

# Nanotechnology in Periodontics: A Review

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**Abstract:** Periodontal disease is one of the common disease which involved tooth and the supporting structures. Maintaining a sound periodontium is essential for improvement of quality of life of the patient that ultimately has its impact on overall health of an individual. Recent developments in nanomaterials and nanotechnology have provided a promising insight into the commercial applications of nanomaterials in the management of periodontal diseases.

**Keywords:** bottom up, microscale, nanoscale, top down, nanorobot, nanoethics etc

## 1. Introduction

The human characteristics of curiosity, wonder and ingenuity are as old as mankind. For many years people around the world have been harnessing their curiosity into inquiry and the process of scientific methodology. Science is the fuel for the engine of technology.<sup>1</sup>

**Nanotechnology** is a field of applied science focused on the design, synthesis, characterization and application of materials and devices on the nanoscale. Nanotechnology is a sub classification of technology in colloidal science, biology, physics, chemistry and other scientific fields and involves the study of phenomena and manipulation of material at the nanoscale, in essence an extension of existing sciences into the nanoscale. Two main approaches are used in nanotechnology; one is a "bottom-up" approach where materials and devices are built up atom by atom, the other a "top-down" approach where they are synthesized or constructed by removing existing material from larger entities.

Nano is derived from *vavoc*, the Greek word for dwarf, and usually is combined with a noun to form words such as nanometer, nanotechnology or nanorobot. A nanometer is 10<sup>-9</sup> meter, or one billionth of a meter. Since it is not easy to visualize the scale of a nanometer, a comparison with concepts and objects of appreciable dimensions is helpful.

The growing interest in the field of nanotechnology is leading to the emergence of a new field called Nanomedicine (including Nanodentistry), the science and technology of diagnosing, treating and preventing disease and traumatic injury, of relieving pain, and of preserving and improving human health, using nanoscale-structured materials, biotechnology and genetic engineering and eventually complex molecular machine systems and nanorobots. The development of "nanodentistry" will make possible the maintenance of near – perfect oral health through the use of nanomaterials, biotechnology, including tissue engineering and nanorobotics.<sup>3</sup>

## 2. Historical Perspective of Nanotechnology

**Richard P. Feynman in 1959** proposed using machine tools to make smaller machine tools, which in turn would be used to make still smaller tools, and so on all the way down to the molecular level. He suggested that such small nanomachines, nanorobots and nanodevices ultimately could be used to develop a wide range of atomically precise

microscopic instrumentation and manufacturing tools. Feynman argued that these tools could be applied to produce vast quantities of ultra small computers and various microscale and nanoscale robots.

**K. Eric Drexler in 1980** popularized the word 'nanotechnology'. He was talking about building machines on the scale of molecules, a few nanometers wide—motors, robot arms, and even whole computers, far smaller than a cell. Drexler spent the next ten years describing and analyzing these incredible devices, and responding to accusations of science fiction. Meanwhile, mundane technology was developing the ability to build simple structures on a molecular scale. As nanotechnology became an accepted concept, the meaning of the word shifted to encompass the simpler kinds of nanometer-scale technology.

**MIHAIL (MIKE) ROCO** of the U.S. National Nanotechnology Initiative has described *four generations* of nanotechnology development.

- The current era, as Roco depicts it, is that of passive nanostructures, materials designed to perform one task.
- The second phase, which we are just entering, introduces active nanostructures for multitasking; for example, actuators, drug delivery devices, and sensors.
- The third generation is expected to begin emerging around 2010 and will feature nanosystems with thousands of interacting components.
- A few years after that, the first integrated nanosystems, functioning (according to Roco) much like a mammalian cell with hierarchical systems within systems, are expected to be developed<sup>3</sup>

### *History of Nanotechnology in Dentistry*

Nanotechnology entered the dental field with advancement in material sciences mainly composites and bonding agents. Nanodentistry will make possible the maintenance of comprehensive oral health by employing nanomaterials, biotechnology including tissue engineering, and, ultimately, dental nanorobotics. When the first micron-size dental nanorobots can be constructed in 10-20 years, these devices will allow precisely controlled oral analgesia, dentition replacement therapy using biologically autologous whole replacement teeth manufactured during a single office visit, and rapid nanometer-scale precision restorative dentistry. New treatment opportunities may include dentition renaturalization, permanent hypersensitivity cure, complete orthodontic realignments during a single office visit and

continuous oral health maintenance using mechanical dentifrobots.<sup>3</sup>

### Potential Risks of Nanotechnology

Potential risks of nanotechnology can broadly be grouped into three areas:

- The risk to health and environment from nanoparticles and nanomaterials;
- The risk posed by molecular manufacturing (or advanced nanotechnology);
- Societal risks.

