipper *et al.* [12;14] and Richards *et al.* [18] this is quite large. However, since K. Iwakiri *et al.* only filtered particles larger than 0.2 µm out of the synovial fluid, this is not surprising.

SHAPE OF WEAR DEBRIS

UHMWPE wear particles do not have a uniform shape; their shape varies between fibrils, flakes and granules.

The particles collected by K. Iwakiri *et al.* [17] from the synovial fluid have a mean aspect ratio (length/width) of 1.88 ± 0.19. Tipper *et*

al. [12] found almost the same result. They measured a mean aspect ratio of 2.16 ± 0.14 µm (range 1.52-2.47 µm)

Particles isolated from the lubricant fluid of the hip simulator by J.L. Tipper *et al.* [14] showed similar morphologies. Smaller and rounder wear debris was abundant but also many Fibril- and flake-like particles were found, these particles commonly formed aggregates.

1.2 Biological response

Short after the implantation of a total joint prosthesis, a capsule forms around the joint similar to a synovial membrane. The inside of this fibrous capsule is covered by a layer of synovial lining cells. These cells produce the synovial fluid, which in normal joints is responsible for cartilage nutrition, removal of metabolites from the joint and joint lubrication. Normally this membrane is thin and contains few cells or vessels. [1]

In contrast, fibrous tissue membrane recovered at the time of revision surgery for aseptic loosening is thick, highly vascular and infiltrated by many, predominantly macrophages and multi-nucleated giant cells and a few lymphocytes [19]. With polarization microscopy, small particles can be seen intracellular in macrophages and lager particles are engulfed by multi-nucleate giant cells (MNGC)[1;3;5;6]. Since there is a constant production of new wear debris the particles induce a chronic foreign body response.

Macrophages and giant cells are part of the non-specific immune response and differentiate from bone marrow-derived monocytes. Their primary role in the immune defense of the host is to detect, phagocytose and degrade foreign material but they are also able to absorb bone tissue [1]. Macrophages orchestrate the processes of inflammation and repair at tissue sites that have been subject to any form of trauma, infection or intrusion by implants. This is done by releasing a range of chemical messages, cytokines, chemokines, oxygen-containing radicals and other molecules or low-molecular-weight inflammatory mediators. UHMWPE is bio-inert and not degradable by macrophages or MNGCs. UHMWP particles however, once phagocytozed, cause macrophages and MNGSs to release even more cytokines and mediators to summon additional cells to the site to help deal with the particles. This makes the particles bio-active.

Bone tissue is constantly being repaired and remodeled. This involves the synthesis of bone matrix by osteoblasts and the coordinate resorption of bone by osteoclasts. Osteoclasts and macrophages have the same lineage and are both derived from the same class of bone marrow precursor cells. Many of the cytokines generated by macrophages in response to activation have been shown to influence osteoclast development and activation. Some cytokines do this directly like for example, tumor necrosis factor α (TNF-α), colony stimulating factors (GM-CSF) and (M-CSF). Others like interleukin-1 (IL-1), interleukin-3 (IL-3), interleukin-6 (IL-6), stem cell factor (SCF) and platelet-derived growth factor (PDGF) influence osteoclast indirect trough osteoblasts or other cells [1;3;5].

Receptor activator of nuclear factor κB ligand (RANKL) is a protein expressed by osteoblastic stromal cells and T- and B-lymphocytes. This protein can bind to receptor activators of nuclear factor-κB (RANK) on osteoclast precursors and is the primary mediator of osteoclast differentiation, activation and survival. C.T. Wang *et al.* [20] discovered that patients with loosened hip prostheses have significantly higher RANKL levels in the synovial fluid than primary patients. Moreover, there was a positive correlation between the levels of inflammatory cytokines and RANKL levels.

