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Investigation of Wear and Wear Particles from a UHMWPE/Multi-Walled Carbon Nanotube Nanocomposite for Total Joint Replacements

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Abstract

Ultra high molecular weight polyethylene (UHMWPE) has been extensively used as a bearing surface in joint prostheses. However, wear debris generated from this material has been associated with osteolysis and implant loosening. Alternative materials, such as polymer composites, have been investigated due to their exceptional mechanical properties. The goal of the present work was to investigate the wear rate, size and volume distributions, bioactivity and biocompatibility of the wear debris generated from a UHMWPE/Multi-walled carbon nanotube (MWCNT) nanocomposite material compared with conventional UHMWPE. The results showed that the addition of MWCNTs led to a significant reduction in wear rate. Specific biological activity and functional biological activity predictions showed that wear particles from the UHMWPE/MWCNT nanocomposite had a reduced osteolytic potential compared to those produced from the conventional polyethylene. In addition, clinically relevant UHMWPE/MWCNT wear particles did not show any adverse effects on the L929 fibroblast cell viability at any of the concentrations tested over time. These findings suggest that UHMWPE/MWCNT nanocomposites represent an attractive alternative for orthopaedic applications.

Keywords: Biotribology, wear debris, ultra high molecular weight polyethylene, nanocomposites, biocompatibility, joint prostheses.

1. Introduction

Joint replacements are considered to be one of the most successful surgical interventions of the 20^{th} century due to their effective treatment of chronic pain and diseases such as osteoarthritis, rheumatoid arthritis, hip fractures or tumors. Ultra high molecular weight polyethylene (UHMWPE) has been extensively used as a bearing surface in total joint replacements. UHMWPE on metal bearing couples are an excellent solution in the short to medium term. However, in the longer term, problems associated with biological responses to wear particle leading to osteolysis and aseptic loosening are the major cause of failure of artificial joints [1]. Since the longevity of joint replacements has been directly related to the wear of their components, interest in developing alternative novel materials with lower wear rates and improved biocompatibility has increased. Highly crosslinked polyethylenes (HXLPEs) have been developed to improve the wear performance of UHMWPE. Previous investigations have shown that crosslinking of the polymer chains through irradiation significantly reduces the wear rate of UHMWPE [2,3]. However, it has been shown that the mechanical properties of polyethylene, such as impact toughness and fatigue, are compromised after crosslinking [4]. In addition, residual free radicals are generated during the irradiation processing in the UHMWPE, making the material more susceptible to in vivo oxidation [5].

An alternative for improving the wear performance of polyethylene is the use of polymer composites. Selected fillers, such as carbon fibres and multi-walled carbon nanotubes (MWCNTs) have been investigated in recent decades. In the 1970's, a carbon fibre-reinforced polyethylene composite was introduced as a bearing material for orthopaedic applications [6]. Although short-term clinical failures, attributed to the lack of bonding between the polyethylene matrix and the carbon fibres, led to the withdrawal of this composite, the long-term performance of the composite has not been fully understood to date. Recently, long-term implanted components (average in vivo duration of retrievals of 11.1 years) of a carbon fibre-reinforced UHMWPE material have been investigated [7]. The results of this study indicated that the reinforced material and historical UHMWPE components had comparable clinical and material performance after long-term implantation. This study also showed that the use of carbon fibres as a reinforcing material did not increase the risk of osteolysis compared to historical UHMWPE. More recently, carbon fibre reinforced polyetheretherketone (CFR-PEEK) has been investigated as an alternative bearing to UHMWPE in the hip. This material composite has shown extremely low wear rates and comparable biological activity to UHMWPE [8]. All these findings may provide motivation for revisiting the use of carbon composites in orthopaedics over the next few decades.

In addition to carbon fibres, MWCNTs provide an attractive alternative for reinforcing polyethylene. MWCNTs have excellent mechanical properties such as high tensile strength and are ultra-light weight [9]. Previous studies have shown the ability of carbon nanotubes to improve the mechanical properties of polymers. Zou et al. [10] reported a 21.5% increase in toughness of neat high density polyethylene (HDPE) at MWCNT content of 1 wt%. Sreekanth et al. [11] found an enhancement of the surface hardness of virgin UHMWPE due to the addition of MWCNTs and Ruan et al. [12] observed that the Young's modulus and yield stress of UHMWPE were enhanced by 25 and 47.6 %, respectively, by the reinforcement of 1 wt% MWCNTs. An improvement in the wear performance of conventional UHMWPE due to the addition of MWCNTs has also been reported [13]. However, it is known that not only the wear rates play a role in the biological reaction to wear debris but also factors such as the morphology, size, volume and composition of the wear particles are important [14] and [15]. Although this fact is a key factor in the success of the bearings, to the author's knowledge, there are no studies which use clinically relevant wear debris generated from this type of nanocomposites or assess the bioactivity of this type of wear particles.

