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P17-35 Characterization of in-situ derived metallic nanoparticles from implant wear as a prerequisite for toxicity assessment

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Background

Metallic micro- and nanoparticles can be generated on the articulating surfaces and modular junctions of orthopedic implants^[1]. The *in situ* formation of wear particles represents a unique toxicological exposure scenario and is associated with adverse local tissue reactions (ALTR) that can lead to osteolysis and aseptic implant loosening while the underlying mechanisms are not fully understood^[2]. The toxicity of micro- and nanoparticles is known to be a function of their shape, size, elemental composition and overall charge (Zeta Potential)^[3]. Furthermore, these physicochemical properties change when introduced into biological fluids such as blood serum or synovial fluid due to adsorption of soluble proteins that form a protein corona on the particles' surface^[4]. This work aims to characterize *in situ* generated metallic nanoparticles from orthopedic implants for their physicochemical properties to identify parameters that might explain the occurrence of ALTRs.

Methods

Sample collection was performed during implant revision surgeries that were conducted due to signs of ALTR. Acquisition of samples focused on implants that were withdrawn from the market due to poor performance. Micro- and Nanoparticles were purified using a two-step enzymatic digestion protocol. The samples were pooled according to the implant type they are derived from with n=11 samples for Metal-on-Metal (MoM) total hip arthroplasty (THA) with CoCrMo metallic adapter sleeve (MAS), n=11 samples for non-MoM THA with CoCrMo dual modular neck (DMN), n=5 for MoM THA without MAS and n=3 for MoM THA with CoCrMo MAS and Ti DMN. After purification, aliquots were taken from each group and introduced to water, synovial fluid and cell culture medium for subsequent analysis using Electron Microscopy for morphology characterizations (size, crystallography, shape) and dynamic light scattering coupled to zeta potential for their characteristics in suspensions.

Results

Particles were isolated from each group in different quantities. The wear particles in each group showed a large heterogeneity in size and morphology, ranging from round or elliptic to needle/rectangular shapes. The range of particle sizes and their elemental composition was different for each implant type. In addition to single dispersed particles, agglomerates/aggregates of micro- and nanoparticles were found in all samples. Introduction to biological fluids was accompanied by an increase in size and a shift in overall charge.

Conclusion

The presented results provide a solid basis for further research focusing on micro- and nanoparticle toxicity. In addition, the need for particle characterization in biological fluids that reflect their environment *in situ* is emphasized, since physicochemical properties strongly depended on the respective liquid. Further investigation of micro- and nanoparticle toxicity *in vitro* will help to correlate their physicochemical properties to observed pathologies such as ALTRs.

References

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