Nanoethics concerns the ethical and social issues associated with developments in nanotechnology, a science which encompasses several fields of science and engineering, including biology, chemistry, computing, and materials science. Nanotechnology refers to the manipulation of very small-scale matter – a nanometer is one billionth of a meter, and nanotechnology is generally used to mean work on matter at 100 nanometers and smaller.

Social risks related to nanotechnology development include the possibility of military applications of nanotechnology (such as implants and other means for soldier enhancement) as well as enhanced surveillance capabilities through nanosensors. However those applications still belong to science-fiction and will not be possible in the next decades. Significant environmental, health, and safety issues might arise with development in nanotechnology since some negative effects of nanoparticles in our environment might be overlooked. Such issues include potential occupational safety and health concerns for those involved in the manufacture of nanotechnologies.

However nature itself creates all kinds of nano objects, so probable dangers are not due to the nanoscale alone, but due to the fact that toxic materials become more harmful when ingested or inhaled as nanoparticles.<sup>3,4,15</sup>

### Nanotechnology in Dental Sciences

#### Salivary diagnostics powered by nanotechnologies

The ability to monitor health status, disease onset and progression, and treatment outcome through noninvasive means is a highly desirable goal in health care promotion and delivery. Oral fluid is a perfect medium to be explored for health and disease surveillance. Specific biomarkers associated with a health or disease state and the development of technologies that can discriminate between the biomarkers was identified.

A recent initiative of the National Institute of Dental and Craniofacial Research has created roadmap to achieve these goals through the use of oral fluids as the diagnostic medium to scrutinize the health and/or disease status of patients. This is an ideal opportunity to optimize state-of-the-art saliva-based biosensors for salivary biomarkers that discriminate between diseases.

#### Oral Fluid Nano Sensor Test

The envisioned product is called the Oral Fluid NanoSensor Test (OFNASET). The OFNASET is a handheld, automated,

easy-to-use integrated system that will enable simultaneous and rapid detection of multiple salivary protein and nucleic acid targets. This salivary biomarker detector can be used in the office of a dentist or another health care provider for point-of-care disease screening and detection.<sup>16</sup>

#### Nanotechnology for Dental Composites

Since the development of hybrid dental products, the quest has been to use smaller and smaller particles, a quest driven by the observation that smaller particles will result in improved polish. From a manufacturing perspective this has simply meant longer and longer milling times, as large particles were ground to make small particles<sup>30</sup>.

**Nanofiller particles** may be of two types Nanomeric, or NM, particles and Nanoclusters or NCs. The **Nanomeric (NM) particles** are monodispersenon aggregated and nonagglomerated silica nanoparticles which is treated with 3-methacryloxypropyltrimethoxysilane, or MPTS. **Nanoclusters (NCs) particles-** The primary particle size of this NC filler ranges from 2 to 20 nm, while the spheroidal agglomerated particles have a broad size distribution, with an average particle size of 0.6 micro meters.<sup>17, 18,22,23,26</sup>

#### Nanoproduct: Nanosolution

Nanosolutions produce unique and dispersible nanoparticles, which can be added to various solvents, paints and polymers in which they are dispersed homogeneously. Adper O Single Bond 2 adhesive incorporates 10% by weight of 5 nm diameter spherical silica particles through a process that prevents agglomeration. As discrete particles, their extremely small size keeps them in colloidal suspension. Thus, the use of nanotechnology in bonding agents ensures homogeneity and so the operator can now have total confidence that the adhesive is perfectly mixed every time<sup>2,21</sup>.

