Application of Nano Technology in Biomedical Engineering

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Abstract

Nanoparticles are defined as solid colloidal particles ranging in size from 10 to 1000 nm. Nanoparticles offer many benefits to larger particles such as increased surface-to-volume ratio and increased magnetic properties. Over the last few years, there has been a steadily growing interest in using nanoparticles in different biomedical applications such as targeted drug delivery, hyperthermia, photo ablation therapy, bio imaging and biosensors. The present scenario demands designing of Nano tools which can respond to the needs of biological problems and prepare more efficient biomedical approaches. This article reviews recent developments in Nano biotechnology with special emphasis on load bearing implants and novel tissue engineered scaffolds. Novel research approaches in Nano medicine and major challenges to practical applications are also highlighted.

Keywords :- Bio- imagine, Hybrid- science, Nano- material, Nano- topology, Nano- robotics.

❖ Introduction

Nano biotechnology; the hybrid science emerging from the mergence of two powerful technologies, biotechnology and nanotechnology, reflects science's growing ability to investigate beyond the molecular level, whereby generating advantageous results. It carefully combines the efficacy of biological materials and the rules and tools of basic sciences like physics, chemistry etc. and genetics to fabricate minute synthetic structures. Materials in nanoscale are expected to integrate well into biomedical devices, as most biological systems such as viruses, biomolecules etc. R&D in different areas of Nano biotechnology aspires to develop highly functional biosensors, Nano sized microchips, molecular switches, and tissue analogs for skin, bones, muscles and other organs of the body

Nanostructured devices used in biological research have emerged in-line with developments in the electronics industry. Metallic, ceramic, polymeric and composite nanomaterials have been investigated extensively for various biomedical applications such as novel tissue engineering scaffolds, targeted drug delivery systems, biosensors etc. In tissue and implant engineering, the enhanced material properties at the nanometer scale dimension such as increased surface area and finer surface roughness is expected to yield better biological responses of osteogenic cells and effective tissue-implant mechanical interlocking. The enhanced hardness and strength of nanomaterials in comparison with their coarser counterparts is attractive in making high wear resistance implants. Computational algorithms and tools applied in biomedical Nano metrics and nanomaterials are helping to generate remarkable new insights into how biological systems function, how metabolic processes interrelate, and how new molecular scale machines can operate.

Nanotechnology plays a central role in the recent technological advances in the areas of disease diagnosis, drug design and drug delivery. The Nano technological applications to disease treatment, diagnosis, monitoring, and to the control of biological systems have been referred to as 'nanomedicine'R&D in different areas of Nano medicine is expected to revolutionize the disease diagnosis and treatment approaches in the near future. Nano sized contrast agents are anticipated to lead way to advancements in understanding biological processes at the molecular level. Nano medical approaches to drug delivery focuses on developing nanoscale particles or molecules to improve the bioavailability of a drug. Special attention has been given to bioassay applications such as biosensors, biomedical devices, and biofuel cells using nanomaterials. Nanotechnology on a chip is a new paradigm for total chemical analysis systems. Nano robotics and Nano manipulation technologies will eventually allow moving and manipulating nanoscale materials and assemble them into Nano systems such as nanoscale robotics. The manipulation techniques can well be used in medicine for the investigation of structures and functioning mechanisms of living things and their interactions at the molecular level.

- **Application In Tissue and Implant Engineering.**

The R&D in this area is thriving to selectively improve the desirable tissue formation and Osseo integration for clinical implant successes. Bioactive surface coatings based on hydroxyapatite (HA) was mainly investigated in this direction. An effective and alternative approach relies on the use of nanomaterials. Nanomaterials and structures such as nanoparticles, Nano surfaces, nanofibers, Nano coatings, and Nano composites are considered for various applications in orthopedics and traumatology. The majority of orthopedic and dental implants currently in clinical use are micrometer scale surface roughened. The available nanotechnology based approaches to enhance the tissue formation can be divided into two:

1. Nano technological modification of biomaterial surfaces.
2. Use of nanomaterials for novel implants.

1.Nanotechnological modification of biomaterials surfaces :

The current research in this area is to uncover novel and economic surface modification strategies for titanium based implants to achieve nanometer scale surface roughness. Bone cells are naturally accustomed to interact with surfaces with a large degree of nanometer roughness. Studies proved that Nano topography alters cellular response through controlled cell growth, protein deposition, increased osteoblast adhesion and proliferation. The enhanced protein and cell binding capacities is attributed to the larger surface areas/roughness degrees and altered surface energies. These nanoscale surface modification strategies belongs to the following two groups:

a) Those which alter a surface topographically

b) Those which introduces nanoscale chemical molecules on a surface.

A) Those which alter a surface topographically :

Although problems do exist (in solvent casting and embossing, distortion during transfer etc.), lithographic technologies continue to be the most widely used techniques for producing Nano topography for biological applications. By functionalizing the surface with poly-L-lysine and dip coating it in a colloidal sol, one can impart Nano topography to a three-dimensional structure such as dental screws. Colloids could act as a mask when modifying the topography using, e.g., a chemical etch. New lithography techniques such as ‘schematic overview of template-directed assembly on an ordered microsphere array’ may limit the possible irregularities occurring in in-plane topographies. Imprint lithography is emerging as an alternative Nano patterning technology to traditional photolithography that permits the fabrication of 2D and 3D structures with high resolution, with operational ease. Other than the lithographic techniques, there are diverse physical and chemical approaches investigated to create Nano patterning on implant surfaces. Self-assembled monolayers can change the topography and chemistry of a surface to impart novel physical and/or biochemical properties. Other physical methods comprise ion beam deposition, nanoparticles deposition etc. Various chemical methods investigated include acid etching and adonization. Methods such as peroxidation and alkali treatment alter both the surface chemistry and the topography. In this direction, few novel approaches have been recently reported. Among them, self-organized nanotube formation through controlled adonization in F- containing electrolytes is particularly attractive. It was shown that the cells cultured on Nano tubular surfaces showed higher adhesion, proliferation, alkaline phosphate activity and bone matrix deposition when compared to those grown on flat titanium surfaces. The bioactivity of such Nano tubular surfaces can be enhanced through growth of nanoscale hydroxyapatite. Prior to the electrodeposition, the Nano tubular titanic surface was subjected to an alkaline treatment, which provided a template for nucleation of the HA inside the nanotubes. This process resulted in a vertical growth of the HA crystals and increased the bond strength of the coating. Bond strength was further improved by annealing the HA coated nonporous titanic in argon atmosphere. It will be desirable if inherent bioactive Nano tubular titanium alloys can be fabricated through incorporation of bioactive elements within the nanotubes. Such a surface will be attractive both in terms of topography and bioactivity. It has been shown that a low temperature heat treatment is essential in biocompatibility point of view of Nano tubular titanium alloys. Analogous to the nanotube formation, few alternative novel approaches were reported. Nanoscale rod arrays were fabricated on it surface by glass phase tonotopy growth method by an interfacial reaction between sodium borate glass coating and the pre-heated titanium substrates at elevated temperature. Uniform Nano nodular structures were developed only on the pre-textured surfaces by either sand-blasting or acid-etching with HCl and/or H2SO4, but not on relatively smooth surfaces, including machined and HF treated surfaces. Biocompatibility and performance of an implant can be significantly improved by localization of biomolecules (peptides, proteins and genes) on the surface through DNA hybridization, ligand/receptor, or antigen/antibody interaction. It was suggested that helical rosette nanotubes (HRN) coated It surface may simulate an environment that bone cells are accustomed to interact with. HRN are a new class of self-assembled organic nanotubes possessing biologically-inspired nanoscale dimensions.

