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The influence of a calcium sulphate bone void filler on the third-body damage and polyethylene wear of total knee arthroplasty

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Objectives

Bone void fillers are increasingly being used for dead space management in arthroplasty revision surgery. The aim of this study was to investigate the influence of calcium sulphate bone void filler (CS-BVF) on the damage and wear of total knee arthroplasty using experimental wear simulation.

Methods

A total of 18 fixed-bearing U2 total knee arthroplasty system implants (United Orthopedic Corp., Hsinchu, Taiwan) were used. Implants challenged with CS-BVF were compared with new implants (negative controls) and those intentionally scratched with a diamond stylus (positive controls) representative of severe surface damage ($n = 6$ for each experimental group). Three million cycles (MC) of experimental simulation were carried out to simulate a walking gait cycle. Wear of the ultra-high-molecular-weight polyethylene (UHMWPE) tibial inserts was measured gravimetrically, and damage to articulating surfaces was assessed using profilometry.

Results

There was no significant difference ($p > 0.05$) between the wear rate of implants challenged with CS-BVF (3.3 mm^3/MC (95% confidence interval (CI) 1.8 to 4.8)) and the wear rate of those not challenged (2.8 mm^3/MC (95% CI 1.3 to 4.3)). However, scratching the cobalt-chrome (CoCr) significantly ($p < 0.001$) increased the wear rate (20.6 mm^3/MC (95% CI 15.5 to 25.7)). The mean surface roughness of implants challenged with CS-BVF was equivalent to negative controls both after damage simulation ($p = 0.98$) and at the conclusion of the study ($p = 0.28$).

Conclusion

When used close to articulating surfaces, a low-hardness, high-purity CS-BVF had no influence on wear. When trapped between the articulating surfaces of a total knee arthroplasty, CS-BVF did not scratch the surface of CoCr femoral components, nor did it increase the wear of UHMWPE tibial inserts compared with undamaged negative controls.

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Keywords: Biotribology, Ultra-high-molecular-weight polyethylene (UHMWPE), Knee arthroplasty, Bone void filler, Calcium sulphate

Article focus

- The aim of this study was to investigate the influence of third-body wear with synthetically manufactured grade calcium sulphate bone void filler (CS-BVF) on a total knee arthroplasty.
- The wear of implants damaged with the CS-BVF were compared with negative controls tested in a clean environment and positive controls where the implant had been scratched to represent severe third-body damage.
- The change in surface topography of the cobalt-chrome femoral components and the wear of the ultra-high-molecular-weight polyethylene (UHMWPE) tibial components were assessed.

Key messages

- Simulating third-body damage with synthetically manufactured CS-BVF did not significantly change the mean surface roughness of cobalt-chrome femoral components compared with negative controls.

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- Third-body wear simulation with synthetically manufactured CS-BVF did not elevate the wear of UHMWPE tibial components compared with negative (unscratched) controls.
- Scratching cobalt chrome femoral components to represent severe third-body damage significantly increased UHMWPE wear compared with unscratched (negative) controls tested in a clean environment.

Strengths and limitations

- This is the first study to investigate the influence of third-body wear by CS-BVF in a whole knee joint simulation study.
- Implants damaged with CS-BVF have been directly compared with both new implants and those damaged to represent severe third-body damage.
- Caution should be taken in the clinical interpretation of these findings, which may not necessarily translate to all bone void filler materials.

Introduction

Total knee arthroplasty (TKA) is a highly successful procedure to restore joint function and reduce pain in patients with osteoarthritis of the knee. Despite a long-term survivorship of >95% at ten years,[1] infection is the primary cause for revision within the first year of implantation,[1] and infection rates are rising.[2] In 2005, infection accounted for 3.5% of all single-stage revision knee procedures,[3] increasing to 5.3% by 2015.[1] Superficial infection is often treated using systemic antibiotics; deep infection, however, usually requires surgical intervention including debridement and washout, often necessitating revision of the implant.[4] Extensive debridement of infected or necrotic tissue can result in dead space, which can provide a potential source of reinfection. Strategies for dead space management must therefore be considered. Allografts and a variety of synthetic materials including non-degradable bone cement, and resorbable materials such as hydroxyapatite, collagen, fibrin, polylactides, calcium phosphate, and calcium sulphate have been used.[5] Due to the presence of infection, clinicians frequently combine these void fillers with antibiotics to enable the release of elevated levels of antibiotic at the surgical site.[6-10]