In vitro studies, show that osteoblasts are also affected by wear debris. Particles smaller than 5-10 µm are capable of being phagocytozed by human and rat bone cells. The effects of particles on cell viability and proliferations are variable and strongly dose dependent. If the particles are non-toxic, the osteoblasts become activated resulting in the up regulation of pro-inflammatory and bone-

resorbing factors and down regulation of factors involved in bone formation. [21]

In summary, the balance between the formation and resorption of bone matrix becomes disturbed due to wear debris. Osteoclasts remove bone around the prostheses while osteblasts are not able to replace it. This ultimately results in bone loss and aseptic loosening of the joint replacement.

2 HIGHLY CROSS-LINKED POLYETHYLENE WEAR DEBRIS

In order to reduce the wear of UHMWPE and thereby reducing the incidence of osteolysis in total joint replacements, highly cross-linked polyethylene's (HXPEs) were introduced as a new biomaterials for joint prostheses. In these designs the UHMWPE acetabular cup is replaced by a cup made from HXPE, the femoral components are still made from metal or ceramic.

2.1 Characteristics of the debris

AMOUNT OF WEAR DEBRIS

C. Heisel et al. [22] compared data from 24 patients with conventional polyethylene cups (Enduron; DePuy), and 34 patients with cross-linked polyethylene (DePuy) as the acetabular bearing. They collected data in radiographic follow-ups with a minimum of 2 years. The group with UHMWPE cups showed a mean linear wear rate of 0.13 mm per year (87.6 mm^3) and the group with HXPE showed a mean linear wear rate of 0.02 mm per year (17.0 mm^3).

CR. Bragdon *et al.* [23] found similar wear rates when they reviewed data from 182 patients (200 hips) with a minimum of 6 year radiographic follow-up. The average steady-state wear rate was 0.002 ± 0.01 mm and 0,026 ± 0,13 mm per year for 28-mm and 32-mm head sizes, respectively. They found no evidence of loosening or osteolytic lesions around the cup or the stem.

The concentration of particles (larger than 0.2 µm) in synovial knee fluid is also less with crosslinked polyethylene (0.09 ± 0.06) x 10^6 particles/ml in comparison to conventional polyethylene. [17]

J. Fisher *et al.* [16] compared the wear rate of highly cross-linked polyethylene (10 MRad) with UHMWPE (both GUR1050) using a hip simulator. They found almost an eight-fold reduction in the volumetric wear rate from the highly crosslinked polyethylene. 35 ± 8 mm^3 versus 4.5 ± 1 mm^3 UHMWPE and HXPE respectively.

SIZE DISTRIBUTION

Fisher *et al.* [16] reported that the size of highly crosslinked polyethylene wear debris generated by a hip simulator is much smaller than UHMWPE wear debris.

K. Iwakiri *et al.* [17] concluded the same when he found that the mean size of HXPE particles (larger than 0.2µm) found in the synovial fluid of artificial knees was 0.64 ± 0.07 µm. This is much smaller than the mean size of UHMWPE particles, 1.21 ± 0.21 µm.

In tissue samples taken at a revision operation from a 73 year old woman the mean equivalent circle diameter of the wear debris was 0.66 ± 0.40 µm. She had for 4 years a hip prosthesis implanted with a HXPE acetabular cup articulating with a 26 mm femoral head made of COCr alloy. The hip prostheses failed due to impaction graft of HA granules. These granules also damaged the HXPE. [24]

SHAPE OF WEAR DEBRIS

The HXPE particles filtered from the synovial fluid by K. Iwakiri *et al.* [17] had a mean aspect ratio of 1.33 ± 0.10. He obtained these particles from the synovial fluid from four knee replacements one year after the operation.

Y. Minoda *et al.* [24] Measured almost the same mean aspect ratio (1.37 ± 0.26) from wear particles seperatated from tissue samples collected from the 73 year old women during the revision operation. They found no fibrils or shreds in the wear debris.

2.2 Biological response

The biological response of the host to wear debris from different materials is almost the same but there are some small differences.

R.L. Illgen *et al.* [25] measured the amount of osteolysis induced by particles with a mean size of 7.01 µm in *in vivo* murine osteolysis models. The amount of bone loss was 34.79% for cross-linked particles (10 MRad) and 9.05% for conventional UHMWPE particles. This leads to the conclusion that cross-linking of PE increases the biological activity of wear debris.