The present study has been focused on UHMWPE/MWCNT nanocomposites with up to 1 wt% MWCNT content. Previous findings suggest that only small amounts of nanofillers can be successfully mixed in a polymer matrix and exceeding this limit can cause embrittlement of the composite [16]. A study performed by Zou et al. [10] showed that the toughness of a HDPE reinforced with MWCNTs was negatively affected when MWCNT content exceeded 1 wt% due to the formation of big filler agglomerates. Thus, the present work has been focused on the investigation of UHMWPE/MWCNT nanocomposites with 0.5 wt% and 1 wt%.

The objective of this work was to investigate the wear rate, size and volume distributions and bioactivity of the wear debris generated from a novel UHMWPE/MWCNT nanocomposite compared with conventional UHMWPE. This study also assessed clinically relevant wear particles, generated by articulation from the novel UHMWPE/MWCNT nanocomposite and conventional UHMWPE, for possible cytotoxic activity.

2. Materials and Methods

2.1 Materials

Two novel UHMWPE/MWCNT nanocomposites, with 0.5 wt% and 1 wt% MWCNTs, were investigated and compared with virgin GUR 1020 UHMWPE. The UHMWPE/MWCNT nanocomposites used in the present study were manufactured with UHMWPE GUR 1020 powder (Ticona, Germany), with an average molecular weight of $3.5x10^6$ g/mol, density of 0.93 g/cm^3 and an average size of particle of 140 μm, and Nanocyl-3150 MWCNTs (Nanocyl, Belgium), with a purity of >95%, a particle diameter of 5-10 nm and a length of 1-5 μm. The nanocomposites were manufactured in house under optimized conditions using a ball milling technique to obtain a homogeneous dispersion [17]. After the compression process, nanocomposites and virgin UHMWPE bar stock were machined into wear pins (contact face= 10 mm in diameter). Smooth (average surface roughness= 0.01 μm) high carbon (>0.2 %

w/w) cobalt chromium alloy plates were used as counterface surfaces. All samples were measured for surface roughness by contact profilometry (Talysurf Series, UK).

2.2 Wear testing

Prior to testing, pins were soaked in distilled water for at least 2 weeks until moisture content levels were stable and then stored for at least 48 hours in a temperature controlled environment to stabilise the material. After this, pins were weighed using a digital precision balance (Mettler Toledo AT21, accuracy ±10 µg, UK,). Each pin was weighed until five measurements within a ± 5µg range were obtained. A six station multidirectional pin on plate wear tester was used for wear tests [18]. Wear pins were articulated against smooth (average surface roughness= 0.01 µm) high carbon (> 0.2 % w/w) cobalt chromium plates. In each test, two pins of each material (virgin UHMWPE GUR 1020, UHMWPE/MWCNT 0.5 wt% and UHMWPE/MWCNT 1 wt% nanocomposites) were tested. Each test lasted 2 weeks (>500,000 cycles) and tests were repeated 3 times with new pins. Tests were carried out under standard hip kinematic conditions, under a load of 160N (nominal contact pressure= 2 MPa),± 30 degrees of rotation, at 1Hz and with a stroke length of 28 mm. Testing was conducted in 25% (v/v) newborn bovine serum, supplemented with 0.03% (w/v) sodium azide solution to inhibit microbial activity. The serum solution was renewed approximately every 350,000 cycles and the components of the wear test rig were cleaned. Unloaded soak control pins of each material were used to provide a correction for moisture content. The weight loss of the pins was calculated every week. The wear factor was determined as follows:

$$Wear\ factor\ (mm^3/Nm) = \frac{Volume\ loss}{Load * Sliding\ distance}$$

The wear test lubricants were kept at -20°C after collection until they were used for wear particle characterization.

2.3 Wear particle characterization

2.3.1 Wear particle isolation

A novel UHMWPE/MWCNT 1 wt% nanocomposite was studied and compared with virgin UHMWPE GUR 1020. UHMWPE/MWCNT 1 wt% material was selected for wear particle characterization from the two initial MWCNT reinforced polyethylenes it had shown superior wear resistance in wear tests.