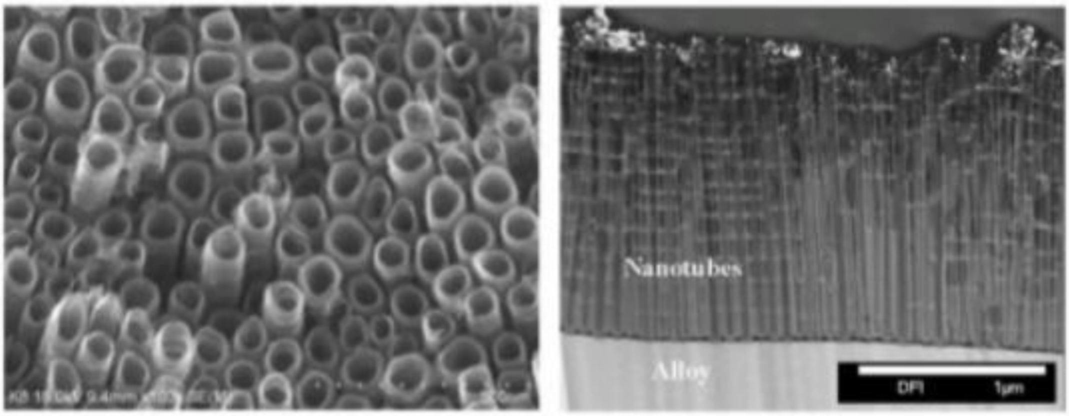

Fig. 1 Nanotubes formed on β type titanium alloy

B) Those which introduces nanoscale chemical molecules on a surface :

Nanoparticles can be deposited onto implant surfaces to alter their surface chemistry. For example, Ag nanoparticles can be used in coating of orthopedic pins to prevent bacterial colonization and, dispersed silver nanoparticles can be used in polymethyl-methacrylate (PMMA) bone cement. First trauma products coated with silver nanoparticles are already in clinical trials. Haiden et al. used nanoscale sol-gel titanic layers with embedded metal salts of Ag, Zn, Hg, Cu, Co and Al deposited on Ti surfaces and the highest bacterial-reduction rate was achieved with Cu. Bone implants with modified titanic and zirconia nanocrystal coatings were investigated for osteointegration and antibacterial effects . The coating comprised of nanocrystal line material comprising nanoparticles of formula AOx- (L-Mn+)i. where AOx represents TiO2 or ZrO2; Mn+ is a metallic ion having antibacterial activity, n = 1 or 2, L is a bi functional organic molecule which can simultaneously bind to the metal oxide and to the metallic ion, i is the no. of L-Mn+ groups bound to one nanoparticle of AOx. Nanoparticles promoting osteointegration can be deposited on pre-roughened surface though exposure to nanoparticles solution.

Nano ceramic coatings Nanoceramic coatings are attractive in terms of enhancement of mechanical properties (hardness, toughness, friction coefficient) and/or bioactivity. Nano-HA based bioactive coatings are expected to have improved mechanical and osteoconductive properties for both dental and orthopedic implant applications. Different methods such as sol-gel, electrophoretic and electrolytic deposition, high velocity oxy-fuel process, electro hydrodynamic spray deposition, ion implantation, cathodes arc plasma deposition, RF magnetron sputtering and pulse laser deposition were investigated for fabricating HA based Nano coatings on implants. Sol-gel-derived coatings demonstrated promise owing to their relative ease of production, ability to form a physically and chemically pure and uniform coating over complex geometric shapes and potential to deliver exceptional mechanical properties owing to their nanocrystal line structure. Many efforts are going on to make effective HA based composite coatings that particularly enhances mechanical properties. Addition of carbon nanotubes increased the bonding strength of the EPD-formed layers to the metallic substrate and is cost-effective. Although ceramics based implants are good in terms of wear resistance, they are unattractive in terms of cost and brittleness, and have catastrophic failure modes. Hence development of high wear resistance biocompatible ceramic Nano coatings on metallic implants possesses significance. Nanostructured metalorganic coatings (Cr-Ti-N) were extensively investigated as wear resistant coatings. Various surface hardening processes such as nitrogen ion implantation, plasma ion nitrating, and PVD of various coatings have been evaluated in this direction. It is well known that nanostructured diamond and diamond like coatings are biocompatible and have extreme hardness, wear resistance, low friction and biocompatibility. Nanostructured diamond coatings and metalorganic coating increases the corrosion resistance of stainless steels and cobalt based alloys.