#### Nano-Ceramic Technology

The Organically Modified Ceramic nano-particles comprise a polysiloxane backbone. The chemical nature of the siloxane backbone is similar to that of glass and ceramics. Methacrylic groups are attached to the backbone via silicon-carbon-bonds. These Nano-Ceramic particles can be best described as inorganic-organic hybrid particles where the inorganic siloxane part provides strength and the organic methacrylic part makes the particles compatible and polymerisable with the resin matrix. The good resistance to micro-crack propagation might be related to the strengthening effect of the nano-ceramic particles. Propagating cracks are either more often reflected or absorbed by the nano-ceramic particles<sup>20</sup>. The Organically Modified Ceramic nano-particles comprise a polysiloxane backbone. The chemical nature of the siloxane backbone is similar to that of glass and ceramic.

#### Nanotechnology for Glass Ionomer Cement

**Nano Light Curing Glass Ionomer Restorative is comprised of:**

##### Two part system

Aqueous paste (acidic polyalkenoic acid, reactive resins and nano fillers)

Non aqueous paste (FAS glass, reactive resins, and nano fillers)

#### Filler content (69%)

27% FAS glass (acid and free radically reactive)

42% methacrylate functionalized nano fillers (acid and free radically reactive)

#### Cure and Setting reactions

Light curing (required)

Long term glass ionomer reaction (water, glass ionomer filler, polyacid, monomers, initiators)<sup>20</sup>

#### GIC Nano Primer

Nano primer is a one part, visible light-cure liquid specifically designed for use with GIC Nano restorative. It is comprised of the Vitrebond copolymer, HEMA, water, and photoinitiators. The primer is acidic in nature. Its function is to modify the smear layer and adequately wet the tooth surface to facilitate adhesion of Nano restorative to the hard tissue. In use, Nano primer is applied to the surface for 15 seconds, and air dried. The primer is then light cured for 10 seconds. Adequately air drying followed by light curing of the primer before placement of GIC Nano restorative provides adhesion to tooth structure<sup>19, 20</sup>.

#### Nanotechnology For Impression Materials

Nanofillers are integrated in vinylpolysiloxanes, producing a unique addition of siloxane impression materials. The materials has a better flow, improved hydrophilic properties, and enhanced detail precision.<sup>2,15</sup> Formulated with proprietary nano-particulate fillers for enhanced performance, *Correct Plus* Fast Set Impression Material exhibits outstanding tear strength and dimensional stability pour after pour. A low contact angle of 30° helps deliver exceptionally detailed and accurate impressions in the oral environment. To facilitate the pouring of stone models, *Correct Plus* Fast Set outgasses in 15 minutes or less ensuring optimal performance in the hands of the lab technician.

#### Nanoadhesive-POSS4

Polyhedral Oligomeric Silsesquioxanes (POSS) enable the design of additives that make plastics that are unusually lightweight, durable, heat tolerant and environmentally friendly. POSS combines organic and inorganic materials in molecules with an average diameter of 1.5 nanometres. They can be used as either additives in or replacements for traditional plastics. Current applications of POSS include dental adhesives in which a strengthened resin provides a strong interface between the teeth and the restorative material.<sup>21</sup>

#### Nano aluminium oxide fibers - Nanoceram3

Nanostructural aluminium oxide fibers provide added strength and improved performance to metals, plastics, polymers and composite materials. This new fiber, designated as nanoceram, represents a major breakthrough in ceramic fibers. The breakthrough advantage of the fiber technology is its ultra small 2 nanometer diameter with a high surface area of 300-600 m<sup>2</sup>/g. X-ray diffraction shows that the fibers are principally boehmite (AlOOH) with minor phases of gamma alumina and Al(OH)<sub>3</sub>.