The presence of loose particles around a TKA means there is potential for them to become entrained between articulating surfaces acting as third-body particles. Retrieval studies of TKAs have shown particles such as bone fragments, bone cement, and porous-coating beads embedded in the polyethylene tibial component; where these particles have articulated against cobalt chrome (CoCr) femoral components, linear scratches have been observed on the implants.[11,12] Experimental wear simulation has shown that counterface roughness has a strong influence on the wear of ultra-high-molecular-weight polyethylene (UHMWPE), and scratches to CoCr counterfaces with a lip height as low as 1 µm can influence UHMWPE wear rate.[13] The directionality of the scratches, relative areas of contact, and the lip height of the scratches all influence the severity of polyethylene wear, therefore more thorough investigations on the effects of third-body particles are required.

Previous experimental studies have replicated third-body wear in total joint arthroplasty either by introducing third-body particles into the lubricant[14] or by scratching the metallic surface of implants directly.[15] There are advantages and limitations to both methods, therefore the method adopted should be determined by the research question. Considering third-body wear of TKAs, Ries et al[16] tumbled CoCr knee femoral components with alumina to create a roughened surface with a random orientation of scratches. This method of damage simulation elevated UHMWPE wear ten-fold.[16] The introduction of cement particles between the articulating surfaces of a TKA or unicompartmental knee arthroplasty (UKA) has been shown to increase the wear rate of metal-on-polyethylene (MoP) implants and to scratch CoCr femoral components.[17,18] The small number of studies carried out suggest that the type of particles (e.g. poly(methyl methacrylate) (PMMA) cement or bone) and their abrasiveness have more influence on UHMWPE wear than particle size.

When replicating third-body damage *in vitro* with particles, a number of difficulties must be overcome. First, controlling the number of particles trapped between the articulating surfaces is difficult, especially with the low-conforming nature of TKA and the tendency for the lubricant to agitate the particles, washing them away from the articulating surfaces. Zietz et al[17] overcame this problem by adding particles of bone cement to tibial components, running the simulator without lubricant to create damage, before adding the lubricant and continuing the wear test. Dosing of the lubricant with particles was carried out to replicate the extended duration the non-resorbable cement particles would be present in the joint. In MoP implants, difficulties can also be encountered in assessing wear gravimetrically due to the potential for particles to become embedded in the polyethylene.[17]

The third-body particle of interest in this study was a calcium sulphate bone void filler (CS-BVF) used for dead space management in arthroplasty surgery, which typically resorbs within six to eight weeks.[19] The influence of calcium sulphate on third-body wear has been previously investigated in the hip[20] and in simple geometry pin-on-plate/pin-on-disc studies.[21,22] In all studies, calcium sulphate did not scratch the surface of CoCr counterfaces with a lip height of sufficient magnitude to influence polyethylene wear rate. The hip simulation study, however, showed an elevated wear rate while calcium sulphate was present in the lubricant.[20] The pin-on-plate study by Cowie et al[21] compared calcium