The wear particles were isolated from the wear test lubricants previously collected. Four samples per material (virgin UHMWPE and UHMWPE/MWCNT 1 wt% nanocomposite) of the serum lubricant were selected randomly from the replicate wear tests. A volume of serum containing a minimum of 1 mm^3 of wear debris per sample was digested and analysed according to the method of Richards et al [19]. After isolation, samples were prepared for observation using a high-resolution scanning electron microscope (Leo 1530 FEGSEM). Images of the filters were taken at 3kV and 3 mm working distance over different magnifications (x400 – x90K) and at least 60 images were captured for each sample.

2.3.2 Wear particle analysis

Images were analysed using Image Pro Plus (Media Cybernetics, USA). At least 150 particles per sample were analysed. Area, aspect, ratio, perimeter and maximum length and width measurements were taken in each image to obtain particle size and area distributions for the wear particles from both materials. Considering a constant thickness, the volumetric concentration as a function of particle size was calculated. The resulting data was analysed by one-way ANOVA and the Tukey method was used to determine significant differences between groups [20].

2.4 Prediction of biological activity of wear particles

The specific biological activity (SBA) index and the functional biological activity (FBA) index of the wear debris generated from the UHMWPE/MWCNT 1 wt% nanocomposite and UHMWPE GUR 1020 were predicted and compared following the study of Fisher et al. [21]. This method can be used for preclinical evaluation of alternative bearing materials, allowing the prediction of the osteolytic potential of the wear particles generated.

2.5 Cytotoxicity of UHMWPE particles with and without MWCNTs in L929 fibroblast cells

2.5.1 Aseptic generation of wear debris

Clinically relevant wear particles for cell culture experiments were generated under aseptic conditions following a well-established protocol [22]. These particles have been shown to be comparable in both morphology and size distribution to those generated in vivo [23]. Test pins from virgin UHMWPE GUR 1020 and UHMWPE/MWCNT 1 wt% were used for the generation of sterile clinically relevant wear particles for cell culture experiments. Rough (Ra 0.07-0.08 µm) high carbon (>0.2 % w/w) cobalt chromium alloy plates were used as counterface in order to generate large volumes of wear particles. Prior to generation of particles, pins were soaked for a minimum of two weeks in distilled water to stabilize moisture content levels and then stored in a temperature controlled environment to stabilise the material. After this, pins were weighed as described previously. The weighed test pins were washed with a brush using general household detergent, and then surface disinfected using sodium hypochlorite (10% v/v) for 10 min. After cleaning, the pins were cultured in 10 ml of nutrient broth for 48 hours at 37°C. If nutrient broth remained clear, this indicated no bacterial contamination of pins. Test pins were then stored in sterile filtered 70% (v/v) ethanol until ready to use.

Wear test rig components and the rough high carbon cobalt chromium plates were washed in soapy water with a toothbrush and then rinsed thoroughly in distilled water. After thorough cleaning, components were cleaned in Virkon solution (1% w/v) for 10 mins and rinsed in distilled water. The components were then placed in a sonicating water bath in 70% (v/v) iso-propanol for 20 minutes in order to remove particulate material and then rinsed with distilled water. Components were then wrapped in tin foil and sterilised in a hot air oven at 190°C for 4 hours to destroy endotoxins. A multidirectional pin on plate wear simulator operating under aseptic conditions was used to ensure sterile endotoxin-free wear particle generation. Tests were carried out under standard kinematic conditions, under a load of 160N (nominal contact pressure= 2 MPa), ± 30 degrees of rotation, at 1Hz and with a stroke length of 28 mm. Each test lasted 1 week. The lubricant used was Dulbecco's modified Eagles medium (DMEM, Lonza, UK) supplemented with 25% (v/v) bovine serum. The use of DMEM as lubricant allowed the wear particles generated to be taken directly from the wear rig to culture them with the cells. The level of lubricant was controlled using a syringe driver at a rate of 1ml/h. For assessing the presence of microbial contamination, samples of lubricant were taken daily, plated onto nutrient, heated blood and sabouraud agar plates and incubated at 37°C, 37°C, and 28°C, respectively, for a period of 3 days. After the tests, lubricants were kept at -20°C after collection until they were used for cell culture studies and a small aliquot was retained for particle size and morphology analysis.