Another reason for a higher biological activity of HXPE wear debris is the smaller size of the particles. Smaller particles, which can be phagocytozed by macrophages, are more biologic active than larger particles. Wear debris with a diameter of 0.1-1 µm bring about the most severe response [3;26]. HXPE has relative more wear debris in this size range than UHMWPE.

3 METAL ON METAL WEAR DEBRIS

Metal on metal articulations were widely used during the late 1960 and early 1970s, but the early clinical results were disappointing. At the same time metal on polyethylene prostheses became a success, which led to a decline in the use of metal on metal hips until 1980. After the discovery of the problems with wear debris formed by UHMWPE, a new interest in the metal on metal joint replacements arouse. This was strengthened due to the observation that some of the metal on metal prostheses had survived for over 20 years. It is thought that many early metal on metal implants failed due to small geometric irregularities. These caused wrong loading and implant loosening [27].

The second generation of metal on metal implants are made from different cobalt and chroom alloys. The wear characteristics of these prostheses are highly dependent on the material, the tribological design and the finishing technique.

3.1 Characteristics of the debris

AMOUNT OF WEAR DEBRIS

H.P. Sieber *et al.* [28] analyzed 118 second generation metal on metal retrieved hip implants. The prostheses were made of wrought Co-28Cr-6Mo-0.12C alloy (ASTM F-1537). 115 had a diameter of 28 mm and three of 32 mm. Only 45% of the revisions was due to loosening of the stem or the cup. A steady state volumetric wear rate was found of 0.3 mm^3 per year and a linear rate of 5 µm was found. In the first year after implantation, the wear rate was 25 µm.

M. Silva *et al.* [29] have reviewed wear results from 12 different first generation metal on metal prostheses from different authors. He calculated an average linear wear rate on the retrieved heads of 0.004 mm per year, with an average volumetric wear rate of 1.5 mm^3 per year.

Firkins *et al.* [30] preformed a hip simulator study on the wear of medical grade wrought cobalt chrome alloys (according to ASTMF1537). They used a prostheses with a head size of 28 mm. During the first million cycles the prostheses had a high wear rate, which than settled to a lower steady state wear rate of 0.023 ± 0.038 mm^3 per million cycles. The wear rate of cobalt chrome alloy with a low carbon content (<0.07% instead of >0.2%) was 0.322 ± 0.111 mm^3 per million cycles

SIZE DISTRIBUTION

C. Brown *et al.* [31] performed a simulator study with hip prostheses made from a medical grade wrought cobalt chrome alloy (according to ASTMF1537) and a head size of 28 mm. They used two different simulators; the standard simulator gave a mean size of 34.72 ± 1.29 nm. During normal walking, the acetabular cup and the head in the hip joint are sometimes separated. The second simulator also included these microseparations of 0.8 mm. The head separates from the cup during the swing phase an relocates in the stance phase after rim contact. The microseparations leaded to a slightly smaller mean size of 31.16 ± 1.82 nm. The particles were typical less than 40 nm

and more than 95% of the particles was smaller than 100 nm.

Doorn *et al.* [32] collected periprosthetic tissue samples from around 13 revised metal on metal prostheses. They used a enzymatic digestion method to separate the particles from the tissue and used TEM to visualize them. The mean size of the particles found was 81 nm and the size range was 51 to 116 nm.

Firkins *et al.* [30] also used a hip simulator to generate wear debris. They found particles with a mean maximum diameter of 25-36 nm.

SHAPE OF WEAR DEBRIS

Doorn *et al.* [32] found that the majority of Co-Cr particles were round in shape, although a small proportion were shard or needle-like in morphology.

C. Brown *et al.* [31] found the same in both simulators both, the standard and the simulator with micro speparations, produced irregular shaped but typically rounded particles.

Firkins *et al.* [30] found only round shaped particles.