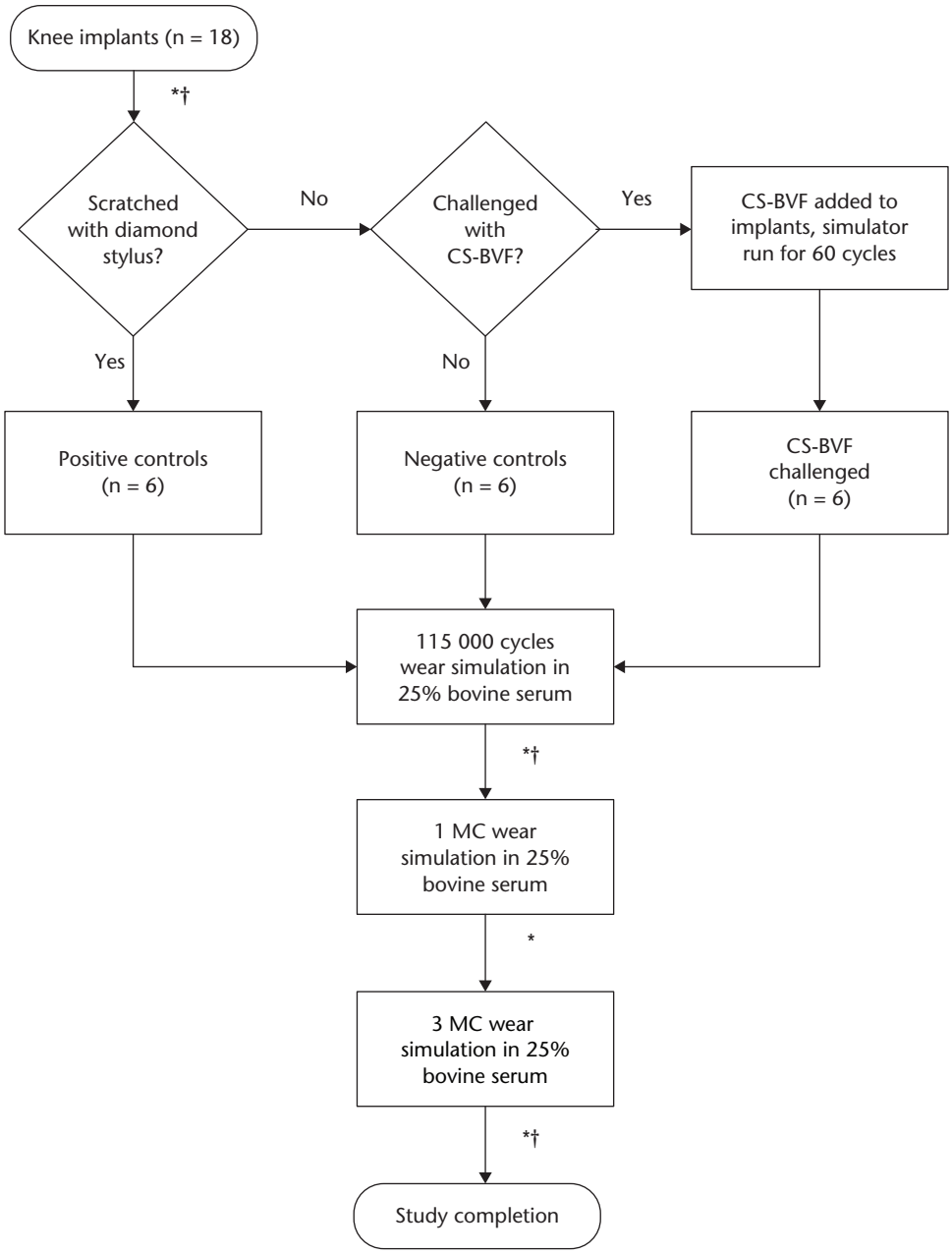

Fig. 1

Flowchart showing the different test conditions. *Gravimetric analysis. †Surface topography assessment. CS-BVF, calcium sulphate bone void filler; MC, million cycles.

sulphate products of similar composition differing by the processing route of the base material and therefore their purity. Hard earth impurities in one of the calcium sulphates tested were thought to contribute to scratching of CoCr counterfaces, although the lip height of the scratches was not of sufficient magnitude to influence polyethylene wear. However, these tests were carried out in a simple geometric configuration and over a relatively short duration.[21]

The aim of this study was to investigate the influence of CS-BVF on the third-body wear of TKAs using experimental simulation. The implications to the wear of the UHMWPE tibial component and the surface topography of the CoCr femoral components were considered if loose beads of CS-BVFs acting as third-body particles were to become trapped between the articulating surfaces. It was hypothesized that CoCr would not be scratched sufficiently by the CS-BVFs to influence the wear of UHMWPE tibial components.