2.5.2 Culture of L929 fibroblasts with wear particles

L929 fibroblast murine cell line was used for culture with UHMWPE GUR 1020 and UHMWPE/MWCNT 1 wt% wear particles. DMEM (Lonza, UK) supplemented with foetal bovine serum (10% v/v), L-glutamine (2 mm), and penicillin-streptomycin (100µg/ml) (Invitrogen, Paisley, UK), was used as culture media for the cells. Particles were evaluated at ratios of 0.005, 0.05, 0.5, 5 and 50 μm^3 per cell. L929 cells were seeded at 1×10^4 cells per well into 96- well culture plates and cultured with the particles for five days at 37°C in 5% (v/v) CO_2 in air. Each concentration was cultured with the cells in six replicate wells. Negative controls consisted of only cells. As a positive control, cells cultured with camptothecin, a compound that induces apoptosis of cells, were used at a concentration of 2 µg/ml.

2.5.3 Cell viability assay

The effect of the wear particles on the L929 fibroblasts was monitored every 24h for five days using the ATP-Lite assay (Perkin Elmer, UK) to assess for possible cytotoxic activity. The levels of ATP produced by the cells with different concentrations of wear particles were determined in counts per second (CPS). Data was analysed by one-way ANOVA and the Tukey method was used to determine significant differences between the control and the cells cultured with wear particles. The viability of the cells was determined with reference to the cells without particles (negative control).

3. Results

3.1 Wear testing

The wear rates (mm^3/Nm) for the three material pins (virgin UHMWPE GUR 1020, UHMWPE/MWCNT 0.5 wt% and UHMWPE/MWCNT 1 wt%) sliding against smooth (average surface roughness= 0.01 µm) high carbon cobalt chromium plates are shown in Fig. 1. The results indicated that the highest wear factor was for the virgin UHMPWE GUR 1020 and the wear factor decreased with increasing concentration of MWCNTs. The wear factors for the UHMWPE/MWCNT 0.5 wt% and UHMWPE/MWCNT 1 wt% materials were significantly lower ($p<0.05$ ANOVA) compared to the virgin UHMWPE GUR 1020 material. The addition of 0.5 wt% MWCNTs reduced the wear rate by approximately 30%. The wear rate was reduced slightly further by the addition of 1 wt% MWCNTs but there were no statistically significant differences between wear rates for the UHMWPE/MWCNT 0.5 wt% and UHMWPE/MWCNT 1 wt% materials.

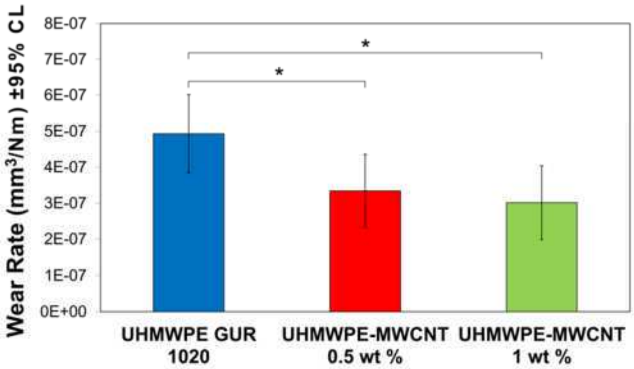


Figure 1. Wear rates (mean±95 per cent confidence limits) for UHMWPE GUR 1020, UHMWPE/MWCNT 0.5 wt% and UHMWPE/MWCNT 1 wt% against smooth high carbon cobalt chromium plates (* p <0.05 ANOVA)

3.2 Wear particle characterization

Wear particles isolated from UHMWPE GUR 1020 were similar in morphology to the particles isolated from the UHMWPE/MWCNT 1 wt% nanocomposite. Scanning electron micrographs of large flakes from the virgin UHMWPE and the MWCNT reinforced UHMWPE are shown in Fig. 2 (a-b). Submicrometre-sized and nanometer-sized wear particles from both materials are shown in Fig. 2 (c-d).