3.2 Biological response

Where polyethylene particles have been shown to induce a chronic foreign body reaction, cobalt chrome particles have a different effect on cells. Generally, histology studies of tissues retrieved from revised metal on metal prostheses show a mild to moderate macrophage infiltration. Since the wear debris generated by metal on metal joints are in the nanometer range, single particles cannot be phagocytosed by macrophages. However, these macrophages are able to phagocytose agglomerates consisting of multiple particles [3;33]. Once phagocytosed, the Co-Cr particles corrode quickly due to the acidic environment in the phago-lysosome. This releases high concentrations of ions within the cell which can be toxic and rapidly kill them [34].

The cobalt chrome alloys, like al metals, are subject to corrosion. The genotoxic potential of the cobalt and chrome ions is a major cause of concern. While high concentrations of cobalt and chromium ions may directly kill cells, sub-lethal concentrations may cause DNA damage and genotoxicity [33]. Both cobalt and chromium are recognized as human carcinogens by the International Agency for Reasearch on Cancer commissioned by the European Union.

However, the small size of the metal particles prevents severe macrophage activation, it also allows them to disperse throughout the body. Metal wear debris has been found in lymph nodes, liver and spleen. Thus, Co-Cr wear debris can cause problems throughout the whole body. [35]

Joint replacements made from cobalt chrome alloys can also induce hypersensitivity to metals. This could cause pseudotumors near the hip prostheses [36]. Besides macrophages, T lymphocytes can be found in tissue around loose artificial hips [1;3;5;6]. T lymphocytes mediate type IV hypersensitivity. In the earlier days of metal on metal hip prostheses, it was discovered that patients showed a higher incidence of metal sensitivity on the skin than people without or with UHMWPE on metal prostheses; which led to the conclusion that metal on metal implants can cause sensitization. Evans *et al.* [37] also found that patients with loosened prostheses often were sensitized while no sensitivity was present in patients with well-fixed prosthetic joints. More evidence for immunological processes and the role of T-lymphocytes in aseptic loosening is described by Revell *et al.* [1]

4 CERAMIC ON CERAMIC

Ceramics were initially used in total hip arthroplasty and in total knee arthroplast more than 35 years ago. The high failure rates of the first generation of metal on metal and the high wear rates of metal on polyethylene bearings let researchers investigate new advanced materials for joint replacements. Alumina (Al_2O_3) was the first ceramic material being applied in total hip replacements by P. Boutin *et al.* [38] in 1970. A striking disadvantage of alumina ceramic is its brittleness and lower tensile strength. Early

ceramic on ceramic joint replacements often failed due to femoral head fractures and catastrophic breakage of the ceramic sockets [3]. Improvements in design, the use of better quality alumina, and advancing operation techniques with better positioning of the prostheses have reduced these problems considerably. Long term fixation was the next problem with ceramic prostheses. This was solved with hydroxyapatite-coated Ti backing. In the most recent ceramic prostheses zirconia (ZrO_2) is introduced as a composite with alumina. Zirconia is like alumina an oxide ceramic, but has a biphasic structure this causes a flexural strength almost twice as high as alumina. In the composite the zirconia increases the fracture toughness of the ceramic compared to alumina alone. [39]

4.1 Characteristics of the debris

AMOUNT OF WEAR DEBRIS

The amount of wear found in ceramic on ceramic hip prostheses varies greatly between different studies and individuals. Most of the time wear rates can be divided in two groups, very low wear rates and severe wear rates [3;39]. Retrieved first-generation alumina-alumina hip joints typically have shown a stripe of wear on the femoral heads which has been associated with high wear [40]. Wrong positioning also can cause severe wear. Very low wear rates can however be achieved with good surgical techniques and newer designs. Several first generation ceramic wear studies reviewed by E. Ingham *et al.* [3] show low linear wear rates in the order of 5 µm/year and volumetric wear rates of 1-5 mm^3 per year

A more recent study by P.J. Lusty *et al.* [41] showed much lower wear rates of 0.2 mm^3 per year. They analyzed a series of 301 third generation alumina on alumina cementless total hip replacements all implanted between 1997 to 1999. Seven ceramic bearings that had been retrieved more than six months after implantation were analyzed for signs of wear. After seven and a half year, the prosthetic survival rate was 96%.