The large number of hydroxyl groups available on the nanofibers generates a positive charge in water solution such that it will attract and retain negatively charged particles, including bacteria, virus, organic and inorganic colloids and negatively charged macromolecules.<sup>20</sup>

#### Hypersensitivity Cure

Dentin hypersensitivity is another pathologic phenomenon that may be amenable to a nanodental cure. There are many therapeutic agents for this common painful condition that provide temporary relief, but reconstructive dental nanorobots could selectively and precisely occlude selected tubules in minutes, using native biological materials, offering patients a quick and permanent cure.<sup>27</sup>

#### Tooth Repair

Nanodental techniques for major tooth repair may evolve through several stages of technological development, first using genetic engineering, tissue engineering and tissue regeneration, and later growing whole new teeth in vitro and installing them. Ultimately, the nanorobotic manufacture and installation of a biologically autologous whole replacement tooth, including both mineral and cellular components - e.g., complete dentition replacement therapy.<sup>24</sup>

#### Inducing Anesthesia

To induce oral anesthesia in the era of nanodentistry, a colloidal suspension containing millions of active analgesic micron-size dental nanorobots will be installed on the patient's gingiva. After contacting the surface of the crown or mucosa, the ambulating nanorobots reach the dentin by migrating into the gingival sulcus and passing painlessly through the lamina propria or the 1-3 micron thick layer of loose tissue at the cemento-dentinal junction. Upon reaching the dentin, the nanorobots enter the 1-4 micron diameter dentinal tubule holes and proceed towards the pulp, guided by a combination of chemical gradients, temperature differentials, and even positional navigation, all under onboard nanocomputer control<sup>24</sup>.

Assuming a total path length of about 10mm from tooth surface to pulp, and a modest travel speed of 100 microns/see, nanorobots can complete the journey into the pulp chamber in 100 seconds.

Once installed in the pulp and having established control over nerve impulse traffic, the analgesic dental nanorobots may be commanded by the dentist to shut down all sensitivity in any particular tooth that may require treatment. When the dentist presses the icon for the desired tooth on the handheld controller display, the selected tooth immediately numbs (or conversely later, upon command, awakens). After the oral procedures are completed, the dentist orders the nanorobots (via the same acoustic data links) to restore all sensation, to relinquish control of nerve traffic, and to egress from the tooth by similar pathways used for ingress, followed by aspiration.

Nanorobotic analgesics offer greater patient comfort and reduced anxiety, no needles, greater selectivity and controllability of analgesic effect, fast and completely reversible switchable action, and avoidance of most side effects and complications<sup>11</sup>.

**Nanoneedles**

Suture needles incorporating nano sized stainless steel crystals have been developed.

Trade name: SandvikBioline, RK 91™ needles. Nanotweezers are also under development which will make cell surgery possible in the near future<sup>15</sup>.

**Orthodontic nanorobots**

Orthodontic nanorobots could directly manipulate the periodontal tissues, including gingiva, periodontal ligament, cementum and alveolar bone, allowing rapid and painless tooth straightening, rotating and vertical repositioning within minutes to hours. This is in contrast to current molar uprighting techniques, which require weeks or months to complete<sup>31</sup>

**Nano Bone Replacement Materials**

**Hydroxyapatite nanoparticles used to treat bone defects are;**

- Ostim ® (osartis GmbH Germany) HA.
- VITOSS ® (orthovital Inc, USA) HA+ TCP.
- NanOss™ (Angstrom Medica, USA) HA.<sup>15</sup>

**Nanotechnology in Periodontics****Nanorods/Nanofibers/Nanotubes as Dental Materials**

Nanoparticles are being developed for a host of biomedical and biotechnological applications including drug delivery, enzyme immobilization and DNA transfection. Spherical nanoparticles are typically used for such applications as discussed above, but this only reflects the fact that spheres are easier to make than other shapes. Nanofibers that are less than 100 nm in diameter, including nanorods, nanoplatelets, nanotubes, nanofibrils, and quantum wires, are other major nanomaterials being widely explored for various applications, of which management of the periodontal diseases could be a prime target.<sup>42</sup>

**Nanorods**

The application of surfactants as reverse micelles or microemulsions for the synthesis and self assembly of nanoscale structures is one of the most widely adopted methods in nanotechnology. Chen et al. took advantage of these latest developments in the area of nanotechnology to mimic the natural biomineralization process to create the hardest tissue in the human body, dental enamel, by using highly organized microarchitectural units of nanorod-like calcium hydroxyapatite crystals arranged roughly parallel to each other. As detailed above, fully developed mature dental enamel is made of enamel prisms, highly organized microarchitectural units, which consist of bundles of nanorod-like calcium hydroxyapatite crystals arranged roughly parallel to each other. This structure spans the entire enamel thickness and is likely to play an important role in determining the unique physicochemical properties of the enamel.<sup>41</sup>

