Reduction in Joint Implant Loosening
Using NanoAccel™ Surface Modification Process

Implant loosening is the number one reason for total joint replacement or revision for both hip and knee. Reliable fixation is a key challenge in orthopedics. Improving implant to bone interface is critical to the longevity of total joint arthroplasty.

Primary Causes of Implant Loosening

1. Bone loss due to biological reactions to wear debris (see pages 2-5)
2. Insufficient bonding of host bone to implant surface (see page 6)
3. Bone loss as a result of stress shielding (see page 7)

Exogenesis Corporation's NanoAccel™ process addresses each of the primary causes of implant loosening. Implementation of the NanoAccel surface modification process may significantly improve long-term clinical outcomes providing a competitive advantage to joint implant manufacturers, suppliers and distributors.

Exogenesis Technology

Exogenesis' NanoAccel technology has the unique ability to produce important atomic level surface modifications without coatings or additives. Gas cluster ion beam (GCIB) surface modification is accomplished through bombardment of a surface by charged clusters of accelerated atoms bound together by weak interatomic forces. Using inert, non-toxic argon gas leaves no surface residuals following exposure. Each bombarding cluster of atoms has very high total energy, but the energy is shared over all the atoms in the cluster, such that each individual atom has very low energy not sufficiently energetic to allow them to penetrate more than a few atomic layers (<10 nanometers) into the target surface.

Exogenesis has developed a new technique called accelerated neutral atom beam (ANAB) for ultra-shallow processing of surfaces. In ANAB, a beam of accelerated gas cluster ions is initially produced as in GCIB, but the charge is removed making the clusters unstable releasing large numbers of their constituent neutral atoms. Upon target impact, the accelerated neutral atom beams produce surface modification comparable to those associated with GCIB, but to substantially shallower depths (≤ 3 nanometers) and with appreciably greater precision and control.

Exogenesis' two processes can be employed to achieve objectives for improving an articulating and integrating implant surface:

- **Accelerated Neutral Atom Beam** (ANAB) which provides nano-scale smoothing, removal of asperities and polishing debris, increases surface energy and hydrophilic properties, and reduces surface crystalinity and oxide layer formation potentially:
    - Reducing corrosion and metal ion release,
    - Reducing 3rd body wear, and
    - Reducing abrasive wear.
- **Gas Cluster Ion Beam** (GCIB) which provides a nano-scale surface texture, surface energy and hydrophilic properties resulting in accelerated and improved cell adhesion, proliferation and differentiation potentially:
    - Improving adhesion between implant material interfaces and implant to bone interfaces,
    - Improving bone integration with implantable metals and polymers, and
    - Promoting bone integration with polymers.

NanoAccel™ Surface Modification Process
Decreases Bone Loss due to Biological Reactions to Wear Debris

Implant loosening is the number one reason for total joint replacement/revision for both hip and knee (representing 50% of revision rate). Reliable fixation is a key challenge in orthopedics. Improving implant/bone interface is critical to the longevity of total joint arthroplasty.

Bone loss due to biological reactions to wear debris is a primary cause of implant loosening.

Modes of Wear[1,2,3]

- Joint articulation
- Articulation between intentional bearing surfaces in the presence of 3rd body component
- Articulation between two nonbearing secondary surfaces, e.g. Back of polymer insert and metallic tray, fretting wear of modular femoral components
- Unintended wear
    - Femoral head and metal backing of acetabular cup (through worn poly lining)
    - Femoral condyle and metal backing of patellar component (through worn poly lining)

Mechanisms of Wear[2,3,4]

- **Corrosion** – metal ion release may cause cytotoxicity and osteolysis and debris may act as an abrasive 3rd body
- **Adhesion** – bonding of asperities between surfaces when load is stronger than the inherent materials
- **Abrasion** – microroughened regions and small asperities on metal surface plow through polymer surface
- **3rd body** – metallic (asperities), bone particles or bone cement embed in polymer bearing
- **Fatigue** – polymer delamination and cracking leading to poly particle release

Exogenesis Theory

- Removal of metal asperities using NanoAccel may reduce initiation point for **corrosion** and release of metal ions.
- Reduce surface crystalinity using NanoAccel may reduce **corrosion** and fretting wear between modular components (femoral hip and tibial plate components).
- Reduce surface crystalinity and oxide layer formation using NanoAccel may reduce **corrosion** and release of metal ions.
- Removal of metal asperities using NanoAccel may reduce **abrasive** and **3rd body** wear.
- Overall smoothness of the articulating surface using NanoAccel may reduce **adhesion** and **abrasive** wear.
- Removal of polishing debris (carbon/silicon) using NanoAccel may reduce **abrasive** and **3rd body** wear leading to release of metal ions.
- NanoAccel enhances the surface energy and hydrophilicity of metal and polymer articulating surfaces increasing joint lubrication and decreasing **abrasion**.