Materials and Methods

Materials. The third-body particles were hemispherical beads, 3 mm in diameter, prepared from commercially available CS-BVF (Stimulan Rapid Cure; Biocomposites

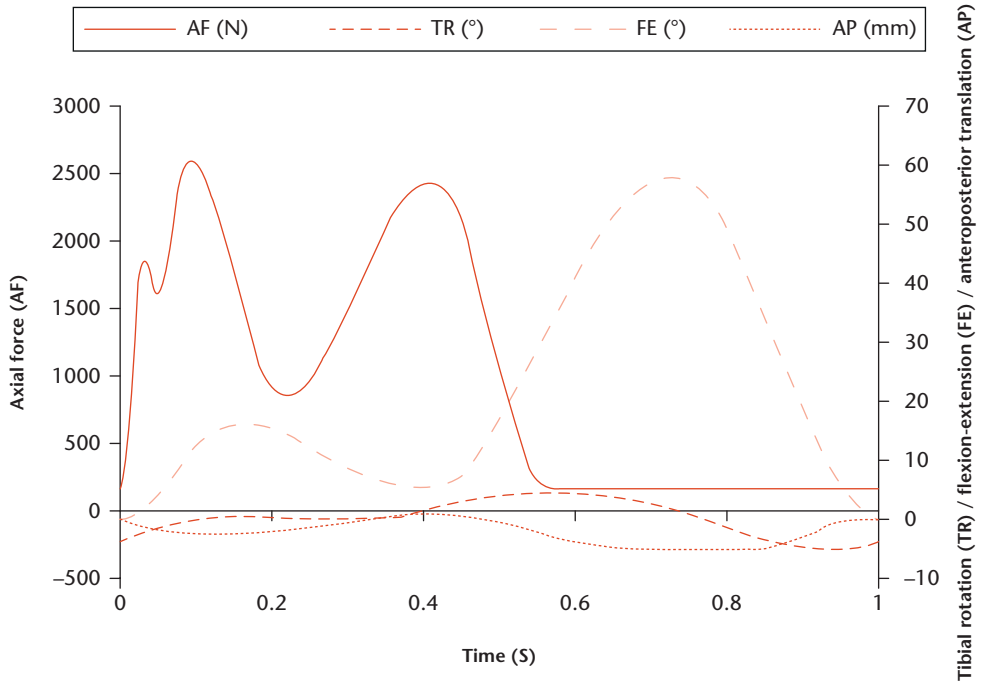

Fig. 2

Chart showing the input kinematic conditions to knee simulator.

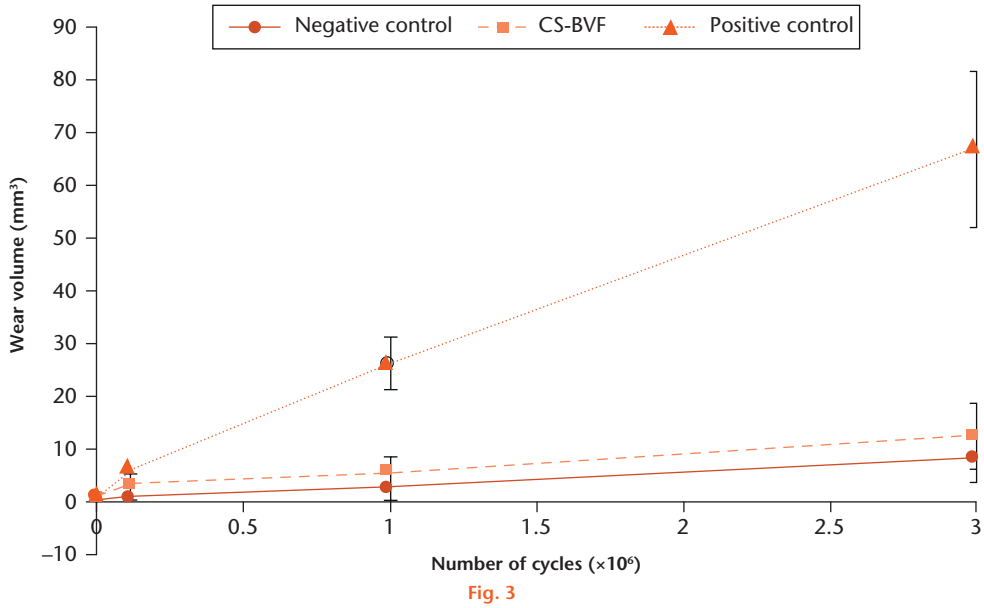

Fig. 3

Chart showing mean wear volume (mm^3) and 95% confidence intervals of ultra-high-molecular-weight polyethylene (UHMWPE) tibial components (n=6). CS-BVF, calcium sulphate bone void filler.