**Nanotubes**

Kolhi & Martin indicated that micro- and nanotube structures that resemble tiny drinking straws are alternatives and may offer advantages over spherical nanoparticles for some

applications. Examples of nanotubes include organosilicon polymer nanotubes, self-assembling lipid microtubes, fullerene carbon nanotubes, template-synthesized nanotubes, and peptide nanotubes. They offer some interesting advantages relative to spherical nanoparticles for biotechnological applications. For example, the large inner volumes (relative to the dimensions of the tube) can be filled with any desired chemical or biochemical species ranging in size from proteins to small molecules. In addition, the distinct inner and outer surfaces can be differentially functionalized chemically or biochemically. The open mouths may also make the inner surface accessible and make incorporation of species within the tubes particularly easy.<sup>43</sup>

**Nanomaterials for Periodontal Drug Delivery**

Nanomaterials are of interest from a fundamental point of view because the properties of a material (e.g. melting point, electronic properties, optical properties) change when the size of the particles that make up the material becomes nanoscopic. Recently, Pinon Segundo et al. produced and characterized triclosan-loaded nanoparticles by the emulsification-diffusion process, in an attempt to obtain a novel delivery system adequate for the treatment of periodontal disease<sup>44</sup>. The nanoparticles were prepared using poly(D,L-lactide-co-glycolide), poly(D,L-lactide) and cellulose acetate phthalate. Poly(vinyl alcohol) was used as stabilizer. Batches were prepared with different amounts of triclosan in order to evaluate the influence of the drug on nanoparticle properties. Solid nanoparticles of less than 500 nm in diameter were obtained. These triclosan nanoparticles behave as a homogeneous polymer matrix type delivery system, with the drug (triclosan) molecularly dispersed. Release kinetics indicates that the depletion zone moves to the center of the device as the drug is released. This behavior suggests that the diffusion is the controlling factor of the release. A preliminary in vivo study using these nanoparticles has been performed in dogs with only the gingival index (GI) and bleeding on probing (bleeding on probing) being determined. With respect to the gingival index (GI), at days 1 and 8, it was found that a severe inflammation was detected in control and experimental sites (GI ¼ 3). It was concluded that triclosan nanoparticles were able to effect a reduction of the inflammation of the experimental sites. This study has specifically tackled periodontal management; however, nanomaterials including hollow sphere, core-shell structure, nanotubes and nanocomposite have been widely explored for controlled drug release. It is conceivable that all of these materials could be developed for periodontal drug delivery devices in the future. Drugs can be incorporated into nanospheres composed of a biodegradable polymer, and this allows for timed release of the drug as the nanospheres degrade. This also allows for site-specific drug delivery<sup>45</sup>.

A good example of how this technology might be developed is the recent development of Arestin<sub>in</sub> in which tetracycline is incorporated into microspheres for drug delivery by local means to a periodontal pocket.

**Nanomaterials for Periodontal Tissue Engineering**

Currently, tissue engineering concepts for periodontal regeneration are focused on the utilization of synthetic

scaffolds for cell delivery purposes. Although the utilization of such systems offers promise, it is very likely that the next generation of materials will rely heavily on nanotechnology and its potential to produce nonbiologic self-assembling systems for tissue engineering purposes. Current materials available for such constructs are metals, ceramics, polymers, and even composite materials, the like of which have not yet been developed. The clinical utility of these nano-constructed self-assembling materials is their capacity to be developed into nanodomains or nanophases, leading to unique nanobuilding blocks with inbuilt nanocontrol and nanodelivery capabilities. Our present capacity to create polymer scaffolds for cell seeding, growth factor delivery and tissue engineering purposes is well recognized. In the future these processes may well be manipulated via nanodevices implanted to sites of tissue damage<sup>45</sup>

#### Nanorobotic Dentifrice (Dentifrobots)

Subocclusal-dwelling nanorobotic dentifrice delivered by mouthwash or toothpaste could patrol all supragingival and subgingival surfaces at least once a day, metabolizing trapped organic matter into harmless and odorless vapors and performing continuous calculus debridement. Properly configured dentifrobots could identify and destroy pathogenic bacteria residing in the plaque and elsewhere, while allowing the 500 or so species of harmless oral microflora to flourish in a healthy ecosystem.