Exogenesis Response and Evidence

- Exogenesis' ANAB technology reduces surface texture
    - The effect on traditionally polished CoCr coupons demonstrates 50% reduction in Ra by AFM (Figure 1).

- The effect on traditionally finished UHMWPE demonstrates 30% reduction of Ra by AFM imaging (Figure 2).

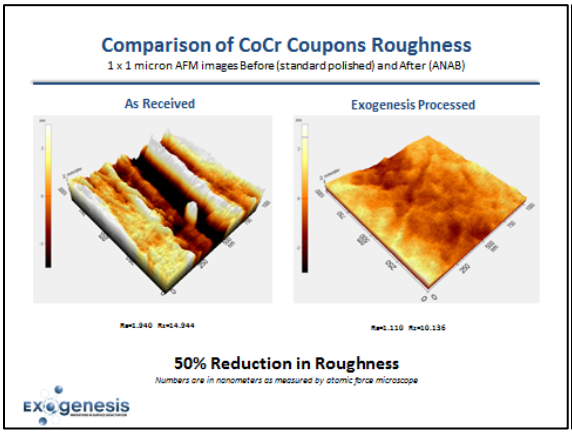

Fig. 1 – Smoothing of CoCr

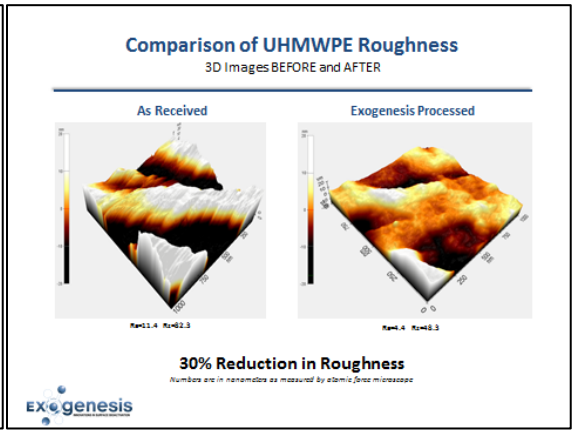

Fig. 2 – Smoothing of UHMWPE

- The driving force behind metal on metal (MOM) joint replacement was due to concern associated with wear particles inducing osteolysis from metal on polyethylene articulating surfaces. Exogenesis demonstrated reduction of wear particles through surface smoothing and removal of asperities and polishing debris in a MOM cyclic wear model (Figure 3). Exogenesis technology was never commercially implemented. Subsequently, MOM clinical experience demonstrated poor clinical outcomes likely due to wear particles and metal ion release promoting osteolysis leading to pain and early failure.

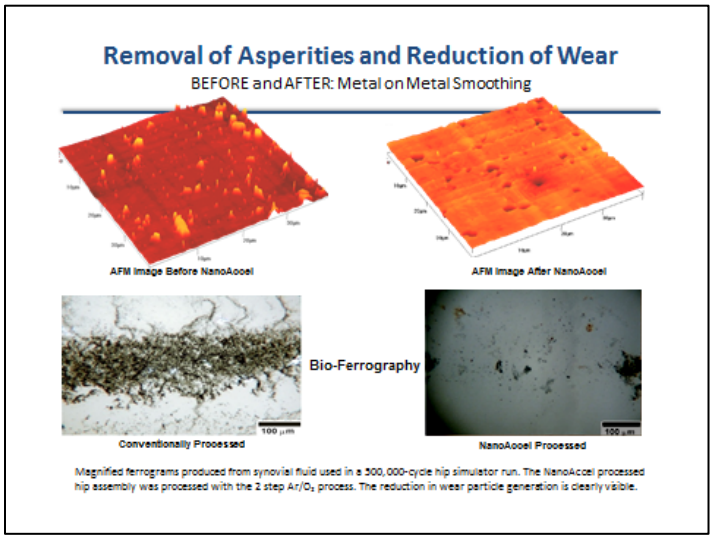

Fig. 3 – Removal of asperities and reduction in wear particles

- Although changes have been made to polyethylene materials used in articulating joints in recent years, the roughness, asperities, and residual polishing debris of the metal component may continue to serve as the hard file on a soft articulating surface. Wear studies indicate an abrasion or scratch of only 2 microns in the metal surface increase polyethylene wear by 30-70 fold.[5] Occurrence of osteolysis due to polyethylene wear has been reported in the literature.[6,7] Highly cross-linked polyethylene may not eliminate osteolysis.[8,9,10]
- Furthermore, studies show that the interface between the polyethylene inserts and metal tibial tray of fixed-bearing total knee replacement components can be a source of substantial

amounts of wear debris due to fretting micromotion. The greatest reduction in polyethylene wear is achieved by highly polishing the metal surface. [10]

