PMMA Third-Body Wear after Unicondylar Knee Arthroplasty Decuples the UHMWPE Wear Particle Generation In Vitro

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Introduction. Overlooked polymethylmethacrylate after unicondylar knee arthroplasty can be a potential problem, since this might influence the generated wear particle size and morphology. The aim of this study was the analysis of polyethylene wear in a knee wear simulator for changes in size, morphology, and particle number after the addition of third-bodies.

Material and Methods. Fixed bearing unicompartmental knee prostheses (UKA) were tested in a knee simulator for 5.0 million cycles. Following bone particles were added for 1.5 million cycles, followed by 1.5 million cycles with PMMA particles. A particle analysis by scanning electron microscopy of the lubricant after the cycles was performed. Size and morphology of the generated wear were characterized. Further, the number of particles per 1 million cycles was calculated for each group. Results. The particles of all groups were similar in size and shape. The number of particles in the PMMA group showed 10-fold higher values than in the bone and control group (PMMA: \(10.251 \times 10^{12}\); bone: \(1.145 \times 10^{12}\); control: \(1.804 \times 10^{12}\)). Conclusion. The addition of bone or PMMA particles in terms of a third-body wear results in no change of particle size and morphology. PMMA third-bodies generated tenfold elevated particle numbers. This could favor an early aseptic loosening.

1. Introduction

Unicompartmental knee arthroplasties (UKA) in the meanwhile show excellent results in the treatment of a medial compartment osteoarthritis, which is certainly due to the sparing of soft tissues that results in better tibiofemoral and patellofemoral kinematics [1] and an increased range of motion compared to total knee arthroplasty (TKA) [2]. While the 10-year-survival rates of UKAs have been shown to be equivalent to those of modern TKA [3], clinical evidence has demonstrated a higher revision rate of UKA compared to TKA [4]. It is commonly accepted that accumulating wear debris after total joint arthroplasty finally leads to an aseptic loosening of the prosthesis, although the exact mechanism of this inflammatory process is not understood in detail yet [5, 6]. But in several studies it could be demonstrated that number, size, and shape of the wear particles influence the extent of the inflammatory biological reaction resulting in periprosthetic osteolysis [7–9]. Submicron particles, especially, increase the biological reaction [8]. It can be assumed that even minor changes in the wear rate have distinctive effects on the amount of accumulating wear particles. This correlation between the gravimetric wear rate of tibial inserts in knee simulator tests and the particle number analysis could be shown in a previous study, as minor changes in the particle size or wear rate showed considerable effects on the particle number [10]. Third-body wear after UKA, especially, might influence the wear generation and the particle morphology and thus lead to an early failure of the prosthesis. Bone and cement fragments (polymethylmethacrylate, PMMA) that occur during the implantation of the prosthesis can easily be missed in the posterior regions of the femorotibial joint gap relating to the minimally invasive approaches [11].

The aim of this study was to analyze the influence of third-bodies (bone- and PMMA-particles) on number, size, and shape of wear debris generated in an UKA joint simulator.
First it was hypothesized that an occurrence of third-body debris can lead to elevated particle numbers. The second hypothesis was that bone as well as PMMA debris alters size and shape of the generated particles.

2. Materials and Methods

The simulator experiments have been described in a previously published study [12]. Sections 2.1–2.3 summarize the simulator tests.

2.1. Prostheses. For this investigation, fixed bearing unicompartmental knee prostheses (Univation-F, Aesculap, Tuttingen, Germany) were used with a metal on polyethylene articulation.

The intermediate-sized femoral and tibial (F3/T4) components were made from CoCr29Mo6 alloy and the gliding inserts were composed of UHMWPE (GUR 1020, Germany) were used with a metal on polyethylene gliding articulation. Sections 2.1–2.3 summarize the simulator tests.

2.2. Simulator Specifications. Before wear testing the gliding surfaces were preconditioned in the test solution until no increase of weight was measurable. The test fluid simulated synovial liquid with a protein content of 30 g/L. The applied lubricant was changed every six days (25% (v/v) new born calf serum (Biochrom, Germany) with 0.1% (m/v) sodium azide solution in sterile water with EDTA (AppliChem, Germany) as a fungicidal). The lubricant was changed every 0.5 million cycles. The specimens were tested on a servohydraulic knee simulator (EndoLab, Germany) with four test stations; the test phase after adding the different particles with zirconium dioxide as radiolucent (Palacos R, Heraeus Medical, Germany) were mixed within the simulator lubricant. The simulator was stopped after every 500000 cycles; the test solution was contaminated into three parts. The first part was a standard test with 30 ± 2 kGy). The inserts were fixed at the tibial baseplate component by a snap-fit mechanism. The medial side of the meniscal bearing had a concave shape and the lateral side was planar. Before testing, the bearings were accelerated aged, according to the standard as described in the "ASTM F2003 - 02(2008)" to simulate the oxidation process of UHMWPE in air [14].