J.L. Tipper *et al.* [42] used a standard hip simulator and a simulator with micro separation to determine the wear of alumina on alumina hip replacements. They have tested the first generation of 'BIOLOX' and the modern 'BIOLOX forte' prostheses (Zimmer, Ltd). Under standard circumstances, they found volumetric wear rates of respectively 0.11 and 0.08 mm^3 per million cycles. With micro separation the wear rates were much higher, 1.74 and 1.24 mm^3 per million cycles.

Other studies have shown even lower wear rates of 0,05 mm^3 per million cycles under ideal conditions [16] and 1,2 mm^3 per million cycles when micro separation was included in the hip simulator testing [43].

SIZE DISTRIBUTION

A. Hatton *et al.* [44] analyzed tissue retrieved from around 10 uncemented Mittelmeier alumina ceramic on ceramic total hip replacements using histological methods. They also isolated wear debris using laser capture microdissection. Transmission electron microscopy of the laser-captured tissue revealed the presence of very small alumina wear debris in the size range of 5-90 nm and a mean size of 24 ± 19 nm. Scanning electron microscopy with a lower resolution also showed larger particles in the 0.05-3.2 µm range.

The hip simulator tests of J.L. Tipper *et al.* [42] showed that this bifurcation in the size range of the particles is probably caused by the microseparation in the artificial joint. The standard hip simulator produced only nanometer sized particles in a range of 2-27.5 nm while under microseparation two size ranges were found, 1-35 nm and 0.02-0.94 µm.

SHAPE OF WEAR DEBRIS

The majority of the small alumina ceramic wear debris found by J.L. Tipper *et al.* [42] in the hip simulator tests were oval to round in shape and appeared as electron dense aggregates of wear particles. These particles are believed to be produced by relief polishing of alumina ceramic grains. The larger wear particles generated under microseparation testing were also oval to round with some polygonal particles. These particles are thought to originate from within

the wear stripe, and are released by grain boundary fracture of the alumina ceramic.

4.2 Biological response

A. Hatton *et al*. [44] found in histological analysis of the retrieved tissue from Mittelmeier aluminia ceramic implants a mixed pathology. Some areas had no obvious pathology whereas other areas were relative rich in macrophages and showed necrosis of tissue. Ceramic particles could be seen inside macrophages as agglomerates. The macrophage response was however not as intense as observed in tissue collected around metal on polyethylene implants.

Clinical, radiographic, laboratory and microbiological data from 30 patients with failed alumina on alumina arthroplasties was collected and reviewed by L. Savarino *et al.* [45]. They found variable wear and tissue macrophage reaction and no activation of giant cells or osteoclasts. A correlation between the inflammatory reaction and the level of osteolysis was not found. This indicates that unlike polyethylene particles and like metal particles, ceramic particles do not induce a severe foreign body reaction.

A. Tsaousi *et al.* [46] performed *in vitro* genotoxicity tests of nanometer and micrometer sized alumina ceramic particles. They found that the ceramic particles were weakly genotoxic and not cytotoxic on human fibroblasts. The size of the particles did not change the genotoxicity of the ceramic. The number of micronucleated binucleated cells induced by the nano-sized particles (average size of 20 nm) was not significantly higher than the number induced by miron-sized particles (average size of 2 µm). When fibril shaped particles where added, in low concentrations, significant more cells became micronucleated binucleated, compared to spherical particles.

5 CONCLUSION

UHMW- and HX-Polyethylene, cobalt chrome and alumina or zirconium wear particles all have different characteristics. On the next pages in a table on the next pages, all the information given in this review about the amount, size and shape of wear debris from different materials and retrieved using different methods is summarized.

UHMWPE on metal or ceramic hip prostheses produces the largest volume of wear debris with approximately 40-90 mm^3 wear per year. Crosslinking of Polyethylene helps but still produces wear rates of approximately 7-20 mm^3 wear debris per year. Much lower wear rates are reached with metal on metal prostheses of approximately 0.3-2.0 mm^3 particles per year. When ceramic on ceramic prostheses are placed correctly similar wear rates can be reached of 0.1-2.0 mm^3.