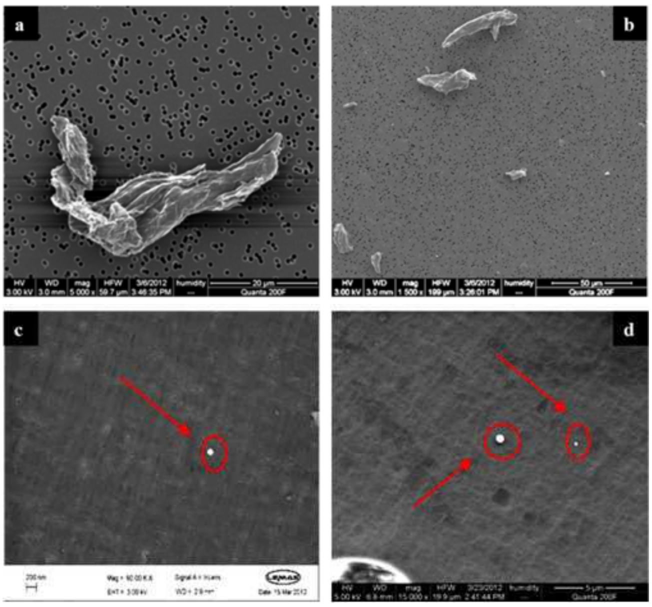
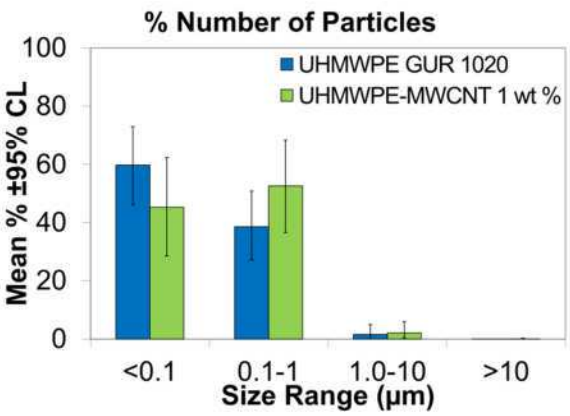


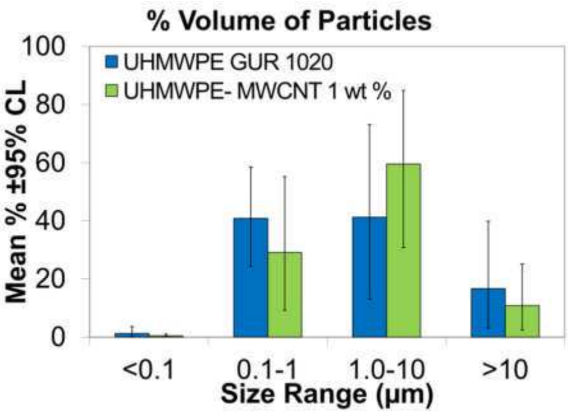
Figure 2. FEGSEM micrographs of large flakes from (a) UHMWPE GUR 1020 (magnification x 5,000) and (b) UHMWPE/MWCNT 1 wt% (magnification x 1,500) and nanometer- and submicrometre-sized wear particles from (c) UHMWPE GUR 1020 (magnification x 60,000) and (d) UHMWPE/MWCNT 1 wt% (magnification x 15,000)

In terms of size (Fig. 3a), no statistically significant differences were found between the reinforced UHMWPE and the virgin UHMWPE. For UHMWPE GUR 1020, the trend showed that most of the particles isolated from the wear test lubricants were in the nanometer size range. For the UHMWPE/MWCNT 1 wt% nanocomposite, the trend showed that the majority of the particles were in the 0.1-1-0 µm size range. For both materials, very few particles larger than 1.0 µm were isolated. There were no significant differences between the numbers of particles in each size for both materials.

In terms of volume distribution (Fig. 3b), no statistically significant differences between the reinforced UHMWPE and the virgin UHMWPE were found. However, the trend showed a lower volumetric concentration of particles in the 0.1-1.0 µm size range in the UHMWPE/MWCNT 1 wt% nanocomposite compared to the UHMWPE GUR 1020.



(a)



(b)

Figure 3. Frequency distributions (a) and volumetric concentration distributions (b) as a function of particle size for wear particles isolated from UHMWPE GUR 1020 and UHMWPE/MWCNT 1 wt% materials (± 95% confidence limits)

3.3 Prediction of biological activity of wear particles

The volumetric concentration distributions of the isolated particles were used to calculate the SBA indices from the virgin and the MWCNT reinforced material. The virgin UHMWPE GUR 1020 material had a higher SBA index compared to the UHMWPE/MWCNT nanocomposite, but the difference was not statistically significant (Table 1). For the FBA indices of the particles, the results showed that the UHMWPE/MWCNT 1 wt% nanocomposite had significantly lower index of FBA compared to the virgin UHMWPE (Table 1).