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2.3. Wear Particle Generation. The simulator was stopped at 8.0 million cycles; the overall test period was divided into three parts. The first part was a standard test with 5.0 million cycles as prescribed by the ISO [15]. In the following two periods, the test solution was contaminated with third-body wear debris in a concentration of 5.0 g/L. The particles were produced by a micro-bone-mill (Aesculap GB060R, Tuttingen, Germany). Between 5.0 and 6.5 million cycles cortical porcine bone particles were added to the test lubricant. From 6.5 to 8.0 million cycles, cement particles with zirconium dioxide as radiolucent (Palacos R, Heraeus Medical, Germany) were mixed within the simulator lubricant. The test phase after adding the different particles was therefore during the steady state phase of the inserts [12]. The morphologic parameters of the debris can be found in Table I. Mean diameter (MD), equivalent circle diameter (ECD), form factor (FF), aspect ratio (AR), and roundness (R) of the third-body wear debris were recorded [16].

2.4. Particle Isolation. Within every 500000 cycles the simulator was stopped; the serum was removed and digested in the following using the "acid digestion" method [17]. The digested lubricant was then centrifuged at 5000 g for 30 minutes to remove the third-body wear debris (the used bone particles consist of milled cortical bone, which has a density of ≈1.5 g/cm³ [18]; the PMMA particles had a mean density of ≈1.18 g/cm³; the UHMWPE particles had a density of <0.96 g/cm³). The specimen was taken out with a pipette (Gilson, Pipetman, made in France, GD29041) three times 1 mL, while the pipette tip was dunked for about 1 cm in the centre of the Falcon tube. 10 mL of each serum sample supernatant was added to 50 mL of hydrochloric acid (37% v/v; Merck, Darmstadt, Germany) and mixed with a magnetic stir bar at 60°C for approximately one hour. Then, 3 mL of this digestion solution was added to 150 mL of methanol (Merck, Darmstadt, Germany) and filtered through a 0.02 μm polycarbonate membrane (Anodisc 47, Whatman plc, Maidstone, Kent, United Kingdom). The filter membrane was then dried for 6 hours and sputter-coated with gold.

2.5. Particle Analysis. The particles recovered on the filter membranes were imaged by scanning electron microscopy (SEM, Zeiss EVO, Carl Zeiss Microscopy GmbH, Jena, Germany). The particles were analyzed at a magnification of 5000–10000 diameters. 20 random, nonoverlapping fields of view were analyzed per sample. Images of each field of view were captured, and the particles were measured using a digital image analysis program [10] (Leica QWin, Image processing and analysis application, Leica Microsystems, Wetzlar, Germany). The boundary of each particle was defined on the basis of a gray-scale level threshold.

In accordance with the ISO, mean diameter (MD), equivalent circle diameter (ECD), form factor (FF), aspect ratio (AR), and roundness (R) were recorded [16]. According to Sieving et al. [13] the percentage of particles with an AR in the range from 1 to 2.39 and ≥2.4 was calculated. Furthermore, the particle number was calculated using the following formula as reported before \( N_{(p)} \) is absolute particle number; \( n_{(p)} \) is examined particles; \( G_{(p)} \) is volumetric wear rate; \( d_{(m)} \) is equivalent circle diameter) [10]:

\[
N_{(p)} = \frac{n_{(p)} \times G_{(p)}}{\sum_{k=1}^{n} \left( \pi \times d_{(m)}^3 \right) / 6}.
\]

The mentioned wear rate was recently found and described by Schroeder et al. in a recently published manuscript [12].

**Table 1: Size and shape of third-body particulate debris.**

| Parameter          | Porcine bone particles | PMMA particles |
|--------------------|------------------------|----------------|
| Mean diameter (µm) | 671.6 ± 186.4          | 644.2 ± 262.6  |
| ECD (µm)           | 519.0 ± 142.9          | 548.4 ± 237.3  |
| FF                 | 0.41 ± 0.12            | 0.57 ± 0.12    |
| AR                 | 1.74 ± 0.62            | 1.74 ± 0.70    |
| Roundness          | 0.50 ± 0.14            | 0.42 ± 0.14    |
3. Results

3.1. Wear Particle Size and Morphology. Overall the particles of all groups showed similar size distributions of polyethylene wear, with a rounded median ECD of 0.13 μm (min: 0.06 μm; max: 3.38 μm) for the bone group, 0.12 μm (min: 0.06 μm; max: 3.27 μm) for the PMMA group, and 0.12 μm (min: 0.06 μm; max: 2.92 μm) for the control group. All differences were statistically significant (\(P < 0.05\)).