Metal wear particles are all in the nanometer size range (1-40 nm), while in tissue retrieved from around ceramic joints besides nanometer sized particles also some larger particles can be found in the size range of 0.02-0.94 µm. The size of UHMWPE particles varies between 0.1 and 10 µm with most of the particles between 0.1 and 1 µm. HXPE particles are smaller than UHMWPE particles and generally between 0.1 and 0.5 µm.

UHMWPE wear debris does not have a uniform shape but it varies between fibrils, flakes and granules. The average aspect ratio of these particles is between 1.5 and 2.5. Particles found around HXPE hip implants are a slightly rounder with a mean aspect ratio 0f 1.3. Metal particles are almost all round although also shard or needle like particles are reported. Ceramic particles are round or oval shaped.

All these different amounts, sizes and shapes of wear particles evoke different biological responses. But also characteristics of the material itself play a part in this.

The biological reaction to UHMWPE can be described as a chronic foreign body reaction. Near bone the severe inflammation and the many activated macrophages cause osteoclast differentiation, bone loss and ultimately implant loosening. Due to the lower wear rate, this reaction is less severe with HXPE, but not as low, as could be expected looking only at the volumetric wear rate. This is partly because HXPE particles cause in the same

concentration a more fierce reaction. But the main reason is that HXPE particles are smaller.

The biological response to metal particles is of a different kind. Corrosion of cobalt and chrome causes high ionic concentrations, these are cytotoxic and genotoxic. Inside macrophages high concentrations are reached much sooner after they have phagocytosed wear debris. The acid environment inside lysosomes accelerates the corrosion of the metals. Metal wear particles can be found throughout the whole body. This means that metal wear debris can cause harm in other places than the hip joint. Another side effect of metal on metal total hip replacements is that cobalt chrome wear debris can cause hypersensitivity to metals.

Since the wear rates of ceramic on ceramic joints are so low, and the material is quite inert, there is little biological reaction to ceramic wear debris. It can cause some DNA damage but much less than metal particles.

Thus, looking only at the wear generated by total joint replacements ceramic implants seem to be the best choice.

Authors	Material	Method	Average amount of wear debris	Size of the particles	Shape of the particles
J.L. Tipper *et al.* [12]	GUR1120 UHMWPE against Stainless steel	Measurements performed on, and tissue samples taken from around, 18 retrieved Charnley hip prostheses.	59.6 mm^3 per year	Number of particles 0.1 - 0.5 µm = 66.5% 0.5 - 1.0 µm = 16.8% 1.0 - 5.0 µm = 15,8% 5.0 - 10.0 µm = 0.9%	2.16 ± 0.14 µm mean aspect ratio (range 1.52-2.47 µm)
A.P. Elfick *et al.* [13]	UHMWPE against COCrMo	Measurements on 47 porous coated anatomic (PCA) cementless acetabular cups	96 mm^3 per year		
J.L. Tipper *et al.* [14]	moderately cross-linked GUR 1020 GVF UHMWPE (4 MRad) against Alumina	Hip simulator	25.6 ± 5.3 mm^3 per million cycles	Number of particles < 0.1 µm = 58% 0.1 - 1 µm = 41% 1.0 - 10 µm = 1% Volumetric < 0.1 µm = 4% 0.1 - 1 µm = 66% 1.0 - 10 µm = 17% > 10 µm = 9%	Mostly small and round but also many Fibril- and flake-like particles. The particles commonly formed aggregates.
K. Iwakiri *et al.* [17]	UHMWPE	Synovial fluid retrieved from 3 knee replacements after one year (only particles larger than 0.2 µm where filtered out)	(1,49 ± 0.14) x 10^6 particles/mL synovial fluid	Mean size 1.21 ± 0.21 µm Number of particles <1 µm = 55%	1.88 ± 0.19 mean aspect ratio
L. Richards *et al.* [18]	GUR1120 UHMWPE against Stainless steel	Tissue samples taken from around 7 Charnley hip prostheses		Number of particles < 0.1 µm = 17% 0.1 - 1 µm = 68% >1 µm = 15%	
C. Heisel *et al.* [22]	UHMWPE	Radiographic follow-ups of 24 patients with DePuy prostheses	87.6 mm^3 per year and a linear wear rate of 0.13 mm per year		
J. Fisher *et al.* [16]	GUR1050 UHMWPE	Hip simulator	35 ± 8 mm^3 per million cycles		
C. Heisel *et al.* [22]	HXPE	Radiographic follow-ups of 34 patients with DePuy prostheses	17.0 mm^3 per year and a linear wear rate of 0.02 mm per year		