- Corrosion at the modular neck-body junction in dual-tapered stems with a modular cobalt-chromium-alloy femoral neck can lead to release of metal ions and debris resulting in pain and local soft-tissue destruction.[11]
- The asperities and polishing debris may be a significant initiating source of metal ion release. Therefore, removal of asperities and polishing debris may be an area of significant importance.
    - Surface asperities have a very high surface area and may be the initiation point for ionic corrosion. Exogenesis treatment removes asperities (Figure 3) and polishing debris (Figure 4).

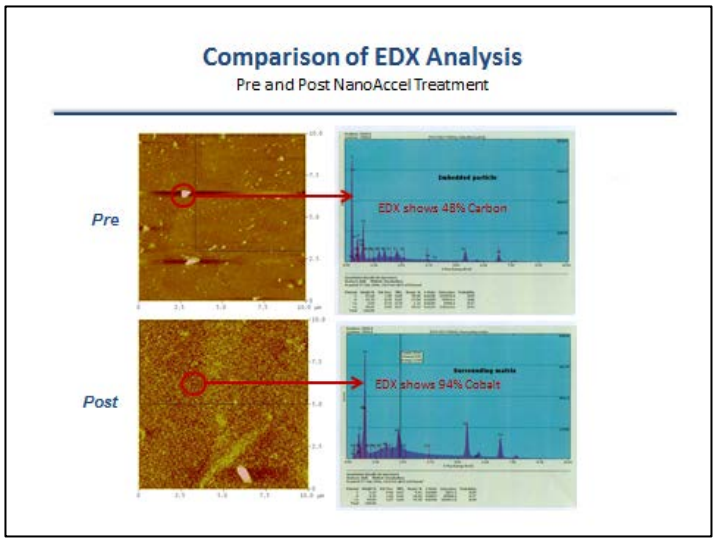

Fig. 4 – Carbon debris pre and Post NanoAccel treatment

- NanoAccel improves the hydrophilic properties of metals and polymers (Figure 5).

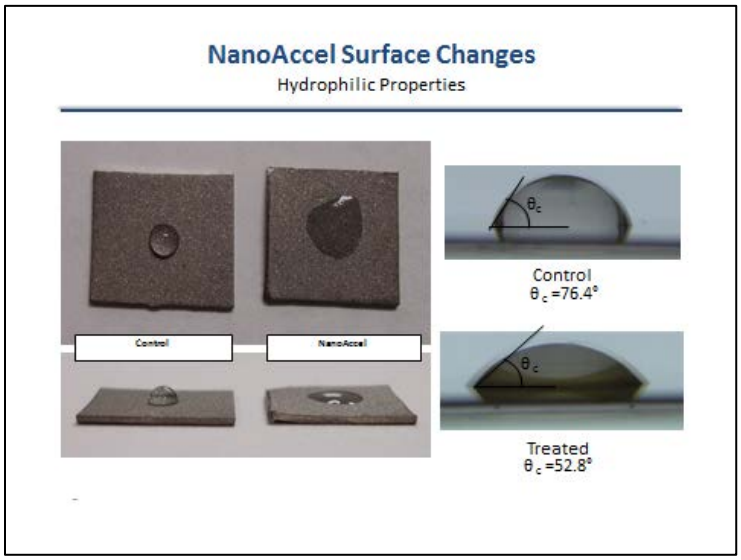

Fig. 5 – Hydrophilic properties pre and post NanoAccel

- **Additional in vitro testing methods**
    - Profilometer and pin-on-disc may not have the sensitivity to measure the important surface changes made by NanoAccel.
    - AFM images are much more sensitive and can clearly document reduction in Ra in addition to removal of asperities and polishing debris.
    - In vitro corrosion tests are being performed to demonstrate decrease in metal ion release using NanoAccel technologies.