2.Nanomaterials for advanced implants :

The majority of fabrication methods used for Nano topographies on planar substrates are unlikely to be capable of providing controlled topographical cues to cells seeded within three dimensional scaffolds. An alternative approach is the use of nonmetric building blocks to fabricate scaffolds. Novel methods for production of high quality nanoparticles with extremely high purity and crystallinity improves the quality of the already existing hydroxyapatite based medical devices, such as bone grafts. Bio inert nanoscale alumina is employed in coronial replacements, maxillofacial reconstructions, couplings of knee prosthesis etc. Ergun et al. investigated osteoblast adhesion on Nano particulate calcium phosphates of various Ca/P ratios. Their study showed that the average nanometer grain size, porosity and the average pore size decreased with increasing Ca/P ratios; the osteoblast adhesion increased on calcium phosphates with higher Ca/P ratios. The main drawback of nano-HA for use in load-bearing implants is their poor mechanical properties. The non matching mechanical properties of an implant to that of natural bone can cause stress shielding effect and can lead to bone resorption and loosening of the implant. To overcome this, biocompatible macromolecules, like biopolymers, proteins and polysaccharides have been widely used and incorporated into Nano sized bone ceramics to form novel bone-like composites. The ideal reinforcement material would impart mechanical integrity to the composite at high loading without diminishing its bioactivity. Among the Nanoceramic protein composites, Nano-HA/collagen composites are widely investigated. Studies showed that incorporation of higher elastic modulus biopolymers such as Ca-cross linked alginate, into Nano-HA/collagen composite systems improved the mechanical properties considerably. It was reported that after mixing biodegradable poly(lactic-co-glycolic acid) with Nano phase alumina, the bending properties of the composites match more closely with the value of human femur bone. In the presence of chitosan some of the limitations of Nano-HA, such as bio resorption and particle migration, can be alleviated. By adding chitosan into HA systems, the fracture strength and micro hardness of the resulting Nano composites were enhanced. Polymer nanofibers are capable of mimicking the size and scale of natural collagen fibers, and can fabricate continuous fibers with controllable alignment. Polymers such as polyploidies, polyploidies, poly (glycoside-co-lactate) are often used as the base materials for implant devices. The integration of composite techniques to fabricate high strength and durable biodegradable polymer-based composites is of a great interest. Properly applying right polymer with the considerations of porous size, degradation rate and surface morphology, as a parent material with mixing with high-strength fibers can indeed provide a good alterative for existing polymer and metallic based biocompatible materials for scaffold applications . Nano fibrous scaffolds designed to elicit specific cellular responses through the incorporation of signaling ligands (e.g., growth factors, adhesion peptides) or DNA fragments are viewed as particularly promising. A Nano-HA-degradable polymer scaffold of a multi-channel configuration can produce an ideal structure that can replace the natural ECM until host cells can repopulate and resynthesize a new natural matrix. A novel bone-tissue engineering scaffold design should mimic the macro- and micro-structure of natural bone. Carbon nanotubes and nanofibers have been investigated as reinforcement material. The versatility of these fibers suggests that there are a large number of possibilities for future designs that could enhance the efficiency of medical implants. For example, carbon nanofibers-polyurethane composites for non-loading orthopedic applications. Carbon nanotubes with their high aspect ratio and excellent mechanical properties have the potential to strengthen and toughen HA without offsetting its bioactivity, thus opening up a wider range of possible clinical uses. PMMA-modified Nano-HA with multi walled carbon nanotubes as reinforcement was projected as new generation biomedical bone cement and implant coatings. Employing freeze-granulation technique, it was possible to increase material homogeneity and also enhance the dispersion of the nanotubes in the composite matrix . Numerous proteins and peptides have been emerging as novel biomimetic nanomaterials due to their ability to self-assemble into nanoscale structures like nanotubes, Nano vesicles, helical ribbons and three dimensional fibrous scaffolds . There is a growing interest in the design of nanotube-nanoparticle hybrid materials. Biomineralisation represents a particularly promising approach in this direction. Protein-mediated formation of Ag nanoparticles on carbon nanotube is a simple and scalable method that uses commercially available proteins which would enable the generation of patterned 1D hybrid nanostructures under mild conditions.

