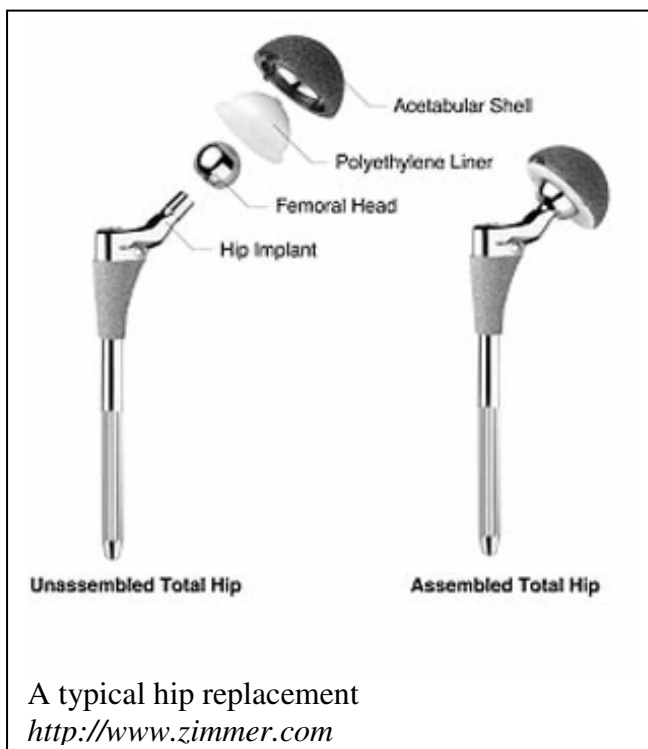


# Nanoparticles generated by the wear of medical implants

The replacement of human bone joints with artificial substitutes, especially knees and hips is now a commonly performed procedure throughout the world – in 2001, 165,000 hip replacements and 326,000 knee replacements in the United States alone<sup>1</sup>. These replacements have a dramatic effect on patients, restoring mobility and removing chronic pain.



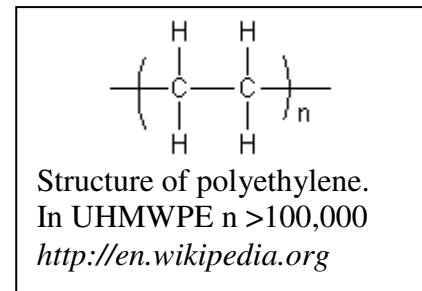
A hip replacement is comprised of two principal components – the main body with its attached femoral head, and the acetabular shell which the femoral head slots into. The acetabular shell is attached to the hip while the body is placed into the femur. A variety of different materials are available for both components of the replacement joint. These different materials offer a variety of different biomechanical and bioactive attributes which require a choice to be made by patients and

surgeons as to which is most appropriate.

For many recipients of hip replacements, there are no issues whatsoever and the lifetime of the prosthesis is often greater than that of the lifetime of the patient. Many receive fifteen years or better without any substantial pain or problems.<sup>2</sup> Some patients however find growing pain and difficulty with movement, resulting in ultimately the need for revision of the implant – often at a time when the patient's age makes surgery a far riskier prospect than at the time of the original replacement. In addition the damage done is often sufficient so as to need substantial repairs,

making revision a more difficult and expensive procedure than the initial installation of the prosthesis.

Typical total hip replacements utilize a cobalt-chrome femoral head and body and a polymer, typically Ultra High Molecular Weight PolyEthylene acetabular shell. Alternatives involve titanium bodies and femoral heads, ceramic femoral



Structure of polyethylene.  
In UHMWPE  $n > 100,000$   
<http://en.wikipedia.org>

heads upon metal bodies, metal and ceramic acetabular cups, as well as proprietary technologies like Oxinium<sup>3</sup> which oxidize a metal surface so as to give it ceramic properties. CoCr/UHMWPE implants have the advantage of being the most established and in many ways easiest to install of the prospective options.