Table 1. Mean SBA and FBA indices for the wear particles isolated from UHMWPE GUR 1020 and UHMWPE/MWCNT 1 wt% materials. (* $p < 0.05$ ANOVA)

Material	SBA±95% CL	FBA±95% CL
UHMWPE GUR 1020	0.41±0.17	2.23±0.63*
UHMWPE/MWCNT 1wt%	0.51±0.15	1.08±0.32*

3.4 Cytotoxicity of UHMWPE particles with and without MWCNTs in L929 fibroblast cells

The effect of UHMWPE GUR 1020 wear particles at different concentrations on L929 fibroblasts cells over the 5-day period is shown in Fig. 4a. The effect of UHMWPE/MWCNT 1 wt% wear particles at different concentrations on L929 fibroblast cells over the same time frame is shown in Figure 4b. The results showed that neither the polyethylene nor the MWCNT reinforced polyethylene wear particles had any adverse cytotoxic effects on the viability of the cells during the five days at any of the concentrations. The positive control (camptothecin) showed a reduction in L929 fibroblast cell viability with time, with a significant reduction in cell viability from day 2 and day 1, respectively.

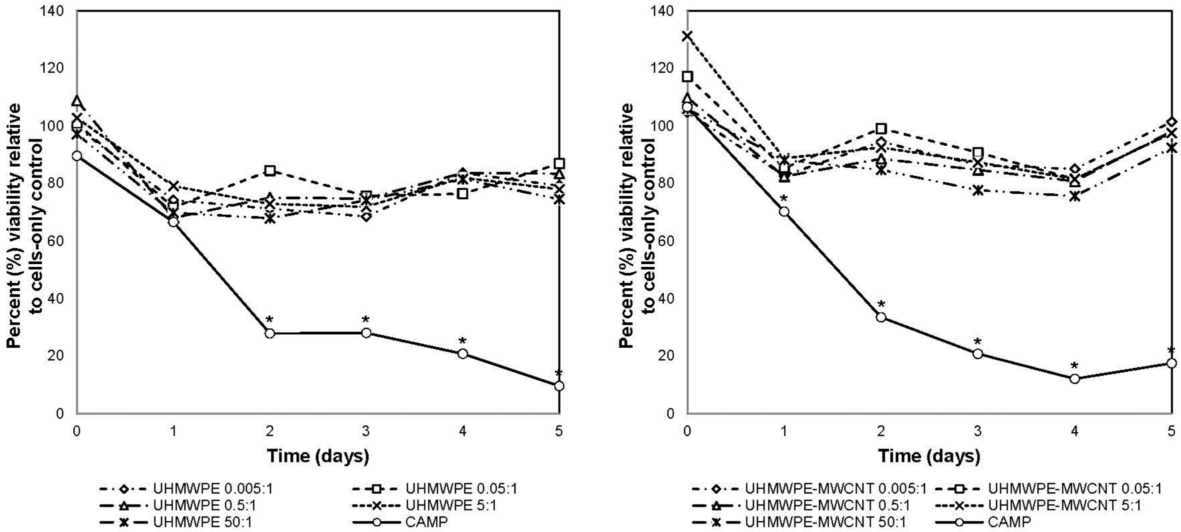


Figure 4. Percentage viability of L929 fibroblasts cultured with UHMWPE GUR 1020 (a) and UHMWPE/MWCNT 1 wt% (b) wear particles at the indicated particles volume (μm^3) to cell number ratios compared to control. * (p <0.05 ANOVA)

4. Discussion

UHMWPE/MWCNT nanocomposites have been previously pointed out as an alternative to conventional UHMWPE for total joint replacements [24] and [25]. However, these studies focused their investigations only on assessing the wear behaviour of these composites and did not consider the importance of wear particle characteristics. Previous studies have demonstrated that wear debris generated by different types or grades of polymers perform differently in terms of biological reactions [26]. For example, a study performed by Ingram et al. [27] showed that GUR 1050 UHMWPE produced a larger volume of particles in the size range of 0.1 to 1 µm, which has been demonstrated to be the most biologically active size range [23], compared to GUR 1020 UHMWPE. Also, the level of crosslinking has shown an influence on the biological activity of polyethylene wear debris [28] and [29]. Thus, critical factors, like morphology, size and volumetric concentration of wear particles generated from UHMWPE/MWCNT nanocomposites need to be identified.