Furthermore, the majority of all analyzed particles were approximately round in shape, smooth, granular, and irregular and had similar AR values (median): 1.34 (min: 1.00; max: 5.93) for the bone particle group, 1.51 (min: 1.00; max: 11.86) for the PMMA particle group, and 1.51 (min: 1.00; max: 9.90) for the control group. All size and shape parameters can be found in Table 2 (statistically significant results, \(P < 0.05\)). The particle size distribution is demonstrated in Figures 1 and 2 using box plots.

99.77% of the particles in the bone group were <1.0 μm, 99.61% in the PMMA group and 99.71% in the control group were in the submicron size range.

In the bone particle group 6.35%, in the PMMA group 13.42%, and in the control group 9.84% of the particles had an AR \(\geq 2.4\) (Table 3). Figure 3 shows example SEM images of the wear particles and gives the impression of mainly round and granular particles. Furthermore, a particle size distribution for each size interval is given in Figure 4.

3.2. Number of Particles. We found differing particle numbers for each group. First, a difference between the running in and the steady state phase was found. In the running in phase \(5.126 \times 10^{12}\) particles were calculated per 1 million cycles. In the steady state phase the particle number decreased to \(1.804 \times 10^{10}\). Interestingly, the addition of bone particles
Figure 3: SEM sample images of all tested groups. (a) and (d) show the debris of the bone debris group; (b) and (e) demonstrate the enormous number of particles in the cement group; (c) and (f) serve as examples for the control group. (a), (b) and (c) are 5000x magnified; (d), (e) and (f) are 10000x magnified.

4. Discussion

This study demonstrated that free cement debris can significantly increase the generation of wear particles in unicompartmental arthroplasty. The first hypothesis could only partly be accepted, as only the addition of PMMA third-body wear debris lead to higher particle numbers, whereas cortical bone particles did not affect the particle generation. The second hypothesis had to be rejected; the particle morphology was not altered by third-body wear debris clearly, although statistical tests showed highly significant differences.

Clinical evidence as well as retrieval studies had disclosed the issue concerning third-bodies after UKA [11, 19]. Schroeder et al. had proven in a simulator-based study that the wear rate is definitely influenced by cement third-body wear debris [12]. But so far, there are no studies known by the authors concerning the influence of third-body wear in UKA on the generated particle morphology and number. It is basically known that particle size, morphology, and number affect the biologic response resulting in an osteolysis that finally leads to an aseptic loosening and consequently to
In order to ensure a SEM analysis that just focuses on the generated wear debris. This step is mentioned neither by the ISO nor by the ASTM [16, 22]. This step was successful as no particles in the size range of the third-body debris could be found. On the other hand the loss of particles, especially of the bigger particles, cannot be excluded against the background that over 99% of the particles were sized submicron.

In this test setup a 0.02 μm pore polycarbonate filter membrane was used. An unknown amount of particles below this size might have been lost before the SEM analysis. Currently, it is known that the pore size of the filter could influence the results of the particle analysis. Scott et al. demonstrated that filtration through 0.05 μm is necessary to isolate a greater number of submicron wear particles [23]. With the 0.02 μm pore size filter which was used the majority of the particles should have been isolated.

In general, joint simulators allow preclinical evaluation of wear of artificial joints in a controlled environment [24]. The results of knee simulator studies, in terms of wear volume and size of the debris produced, have been shown to be similar to those found in early retrieved knee prostheses [25–27].

Overall, the particle size distribution in the present study is comparable to those of former particle analyses of bicondylar knee prostheses. As already mentioned, the most particles were found to be submicron, which correlates with the SEM based findings of a knee simulator based study that compared cross-linked and conventional polyethylene inserts for bicondylar knee systems [10]. In this study the mean diameter of the analyzed particles was between 0.37 μm and 0.48 μm and therefore submicron [10]. In the present study the particles are even smaller with 0.13-0.14 μm (given as median) as demonstrated in Table 2. Furthermore, a recent retrieval study by Minoda et al. verified a mean ECD of wear particles from well-functioning total knee prostheses of various material types and designs in a size range from 0.64 μm to 0.81 μm [28]. In this study a filter with a 0.1 μm pore size was used, which might explain the slightly larger values of the particle size distribution.