Ltd, Keele, United Kingdom) in accordance with the manufacturer's instructions. This is a clinically used, fully absorbable pharmaceutical grade of calcium sulphate, manufactured via a synthetic route.[23] The CS-BVF was supplied as a calcium sulphate hemihydrate powder, which was combined with the mixing solution provided (water) to form a paste. The paste was then transferred to the bead mat supplied, which can be used to make hemispherical beads in three different diameters: 3 mm, 4.8 mm, and 6 mm. The 3 mm diameter beads were selected for this study. Once the beads were set (eight minutes), the bead mat was flexed to remove the beads. A total of 18 fixed-bearing (right, mid-sized (#3)), U2 posterior-stabilized total knee arthroplasty system implants (United Orthopedic Corp., Hsinchu, Taiwan) were tested, consisting of a CoCr-molybdenum (CoCrMo)

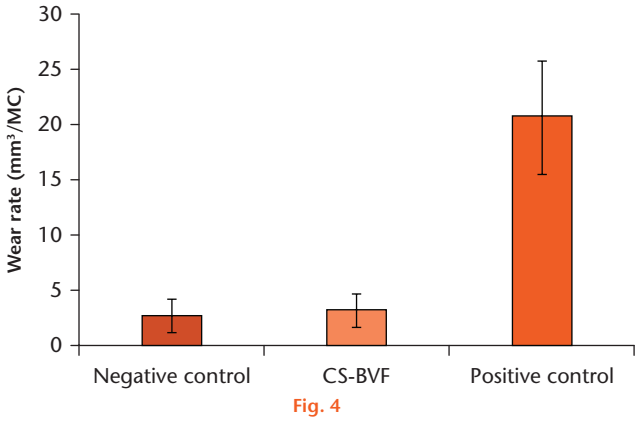

Fig. 4

Chart showing mean wear rate calculated between 115 000 cycles and 3 MC (mm³/MC) and 95% confidence intervals of ultra-high-molecular-weight polyethylene (UHMWPE) tibial components (n = 6). CS-BVF, calcium sulphate bone void filler.

femoral component articulating against an irradiation-sterilized, conventional UHMWPE tibial component fixed into a Ti6Al4V tray. Prior to testing, the UHMWPE tibial components were soaked in sterile water for a minimum of two weeks to maximize moisture uptake. Three experimental groups of six implants were investigated (Fig. 1). New implants (negative controls, initial mean surface roughness (Ra) ~ 0.02 µm) were assessed to give a baseline wear rate for this implant. For the positive controls, the CoCr femoral components were scratched directly with a diamond stylus, representative of 'severe' third-body damage, to demonstrate that scratches with a sufficiently large lip height would influence UHMWPE wear.[24] Scratches were created using a 200 µm radius diamond stylus (Euro Products Ltd., Stourbridge, United Kingdom) in a grid pattern within the articulation zone of both medial and lateral condyles; 15 scratches ran mediolaterally and seven ran parallel to the flexion-extension (FE) axis, with 2 mm spacing. Scratches had a lip height > 3 µm,[13] an initial maximum profile height averaged over the sampling length (Rp) of ~1.3 µm, and an initial Ra of ~0.4 µm.

Methods. Experimental wear simulation was carried out using a six-station Leeds/ProSim electropneumatic knee simulator (Simulation Solutions, Stockport, United Kingdom).[25] The simulator has six degrees of freedom with four controlled axes of motion: axial force (AF), flexion/extension (FE), tibial rotation (TR), and anteroposterior displacement (AP). Abduction-adduction was unconstrained and the mediolateral offset fixed as detailed in the ISO standard.[26] Leeds intermediate kinematic conditions were used (Fig. 2); AF (maximum 2800 N) and FE (0° to 60°) were adapted from ISO 14243-3.[26] Tibial rotation (± 5°) and AP (maximum 5 mm) were driven through the tibial side of the implant and based on the natural kinematics of the knee.[25] Displacement control was used for the AP and TR motion to maintain consistency between the input kinematics irrespective of changes in the surface topography of the articulating surfaces.