Used as a mouthwash containing full of smart nanomachines to identify and destroy pathogenic bacteria while allowing the harmless flora of the mouth to flourish in a healthy ecosystem. The devices would identify particles of food, plaque, or tartar, and lift them from teeth to be rinsed away. Being suspended in liquid and able to swim about, devices would be able to reach surfaces beyond reach of toothbrush bristles or the fibres of floss.<sup>28</sup>

#### BONE REPLACEMENT MATERIALS

Hydroxyapatite nanoparticles used to treat bone defects are

##### Ostim® (Osartis GmbH, Germany) – HA

The bone substitute Ostim® (Medical device product class III) is a completely synthetically manufactured pure, nanocrystalline hydroxyapatite. The crystals are needle-shaped with a mean crystallite size of 18 nm. Due to its nanostructure, Ostim® is fully degradable after implantation. It enhances new bone formation and stimulates bone healing. Ostim is phagocytised by macrophages and osteoclasts; resorption process is completed within 15-20 weeks in animals. The material can be used in traumatology, orthopaedics, spine surgery and maxillofacial surgery.<sup>15</sup>

##### VITOSS® (Orthovita, Inc., USA)

#### An Improved Form of $\beta$ -Tricalcium Phosphate ( $\beta$ -TCP)

##### Highly porous structure

- Engineered to resemble human cancellous bone in porosity and structure
- Approximately 90% interconnected pore space, by volume
- Interconnected pores ranging in size from approximately 1 mm to 1000 mm

- Small pore sizes for high capillarity and good wicking properties
- Larger pore sizes for vascularization and bone ingrowth

#### Similar to the major mineral components in natural bone

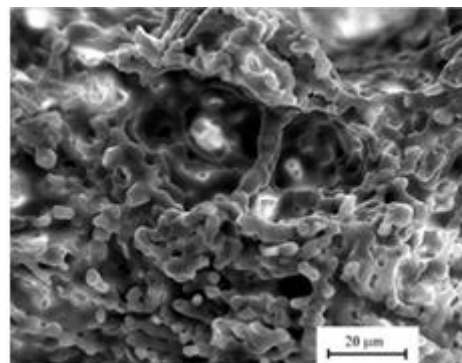
- Nano-sized particles of  $\beta$ -TCP
- Approximately 39% calcium and 20% phosphorus, compared with 35% and 15% in normal bone mineral
- Conforms to American Society for Testing and Materials (ASTM) guidelines for  $\beta$ -TCP for surgical implantation

#### A soluble scaffold for cancellous bone growth

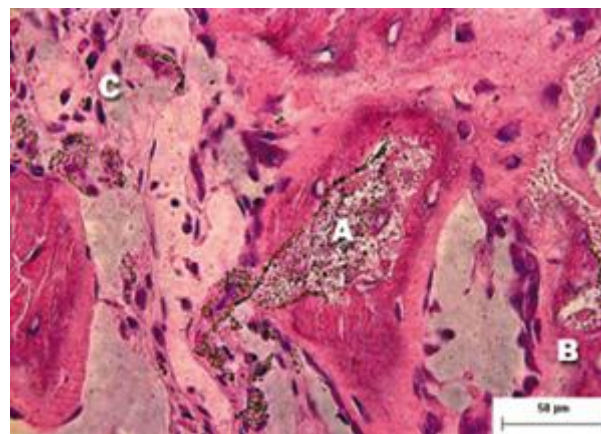
- More readily soluble than synthetic hydroxyapatite
- Resorbable through cell-mediated remodeling processes
- Remains intact long enough for bone ingrowth to take place
- In canine studies, new cancellous bone reached density and structure of existing cancellous bone by 12 weeks

#### The known safety profile of $\beta$ -TCP

- No reports in the literature of untoward responses to  $\beta$ -TCP
- Passed extensive cytotoxicity, sensitization, irritation, toxicity, hemocompatibility, and pyrogenicity testing to demonstrate biocompatibility and safety
- Nonimmunogenic in animal studies
- Appropriate as a substitute for cancellous bone in orthopaedic surgery