CR. Bragdon *et al.* [23]	HXPE	Radiographic follow-up of 200 hips	linear wear rate of 0.002 ± 0.01 mm and 0,026 ± 0,13 mm per year for 28-mm and 32-mm head sizes, respectively		
K. Iwakiri *et al.* [17]	HXPE	Synovial fluid retrieved from 4 knee replacements after one year (only particles larger than 0.2 µm where filtered out)	(0.09 ± 0.06) x 10^6 particles/ml synovial fluid	Mean size 0.64 ± 0.07 µm	1.33 ± 0.10 mean aspect ratio
J. Fisher *et al.* [16]	GUR1050 HX UHMWPE (10 MRad)	Hip simulator	4.5 ± 1 mm^3 per million cycles		
Y. Minoda *et al.* [24]	HXPE against CoCr alloy	Tissue samples taken from failed hip		Mean size 0.66 ± 0.40 µm	1.37 ± 0.26 mean aspect ratio
H.P. Sieber *et al.* [28]	Wrought Co-28Cr-6Mo-0.12C alloy (ASTMF1537)	Analysis of 118 second generation metal on metal retrieved hip implants	0.3 mm^3 per year and a linear wear rate of 5 µm		
M. Silva *et al.* [29]	Metal on metal	Reviewed wear results from 12 different first generation metal on metal prostheses from different authors	Average 1.5 mm^3 per year and a mean linear wear rate of 0.004 mm/year		
Firkins *et al.* [30]	Wrought cobalt chrome alloys (ASTMF1537) with carbon content of <0.07% or > 0.2%	Hip simulator	0.023 ± 0.038 mm^3 per million cycles (>0.2% carbon) 0.322 ± 0.111 mm^3 per million cycles (<0.07% carbon)	Mean size 25-36 nm	Round particles
C. Brown *et al.* [31]	Wrought cobalt chrome alloy (ASTMF1537)	Normal hip simulator and hip simulator with microseparations		Mean size of 34.72 ± 1.29 nm (normal) Mean size of 31.16 ± 1.82 nm (microseparations) 95% was smaller than 0.1 µm	Irregular shapes but typical round particles
Doorn *et al.* [32]	Metal on metal	Tissue samples taken at revision operation		Mean size 81 nm Size range 51 to 116 nm	Majority round with few shard or needle-like particles
E. Ingham *et al.* [3]	Ceramic	Review of several first generation ceramic wear studies	1-5 mm^3 per year and linear wear rate of 5 µm per year		

P.J. Lusty *et al.* [41]	Alumina	Analysis of 7 third generation alumina on alumina cementless hip prostheses	0.2 mm^3 per year		
J.L. Tipper *et al.* [42]	Alumina	Norma hip simulator and hip simulator with micro separations with first generation BIOLOX and modern BIOLOX forte prostheses	0.11 and 0.08 mm^3 per million cycles normal hip simulator 1.74 and 1.24 mm^3 per million cycles micro separation For first generation and modern prostheses respectively	Standard hip simulator: size range 2-27.5 nm Micro separation 1-35 nm and 0.02-0.94 µm	Oval to round shaped and formed aggregates
A. Hatton *et al.* [44]	Alumina	Tissue samples taken from around 10 uncemented Mittelmeier alumina ceramic on ceramic prostheses during revision operations		Size range 5-90 nm and 0.05-3.2 µm	

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