The methodology described by Zietz et al[17] was adapted to simulate third-body wear using a single 5 cc dose of CS-BVF beads, typical of the volume used in infected TKA revision procedures.[19] The beads were placed on both compartments of the tibial component and, to ensure they became entrained within the articulating surfaces, the simulator was run without lubricant for 60 cycles. The test lubricant, 25% bovine serum with 0.03% (v/v) sodium azide solution, was then added to the test cell and the simulator was run for 115 000 cycles. The timepoint replicated the six to eight weeks that the CS-BVF beads are present before their resorption,[19] based on a typical TKA patient completing one million steps per year. This was the only dose of CS-BVF used as, after this duration, the CS-BVF would have resorbed[19] so no further third-body damage would occur.

The surface topography of the articulating surfaces of the femoral components was assessed prior to the start of the study, after 115 000 cycles, and after three million cycles (MC) (Fig. 1), using a Taylor Hobson Form Talysurf with a 2 µm conical tip stylus (Taylor Hobson Ltd., Leicester, United Kingdom). Five measurements were taken across each femoral condyle in a mediolateral direction within the flexion range. Least squares arc form removal and Gaussian filtering with a lower cut-off of 0.25 mm was applied to the measurements in line with ISO 4288:1998.[27] The surface roughness parameters of interest were Ra, Rp, and the maximum valley depth (Rv). To investigate the influence of CS-BVF on third-body wear of UHMWPE, 3 MC of experimental wear simulation were carried out under the previously described test conditions. After every 0.3 MC, the simulator was stopped and cleaned, and the lubricant was replaced. After every 1 MC, the implants were moved to the adjacent station to reduce interstation variability. The wear of the UHMWPE tibial components was assessed gravimetrically at 115 000 cycles, 1 MC, and 3 MC (Fig. 1) using a Mettler Toledo XP205 digital microbalance (Mettler Toledo Inc., Columbus, Ohio) with a resolution of 0.01 mg. Two unloaded soak controls were used to compensate for moisture uptake by the polyethylene.

The data set associated with this article is openly available from the University of Leeds Data Repository.[28]

Statistical analysis. The mean and 95% confidence intervals (CIs) were calculated for the wear rate, and for surface parameters Ra, Rp, and Rv. Statistical analysis was carried out between the three experimental groups using one-way analysis of variance (ANOVA) with a *post hoc* Tukey's test in SPSS 22 (IBM Corp., Armonk, New York). Data were considered significant at $p < 0.05$.

Results

When the beads of CS-BVF were trapped between the components, and the simulator was run without lubricant,

Table I. Mean surface roughness and 95% confidence intervals (CI) of femoral components taken in a mediolateral direction following 115 000 cycles of wear simulation and three million cycles (MC) of wear simulation (n = 6)

	After 115 000 cycles wear simulation			After 3 MC wear simulation		
Parameters	**Negative controls**	**CS-BVF**	**Positive controls**	**Negative controls**	**CS-BVF**	**Positive controls**
Mean Ra, μm (95% CI)	0.020 (0.014 to 0.026)	0.023 (0.018 to 0.028)	0.430 (0.391 to 0.469)	0.057 (0.022 to 0.092)	0.092 (0.045 to 0.139)	0.450 (0.411 to 0.489)
Mean Rp, μm (95% CI)	0.041 (0.027 to 0.055)	0.035 (0.025 to 0.045)	1.327 (1.224 to 1.430)	0.125 (0.047 to 0.203)	0.143 (0.084 to 0.202)	1.361 (1.208 to 1.514)
Mean Rv, μm (95% CI)	0.045 (0.023 to 0.067)	0.042 (0.032 to 0.052)	0.838 (0.743 to 0.933)	0.150 (0.070 to 0.230)	0.240 (0.132 to 0.348)	0.878 (0.797 to 0.959)