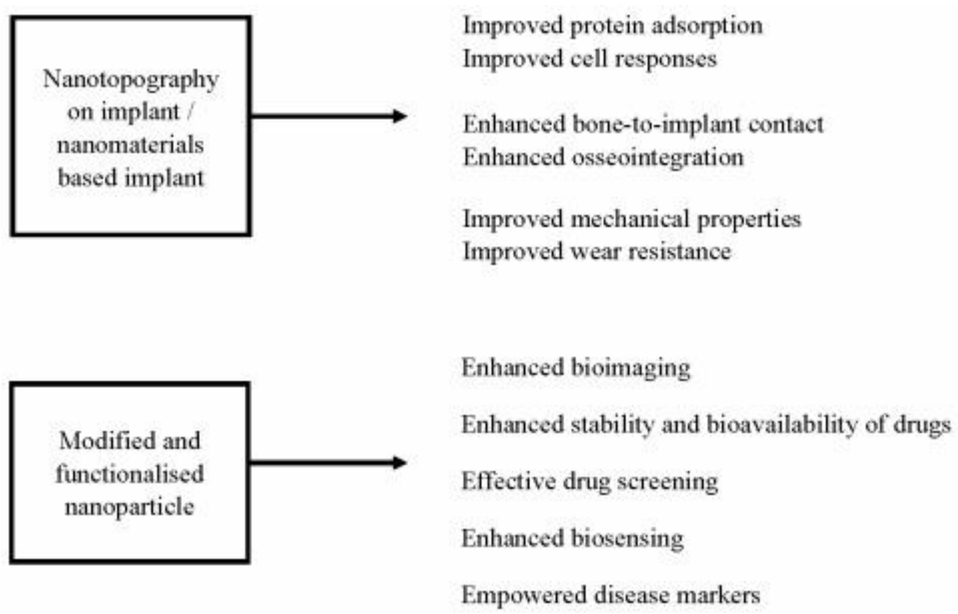

Fig. 2 Expected advantages of nanomaterials in implant engineering and medicine.

❖ Conclusion

Despite the excitement associated with the tremendous progress of nanotechnology applications, evaluation of potential hazards related to nanoscale-material-exposures and its subsequent outcomes have become an important area of study in the toxicology and health risk assessment realm. It is quite contradictory that; those special properties that make nanoscale materials useful are the same, which makes them potentially hazardous in certain aspects. The high specific surface area materials have high interfacial chemical and physical reactivity that can translates to biological reactivity. There exists a need for collective efforts in various directions such as determination of distribution of Nano particulate carriers in the body following systemic administration, development of imaging modalities for visualizing the bio distribution over time, understanding of mass transport across compartmental boundaries in the body, development of mathematical and computer models, establishment of standards/reference materials/consensus testing protocols and realization of analytical toolkits for Nano pharmaceutical manufacturing. Current research trends in Nano biotechnology are reviewed here with special emphasis on tissue and implant engineering. Although not yet truly realized, Nano patterning of functional medical devices offers great potential in implant engineering. Research in the field of Nano medicine is quite promising and is expected to revolutionize the disease diagnosis and therapy in the near future. Pivotal studies, both non-clinical and clinical in the aspects of safety and tolerance are the necessity of recent times in order to formulate potential commercial application.

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