Concerns have arisen however about the biological effects and lifetime of CoCr/UHMWPE total joint replacements. In many patients the bone around the body of the implant becomes worn away, leading to reduced joint function and often renewed pain in the patient. This behaviour was initially ascribed to physical wear, however this seemed surprising as wear between the actual moving parts (the femoral head and acetabular cup) would be expected to be relevant first. This bone loosening is now believed to be caused by osteolysis induced by particulate debris from the implant<sup>4</sup>. In the course of normal use, the femoral head wears on the acetabular cup. This wearing action produced particles of UHMWPE to be removed from the acetabular cup and float free in the body. UHMWPE is biologically inert, making it seemingly a good implant choice. This presence of large amounts of biologically inactive particulate material however triggers an exceptionally strong macrophage response. This leads to the osteolysis of bone material around the implant – specifically at interfaces where the bone is exposed and open to attack.

As such there has been increasing focus on alternative materials for the construction of total joint replacements so as to remove the need for the costly and dangerous revision surgery often necessitated by the osteolysis triggered by UHMWPE particulate debris. Metal-on-metal, notably

cobalt chromium replacements were considered<sup>5</sup>. Despite the general mechanical undesirability of like-on-like bearings, the wear rate in terms of volume is between 10 and 100 times lower than that of CoCr femoral head on UHMWPE acetabular cups. Despite these low levels of wear however, SEM analysis of lab testing shows that in excess of 1 million nanoparticles of cobalt and chrome are generated per step. These particles are biologically active however and do not stimulate an immunogenic response leading to osteolysis<sup>5</sup> as UHMWPE particles do. However there has been shown to be significantly increased metal ion levels in patients receiving metal-on-metal implants. In vitro studies of human cells with particles generated by implant wear demonstrate that the particles do have a dramatic effect on cell viability, killing off most cells within 5 days. While studies show a lack of any cytotoxic effects near the implant site, leading to the belief that the body can dispose of the ions sufficiently quickly, there is significant concern about the genotoxicity of the particles. Chromium has well established genotoxic effects<sup>6</sup> and comet assays performed show signs of genetic damage by cells that come into contact with the metallic nanoparticles.

Ceramic femoral head on ceramic acetabular cup bearings are also a subject of investigation. Some early replacements involving titanium, with a TiN finish on one component and a TiC on the other have been largely abandoned. Usage of alumina (Aluminium Oxide) bearings is however on the increase and a subject of investigation with regards to viability<sup>7</sup>. Wear levels for ceramic-on-ceramic bearings have been shown to be as low as 4000 times less than those of cobalt chrome on UHMWPE cups. In addition, particles produced are less numerous, smaller and less attractive to macrophages than ultra high weight polyethylene particles. However, despite the exceptionally favourable wear properties of ceramic femoral heads on ceramic acetabular cups, there remain several problems with their usage. Installation is difficult – chips frequently are made and need to be repaired during the operation, and any slight misalignment can result in increased wear or the need for early revision. Severe impacts have been known to cause ceramic implants to shatter – this not only requires revision of the implant but can lead to many complications for the patient.

Overall the complete replacement of joints has been a resounding medical success, improving the lives of many patients. However time has shown that the nanoparticulate wear occurring in many implants is a cause of significant problems. As such there has been a move away from the use of UHMWPE and CoCr bearings and towards all-metal or all-ceramic bearings. Which one of these technologies is the safest and will become most prevalent remains to be seen, however the genotoxic concerns with CoCr could spell an end to that technology.

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<sup>1</sup> [http://www.fda.gov/fdac/features/2004/204\\_joints.html](http://www.fda.gov/fdac/features/2004/204_joints.html) (U.S. Food and Drug Administration)

<sup>2</sup> Total Hip Arthroplasty, Clinical Perspective. John J Callaghan MD. Clinical Orthopaedics and Related Research, 276.

<sup>3</sup> <http://www.ceramtec.com/pdf/9thSymp-3-6.pdf>

<sup>4</sup> Mechanism and clinical significance of wear-debris induced osteolysis. HC Amstutz, Pat Campbell, N Kossovsky, I Clarke. Clinical Orthopaedics & Related Research, 276.

<sup>5</sup> The Benefits of Metal-on-Metal Total Hip Replacements. ME Muller. Clinical Orthopaedics & Related Research, 311.

<sup>6</sup> Mechanisms of chromium genotoxicity. V Bianchi, AG Levis. Toxicological and Environmental Chemistry, 1984

<sup>7</sup> Ceramic-on-Ceramic Bearings in Total Hip Arthroplasty. Bierbaum, Benjamin E. MD; Nairus, James MD; Kuesis, Daniel MD; Morrison, J. Craig MD; Ward, Daniel MD. Clinical Orthopaedics & Related Research, 405.