Abstract:
The majority of previous studies that evaluated inflammatory and cytotoxic responses to wear debris from metal-on-metal (MoM) hip implants utilized particles with physical and chemical characteristics that differed from clinically relevant particles released in vivo from MoM implants under normal wear conditions. Additionally, no previous study has attempted to understand the potential difference in biological responses to clinically relevant MoM wear debris generated under normal versus abnormal (e.g., edge-loading) conditions. The goal of this study was to understand the potential cytotoxic and inflammatory response to clinically relevant MoM wear debris generated during normal versus edge-loading conditions. Wear debris particles from each condition were isolated from Pinnacle MoM simulator fluid and sterilized prior to biological testing in a murine macrophage cell line (RAW 264.7). Particles generated from edge-loading conditions were larger and contained more cobalt (Co) compared to particles from normal wear conditions. Particles and ions from normal implant conditions up to 1021 cycles per mL (1000 ppb total Co and chromium (Cr)) did not induce cytotoxicity or inflammation as detected by MTT and TNF-α cytokine release, respectively. In contrast, particles and ions released from edge-loading conditions induced significant cytotoxicity and TNF-α cytokine release when RAW 264.7 cells were exposed to 1021 cycles per mL (61124 ppb total Co and Cr) for 24 hours. The 25% inhibitory concentration (IC25) value of approximately 26,000 ppb (Co and Cr) was calculated for the metal concentration which resulted in a 25% decrease in cell viability. The IC25 value for edge loading particles and ions was over 150-fold greater than metal levels observed in synovial fluid in well-functioning implants. These results indicate that 1) normal wear conditions that generate nano-sized chromium oxide particles are unlikely to result in cytotoxic or inflammatory responses in periprosthetic tissues, and 2) adverse biological responses likely occur only under suboptimal wear conditions that generate a sufficient dose of larger particles with greater amounts of cobalt.