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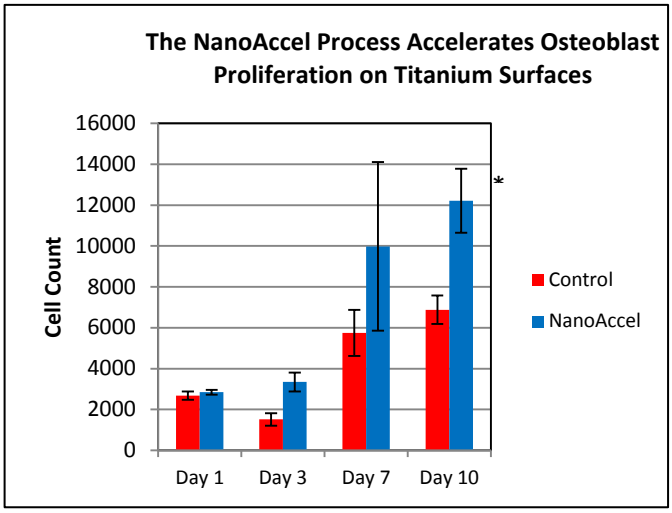
NanoAccel™ Surface Modification Process
Improves Bonding of Host Bone to Implant Surface

Implant loosening is the number one reason for total joint replacement/revision for both hip and knee (representing 50% of revision rate). Reliable fixation is a key challenge in orthopedics. Improving implant/bone interface is critical to the longevity of total joint arthroplasty.

Insufficient bonding of host bone to implant surface is a significant cause of Implant loosening.

- **Exogenesis Response and Evidence**

  - Surface treatment with the NanoAccel™ surface modification process leads to accelerated cell attachment and proliferation in vitro which in turn leads to enhanced osseointegration.
    - There are three key improvements that the NanoAccel process makes to materials that can positively impact cell attachment and proliferation: i) the technology produces a nanoscale textured surface, ii) there is an increase in negative surface charge and iii) the technology creates an amorphous surface. The combination of these three features results in accelerated cell attachment and proliferation.



  - Surface treatment with the NanoAccel™ surface modification process may lead to improvement in adhesion of PMMA bone cement to polymers (data pending).

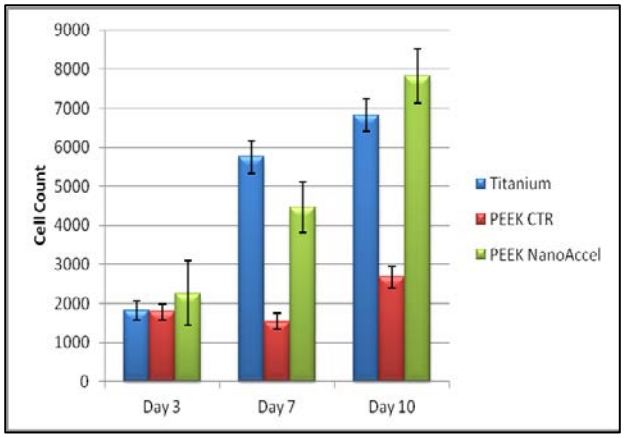
  - Surface treatment with the NanoAccel™ surface modification process may lead to anti-fouling or reduction of biofilm formation leading to insufficient bonding of host bone to implant surface (data pending).

NanoAccel™ Surface Modification Process
Reduces Bone Loss as a Result of Stress Shielding

Implant loosening is the number one reason for total joint replacement/revision for both hip and knee (representing 50% of revision rate). Reliable fixation is a key challenge in orthopedics. Improving implant/bone interface is critical to the longevity of total joint arthroplasty.

Bone loss as a result of stress shielding is a significant cause of implant loosening.

- **Exogenesis Response and Evidence**
  - Polymers have an elastic modulus that more closely match that of bone and therefore reduce stress shielding.
  - Current practice includes a titanium backing plate for bone interface with an attached UHMWPE insert.
  - A drawback of polymers is that due to their inert properties, they fail to integrate with bone.
  - Surface treatment of polymers with the NanoAccel™ surface modification process leads to accelerated cell attachment and proliferation in vitro which in turn leads to osseointegration.
    - There are three key improvements that the NanoAccel process makes to materials that can positively impact cell attachment and proliferation: i) the technology produces a nanoscale textured surface, ii) there is an increase in negative surface charge and iii) the technology creates an amorphous surface. The combination of these three features results in accelerated cell attachment and proliferation.



  - NanoAccel promotes bone purchase and osseointegration of polymer implants as seen in a rat calvarial critical size defect (see below).

Control **NanoAccel Processed**