Nanometre sized wear particles *in vivo*: Conventional and highly crosslinked polyethylene prostheses

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Aim: Longevity of conventional ultra high molecular weight polyethylene (UHMWPE) Charnley prostheses can be comprised by the onset of late aseptic loosening caused by the production of PE wear particles. Particles in the size range 0.1µm-1.0µm are most problematic with a high biological activity. Little is known about particles that are <0.1µm in size and their biological activity. Nanometre sized particles (<0.1µm) have only recently been identified in *in vitro* hip simulator test lubricants and it is yet to be determined if particles in this size range exist *in vivo.* Crosslinking improves the wear properties of PE and decreases the total wear volume generated. However, simulator testing of crosslinked PE has shown a smaller size distribution of particles produced. Particles were isolated from acetabular and femoral tissues which had been explanted from around conventional Charnley prostheses. Also an opportunity arose to study the particles isolated from tissues surrounding a crosslinked UHMWPE prosthesis. The aim was to determine if nanometre sized particles were present *in vivo*.

Methods: Five tissue samples, from conventional Charnley prostheses, were collected at revision operation (sites of explant: samples 1&2 femoral; sample 3 acetabular and sample 4 capsular). Prostheses were gamma irradiated in air (0MRad). The mean implant life was 15.08 years (range 9.25-19 years). All revisions were due to loosening. Also 5 tissue samples were retrieved at autopsy from a patient with a crosslinked acetabular component (28mm Durasul cross-linked inlay, 9.5MRad ebeam irradiated, articulating against low carbon metal ball head); implant time 2 years (four femoral sites; caudal, CD; cranial, CR; dorsal, D; ventral, V and one capsule sample, LR). Tissues were stored in 10% (v/v) formalin at room temperature.
The wear debris was isolated using the method of Tipper *et al.* [1]. The method was optimised to ensure complete digestion and removal of biological contaminants. Samples were filtered through a sequence of 10µm, 1µm and 0.015µm membrane filters. Samples were sputter coated with 5.0nm platinum/palladium and mounted on to aluminum stubs in preparation for FEG-SEM. Five random fields of view were taken over three or four ranges of magnification for each filter pore size. A minimum of 150 particles were counted for each sample. Parameters of area, perimeter, length and width were measured using image analysis software, Image Pro Plus 3.0 (Media Cybernetics, USA).

Results: The wide array of sizes and morphologies of particles isolated from conventional and crosslinked PE prostheses are shown in Figure 1. For the first time nanometre sized particles were identified in the tissue samples explanted from around both conventional and crosslinked UHMWE prostheses. The smallest particle identified was 43.5nm in length (sample LR). The largest particle identified was 1.0mm in length (sample V, Fig 1c). The size and area distributions of particles isolated from the tissue samples are shown in Figures 3&4.

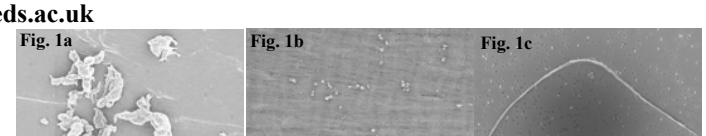

Fig. 1a. Flake/fibril agglomerations isolated from tissue sample 4 (conventional PE), 0.015µm filter, x11K; Fig. 1b&c. Particles isolated from tissue samples explanted from around crosslinked PE prostheses b. Nanometre sized granules (Sample LR, 0.015µm filter, x50K); c. Long fibril (Sample V, 10µm filter, x260);

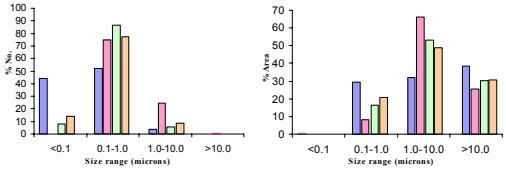

Fig 3a. **Fig 3b.**

Fig 3a. Size and Fig 3b. Area distributions of particles isolated from tissue samples explanted from around conventional PE prostheses: 1 ; 2 ; 3 ; 4

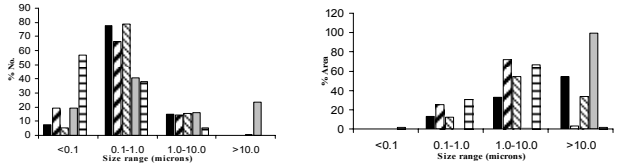

Fig 4a. **Fig 4b.**

Fig 4a. Size and Fig 4b. Area distributions of particles isolated from tissue samples explanted from around crosslinked PE prostheses: CD ; CR ; D V and LR .

Conclusions: Nanometre particles were identified in the tissue samples taken from around both conventional and crosslinked PE prostheses. A high number of nanometre sized particles were identified in the sample, LR which was capsule tissue retrieved from around the crosslinked PE prosthesis. The femoral tissue samples taken from around the crosslinked PE prosthesis had a higher proportion of larger sized wear debris. This suggests that small nanometre sized particles are preferentially transported away from the implant. Galvin *et al.* [2] tested highly crosslinked PE in hip joint simulators, and isolated particles from the simulator lubricant. The distribution showed a high number of particles isolated in the <0.1µm size range compared to the *in vivo* wear of both the conventional and crosslinked PE prostheses. Simulation is carried out in an enclosed environment where dissemination of particles is impossible. *In vivo* particles that are released from articulating implants may disseminate around the body via the body's natural transport systems. Cell culture experiments are currently being performed to assess the biological potential of nanometre sized PE particles.

References:

1. Tipper JL. *et al.,* J Mater Sci Mater Med **2000; 11** (2), 117-124.
2. Galvin AL. *et al.,* Wear **2005; 259**, 977-983.