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EMPLOYING THE FISH EMBRYO TOXICITY (FET) TEST TO ASSESS WEAR DEBRIS FROM BIOMATERIAL CANDIDATES DESIGNATED FOR HIP REPLACEMENT PROSTHESIS

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Summary: Total hip replacement is a common surgical therapy for patients who suffer from hip arthrosis or femoral head necrosis. The femoral head is commonly replaced by a cobalt chromium (CoCr) alloy, articulating against a polymer liner. These materials have to resist a high load, have high fracture toughness and demonstrate a low frictional contact combination. Still, the main cause for prosthesis failure is the biological reaction to wear debris. This reaction is dependent on the particle size, the chemical properties and the quantity of debris. For example, CoCr ions and wear debris may, in rare cases, cause severe side effects such as hypersensitivity, metallosis and pseudotumours.

This prompts for a further need to develop novel materials with high biocompatibility and preferably bioactivity, promoting healing and osteogenesis that simultaneously minimises inflammatory responses. Newly developed biomaterials need to be thoroughly assessed preclinically both in vitro and in vivo, which burdens the use of animal in research. Therefore, we herein employ the fish embryo toxicity (FET) test as a bridge between in vitro and in vivo, for wear particle toxicity assessment. This Zebrafish model is ideal for imaging due to the transparency of the embryos and larvae. In this study, embryos were exposed to increasing concentrations of CoCr or silicon nitride nanoparticles, the latter being a recently investigated material for joint implants. The embryos were later assessed in terms of malformations and survival in correlation to increasing exposure. The fate of the nanoparticle was visualised with confocal microscopy, light sheet imaging and supplementary electron microscopy. The nanoparticles aggregated quickly and adhered to the chorion with minimal migration across the membrane. Malformations and low survival rates of the embryos were seen to a higher extent in the silicon nitride group, at the same (high) concentration. In conclusion, the FET test proved to be a valuable method for biocompatibility testing of nanoparticles, where the complexity of the growing embryo and exposure to a whole organism enabled a more thorough understanding of the in situ behaviour of the biomaterial.