In the present study, a UHMWPE/MWCNT nanocomposite and the wear particles generated were investigated to assess its potential as a new orthopaedic material.

The results showed that MWCNTs have the ability to improve the wear performance of virgin UHMWPE, demonstrating a 30 % reduction in the wear rate compared to virgin UHMWPE after the addition of 0.5 wt% MWCNTs. Further addition of MWCNTs did not show significant differences. These results are in concordance with previous investigations on the effect of MWCNTs on polymer matrices [30,31].

Although the addition of MWCNTs has shown a positive effect on the wear performance of UHMWPE, the use of nanoparticles to reinforce polymer matrices has raised some concerns, since it may lead to an increased wearing of the metallic counterface. However, to date, the wear mechanisms of MWCNT nanocomposites are still not well understood [32] and further contributions are needed to gain knowledge on the tribological performance of these novel nanocomposites and assess the risk of metallic debris generation.

The wear debris generated by the MWCNT reinforced UHMWPE was also analysed and compared it with conventional UHMWPE. The debris characteristics for the virgin UHMWPE GUR 1020 were similar to those reported previously [19]. However, there is no previous data of particles isolated from UHMWPE/MWCNT nanocomposites. The results of the present investigation showed that the addition of MWCNTs for reinforcing UHMWPE did not modify particle morphology, and no significant differences in terms of size and volume distributions were found. However, the volume distribution trend of the wear particles generated from the UHMWPE/MWCNT nanocomposite showed a lower particle volume in the most critical size range (0.1-1 μm) compared to the conventional UHMWPE. This difference, together with the reduced wear factor measured for the MWCNT reinforced material, was evidenced in the SBA and FBA indices. SBA and FBA predictions indicated that wear particles from the UHMWPE/MWCNT nanocomposite had a lower osteolytic potential to those produced from the UHMWPE GUR 1020.

Over recent years, research interest has been focused on the toxicity and biocompatibility of MWCNTs. However, the results of these studies are often contradictory. A study performed by Zhu et al. [33] showed that MWCNTs induced apoptosis in mouse embryonic stem cells. On the other hand, the results of a study by Reis et al. [34] indicated good cytocompatibility of MWCNTs, similar to that of conventional UHMWPE, suggesting its potential for use in orthopedic applications. In order to assess possible cytotoxicity activity of UHMWPE/MWCNT wear particles, the present study used clinically relevant sterile wear debris, which was generated by articulation under aseptic conditions. In a similar study, Germain et al. [35] demonstrated that clinically relevant cobalt-chromium particles reduced the viability of L929 cells at concentrations of 50μm^3 and 5 μm^3 per cell. In the present study, clinically relevant UHMWPE/MWCNT wear particles were shown not to have any adverse effect on L929 fibroblast cells in culture at any of the concentrations tested over time. These findings suggest that UHMWPE/MWCNT nanocomposites may be an attractive alternative for orthopaedic applications.

Our study has shown that non-crosslinked UHMWPE had a higher wear rate than UHMWPE/MWCNT nanocomposites. Since moderately crosslinked and highly crosslinked UHMWPE are usually the materials of choice for total joint replacements, it will therefore be important to investigate in further studies whether there are significant differences regarding wear rates and biological activity of wear particles between crosslinked UHMWPE and crosslinked UHMWPE/MWCNT nanocomposites. Besides, additional work that investigates the effect of UHMWPE/MWCNT wear particles on TNF-α production in human peripheral blood mononuclear cells is currently being performed.

5. Conclusion

As more and more patients require joint replacement surgery, the orthopaedic community is searching for new biomaterials which will extend the life of artificial joints. Through the use of selected fillers, polymer nanocomposites have shown the ability to improve the wear behaviour of virgin UHMWPE in orthopaedics implants. In particular, the following conclusions can be made from this study:

1. MWCNTs have shown the ability to improve the characteristics of UHMWPE without adversely affecting the biocompatibility.

2. UHMWPE/MWCNT nanocomposite material was shown to generate lower wear rates and reduced osteolytic potential, as well as comparable cytotoxicity, compared to conventional virgin polyethylene of the same grade.

3. This study has provided insight into the potential of the UHMWPE/MWCNT nanocomposites as a promising alternative to conventional UHMWPE for use in total joint replacements.

4. Further work concerning the influence of MWCNTs on human health is necessary.

6. Acknowledgements

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