Interestingly three research groups investigated the impact of methodology concerning a standardized particle analysis in a round robin test [29]. They found that several not exactly defined differences in the complex methodology of wear particle analysis significantly influence the results, for instance, the use of different pore size filter membranes or the use of different SEMs [29]. Therefore, the relatively wide interobserver variability is roughly explainable.

The particles found in the present study were mostly round in shape, smooth, granular, and irregular. According to the sizing of Sieving et al. [13] only the PMMA particle group showed a higher percentage of particles with an AR ≥ 2.4 (13.42%) [13]. This is an important fact, as it is known that fibrillar particles with an AR ≥ 2.4 show increased inflammatory reactions compared to round and granular particles [13, 30]. This has to be assessed with regard to the particle size distribution: Green et al. reported that even small differences in the size range (mean size 0.24 μm versus 0.45 μm and 1.71 μm) lead to different reactions of macrophages in vitro [7]. The particles with a mean size of 0.24 μm were the most reactive [7]. As the most particles of
all groups in the present study are even smaller it has to be
assumed that they are in a biologically reactive size range. The
PMMA group, especially, tends towards a higher percentage
of fibrillar particles, which are supposed to be biologically
more reactive.

Respectively, there are no relevant though statistically
significant differences between the groups. The statistical
significance is rather due to the extremely high group sizes.
This problem occurred in a former study as well [10]; the
statistical rating has to be used only carefully.

The most imposing difference between the tested groups
in the present study was yet the absolute number of particles
per million cycles. The particles were calculated using a
previously developed formula [10]. The calculation of the par-
ticles is essentially based on two factors: first, the measured
gravimetric/volumetric wear rate of the polyethylene inserts
and, second, the hypothesized volume of the wear particles.
In the calculation of the volume the three-dimensional shape
of the particle is assumed to be spherical. Therefore, the ECD
of the particles is used as diameter for the calculation. This
is an approximately simplified model of the particle shape, as
the real volume cannot be assessed using SEM. As the most
particles have an AR < 2.39, this assumption seems to be
justified [10]. However, the addition of PMMA third-bodies
lead to tenfold particle generation compared to the steady
state phase and the bone particle group. It is important to
note that the number of particles in a given total volume
increases as the particle size decreases. This might explain
the rather high particle numbers compared to the findings by
Utzschneider et al. [10]. They had found particle numbers in
the range of 5–20 × 10^9 [10].

The findings in the present study have to be associated
with the complex cellular pathogenesis in the development
of periprosthetic osteolysis in response to wear debris [5, 6].
Thus, it has to be assumed that PMMA third-bodies via
the generation of multiple particles, especially, negatively
influence the biologic reaction and finally lead to an increased
inflammatory reaction that ends in an aseptic loosening of the
prosthesis. Other factors, including particle surface texture
and surface chemistry, could influence the cellular response
as well. Further investigation in adequate in vivo models is
mandatory to clarify the biological activity of the wear debris
isolated in this study.

As limitations in the present study the wear simulation
tests have to be named. They were performed in a single series
of 8.0 million cycles divided in four test groups, rather than
different series testing each step. But the advantage in this
setup is the identical positioning of the prosthesis throughout
the 8.0 million cycles allowing identical test conditions for all
groups. Another limitation is the point of time of the addition
of the third-bodies. First, they were added after reaching the
steady state phase which allows using that phase as a control
concerning wear rate and particle generation. This certainly
cannot totally be transferred to the clinical situation, as
the third-bodies are most likely placed already during the
implantation of the prosthesis. The order of the third-body
particles might influence the results as well. As the wear rate
did not change after adding the third-body bone particles
compared to the steady state phase, negligible changes of the
wear pattern were assumed [12].

The particle analysis was performed using a grayscale
detection method. This allows objective particle measure-
ments. On the other hand, small grayscale differences cannot
be captured by the software, which might lead to values
that do not reflect the absolutely correct size and shape of
the particles. Additionally, the geometrical structure of the
particles can only be assumed, as SEM analysis does not allow
a three-dimensional measurement of the particles.

5. Conclusion

The results of the present study demonstrate the evident
effect of PMMA third-body wear particles on the particle
generation after UKA in a knee simulator based study. The
PMMA particles increase the generation of numerous particles and slightly alter the particle morphology towards
fibrillar particles. This might lead to an elevated inflammatory
response after UKA in vivo and, therefore, even lead to an
ever lasting failure of the unicondylar knee prosthesis.

In this regard the careful removal of PMMA debris and
a thorough lavage after UKA implantation is mandatory. In
order to detect missed PMMA pieces, postoperative X-ray
diagnosis should be used to verify hidden third-bodies.

Conflict of Interests

The authors declare that there is no conflict of interests
regarding the publication of this paper.

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