CS-BVF, calcium sulphate bone void filler; Ra, mean surface roughness; Rp, maximum profile height averaged over the sampling length; Rv, maximum valley depth

the calcium sulphate was ground to a fine powder. Figure 3 shows the wear volume of the UHMWPE tibial components over the duration of the study. The wear rate of the UHMWPE tibial components was higher in the CS-BVF group (24.1 mm^3/MC (95% CI 0.9 to 47.3)) and the positive control group (49.9 mm^3/MC (95% CI 43.6 to 56.2)) between 0 and 115 000 cycles than between 115 000 cycles and 3 MC. For the negative controls, the wear rate between 0 and 115 000 cycles was 2.4 mm^3/MC (95% CI 0.6 to 4.2), and there was no apparent change in the wear rate of the negative control components over the duration of the study.

Figure 4 shows the mean wear rate of the UHMWPE tibial components during wear simulation between 115 000 cycles and 3 MC when no CS-BVF particles were present in the test cell. Between these timepoints, the influence of surface damage caused by the CS-BVF on the wear of the UHMWPE could be assessed. The mean wear rate of the negative controls was 2.7 mm^3/MC (95% CI 1.2 to 4.2). Implants challenged with CS-BVF and the positive controls had wear rates of 3.3 mm^3/MC (95% CI 1.8 to 4.8) and 20.6 mm^3/MC (95% CI 15.5 to 27.7), respectively. A one-way ANOVA of all the groups showed a significant difference ($p < 0.001$) in wear rate of the UHMWPE tibial components under the different test conditions; however, *post hoc* analysis showed there to be no significant difference ($p = 0.95$) between the negative controls and implants challenged with CS-BVF. Visual inspection of the tibial components showed no evidence of CS-BVF particles embedded in the polyethylene.

Light scratching was visible on the surface of the CoCr femoral components of both the negative controls and the implants challenged with CS-BVF. The surface roughness of the femoral components was assessed after 115 000 and 3 MC wear simulation (Table I). One-way ANOVA showed a significant difference ($p < 0.001$) in all the surface roughness parameters measured; however, *post hoc* analysis showed no significant difference between the surface roughness of the negative control implants and those challenged with CS-BVF at the conclusion of the study for Ra ($p = 0.28$), Rp ($p = 0.95$), or Rv ($p = 0.20$).

Discussion

This study used experimental full-joint simulation to replicate third-body wear of TKAs with CS-BVF. It was hypothesized that third-body wear with CS-BVF would not influence the wear of polyethylene.[20-22]

The negative controls gave the baseline wear rate for this implant tested under Leeds intermediate kinematic conditions. Under these conditions, a typical wear rate for a moderately conforming fixed-bearing knee arthroplasty with a conventional polyethylene tibial insert would be 8.6 mm^3/MC (95% CI 5.2 to 12).[25] The wear rate of this implant was lower at 2.7 mm^3/MC (95% CI 1.2 to 4.2), but of the same order of magnitude to similar designs tested under the same conditions.[25] Measuring low wear rates (< 5 mm^3/MC) by gravimetric analysis is difficult and brings about the potential for wear to be influenced by random errors in the system. The implants challenged with CS-BVF showed no significant difference in steady state wear rate (3.3 mm^3/MC (95% CI 1.8 to 4.8)) compared with the negative controls. When the beads of CS-BVF were trapped between the components in the simulator, the CS-BVF became a fine powder, visual inspection showed no CS-BVF particles embedded in the polyethylene, and there was no influence on the surface roughness of the implants compared with the negative controls. Previous studies applying a similar experimental approach using cement particles containing hard agglomerates of zirconium dioxide have shown scratching to the CoCr femoral components and an elevated wear rate of UHMWPE;[17,18] however, introduction of bone fragments into the lubricant did not influence wear.[18] Therefore, the abrasiveness of the third-body particle is a strong determinant as to whether the CoCr counterfaces will become scratched by the debris.[18,29] The wear of UHMWPE is influenced by the lip height of the scratches on CoCr counterfaces, which must be above a critical value to elevate wear.[30] In this study, only the scratches on the positive control implants, representative of surface damage at the upper limit of that measured on retrieved femoral knee[31] and hip[24] components, had lip heights of sufficient magnitude to influence the wear rate of UHMWPE (20.6 mm^3/MC (95% CI 15.5 to 25.7)). The approach used to create

scratches on the surface of the CoCr femoral components has not previously been used in the simulation of third-body damage in TKAs; however, this method has been used extensively in simple geometry studies[13] and total hip arthroplasties.[15,32] In a hip simulation study, scratches created with a lip height of 3 µm led to an eight-fold increase in wear compared with undamaged controls.[32] The increase in wear rate seen in this study is of similar magnitude.

Previous studies investigating third-body wear with calcium sulphate in the hip have shown a higher rate of UHMWPE wear while the calcium sulphate was *in situ*.[20] When the third-body challenged implants were subsequently tested in a clean environment, the wear rates returned to values similar to those of the negative controls. An elevated wear rate and a high variability in the wear rate of UHMWPE were also noted in the present study between 0 and 115 000 cycles when CS-BVF was present in the test lubricant (mean wear rate of 24.1 mm^3/MC (95% CI 0.9 to 47.3) between 0 and 115 000 cycles; 3.3 mm^3/MC (95% CI 1.8 to 4.8) between 115 000 and 3 MC). This effect was not seen in the negative controls (mean wear rate of 2.4 mm^3/MC (95% CI 0.6 to 4.2) between 0 and 115 000 cycles; 2.8 mm^3/MC (95% CI 1.3 to 4.3) between 115 000 and 3 MC). However, a similar elevated wear rate was seen in the positive controls (mean wear rate of 49.9 mm^3/MC (95% CI 43.6 to 56.2) between 0 and 115 000 cycles; 20.6 mm^3/MC (95% CI 15.5 to 25.7) between 115 000 and 3 MC), so it was not known whether this was a test artefact perhaps caused by inconsistent moisture uptake by the polyethylene due to the very short test interval (115 000 cycles), or whether the elevated wear rate was a real effect. If the elevated wear rate was a real effect, with the short duration that the calcium sulphate beads remain in the body prior to their resorption, it is not anticipated that this short-term increase in wear rate would accelerate wear-debris-induced osteolysis. Our findings corroborate those of previous studies that have investigated the use of CS-BVF materials and have shown them not to influence the wear of UHMWPE.[20-22]

Following third-body wear, light linear scratching was apparent on the surface of the CoCr femoral components running in an AP direction, the principle direction of sliding. The measured surface roughness of the CoCr femoral components, however, was similar to that of the negative control implants. With the third-body damage methodology used, CS-BVFs were therefore considered to have no influence on the surface topography of the CoCr femoral components. Scratching parallel to the direction of the FE motion commonly occurs during experimental wear simulation of knee arthroplasties, even without the addition of contaminants to the lubricant.[33]

There were limitations associated with this *in vitro* study that must be considered in the clinical interpretation of the findings. One of the limitations was its duration: 3 MC is equivalent to three years *in vivo* in a moderately active patient;[34] a younger, more active patient, however, may complete a greater number of steps, approaching two million per year.[35] Also, the damage simulation was carried out in ~ 30 hours, an equivalent number of cycles to the six to eight weeks in which the CS-BVFs typically resorb. It should also be noted that the calcium sulphate used in this study was a commercially available, synthetically manufactured CS-BVF product and hence had a high purity (>99%). Other similar CS-BVF materials may be manufactured by different processing routes. Medical-grade calcium sulphate, for example, is derived from earth-sourced gypsum rock and is a relatively soft material with a value of 2 on the Mohs scale.[36] However, it may contain insoluble and potentially harder impurities such as quartz (7 on the Mohs scale)[36] or slower-absorbing calcium phosphate constituents that may have an influence on the wear of UHMWPE,[21] meaning that the findings from this study do not translate directly to all bone void filler materials.

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Author contributions

- R. M. Cowie: Designed the study, Acquired and analyzed the data, Wrote the manuscript.
- S. S. Aiken: Designed the study, Prepared the bone void fillers, Wrote the manuscript.
- J. J. Cooper: Designed the study, Wrote the manuscript.
- L. M. Jennings: Designed the study, Analyzed the data, Wrote the manuscript.

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