Scanning electron micrograph of VITOSS at 1000x magnification, showing porous structure



Center of canine humeral defect 6 weeks after implanting VITOSS. Note new bone formation and

**beginning of VITOSS resorption as evidenced by (A) lining of implanted VITOSS by osteoblasts, (B) surrounding osteoid maturing into healthy bone, and (C) implanted Vitoss engulfed by what appear to be multinucleated giant cells or osteoclasts NanOss™ (Angstrom Medica, USA)**

Angstrom Medica harnesses nanotechnology for orthopedic applications. Its flagship product is a patented biomimetic nanostructured material similar in composition to human bone. This novel new material forms the basis for a variety of orthopedic applications including sports medicine, trauma and spine. It can be used in areas where natural bone is damaged or removed, such as in the treatment of fractures, or in lieu of allograft (donor bone) and metallic medical devices. To produce NanOss, calcium and phosphate are manipulated at the molecular level and assembled to produce materials with unique structural and functional properties not seen before in other calcium phosphate-based materials. NanOss is highly osteoconductive and remodels over time into human bone, with applications in the sports medicine, trauma, spine and general orthopaedics markets. The company has also developed Injectable NanOss – endothermic, weight bearing bone cements; and programmable Bioactive Coatings with nanosurfaces.<sup>12,15.</sup>

#### **Dental Implants and Nanotechnology**

Conventional dental implants suffer from a restricted lifetime caused by implant failure. Obviously, this implant lifetime is not long enough, especially for young patients who are faced with frequent, complicated and expensive revision surgery. Therefore, extending the lifetime up to several decades would eliminate considerable patient suffering and save health care costs. Failure rate can be decreased if implant material stimulates rapid formation of new bone or if an implant is firmly fixed within adjacent bone (osseointegration).

Bone is a biocomposite material of which the major constituents are a complex mineral mixture (60-70% by weight) of calcium and phosphate in the form of hydroxyapatite, proteins (20-30%) with predominately type I collagen fibrils, and water (10%). The dimensions of the mineral and organic constituents are on the nanometre scale. Hydroxyapatite is between 2-5 nm in diameter and ~50 nm in length, and the estimated Young's modulus is 110 GPa. X-ray diffraction analysis showed an identical structure to synthetic hydroxyapatite ( $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ ) which is often used as bioactive ceramic coating material on titanium and cobalt-chromium implants. However, chemical analysis indicates presence of impurities such as carbonate, citrate, sodium, magnesium, fluoride and other ions. Collagen fibrils are composed of three identical collagen fibres that are woven in a triple-helix to form a cylinder of ~80-300 nm×1.5 nm. Obviously, bone cells are accustomed to interacting with nanostructured materials, i.e. materials with grain size of <100 nm in at least one dimension. It is assumed that nano-structured materials are very biocompatible. Hydroxyapatite coatings are more accepted in dentistry than in orthopaedics, but the potential in both fields is high. Hydroxyapatite promotes bone formation around the implant, increases osteoblast (bone-forming cell) functions such as adhesion, proliferation, and mineralisation.

However, it is unlikely that bulk synthetic hydroxyapatite will be used as load-bearing implant since fracture toughness (~1.0 MPa·m<sup>1/2</sup>) and flexural strength (<140 MPa) are low. Further research is necessary for long-term in vivo performance. Currently, Inframat, Inc. (Farmington, Connecticut, USA) and Spire Biomedical, Inc. (Bedford, Massachusetts, USA) are developing orthopaedic and dental implants using nanostructured hydroxyapatite coatings. Inframat is developing the next generation nanostructured hydroxyapatite coatings for hip, knee, and dental prostheses using a room temperature electrophoretic deposition technique. Knee and dental implants require high bond strength coatings to accommodate the greater impact loads and related higher stresses than hip prostheses. Spire Biomedical is developing a new family of "smart" nanophase (i.e. grain sizes less than 100 nm in at least one direction) coatings that will enhance bone integration and promote better device fixation. Although hydroxyapatite coatings are now widely used to encourage device fixation and stability, they can lead to undesirable soft tissue, as well as growth of desirable hard tissue. Spire's nanophase hydroxyapatite coatings are modified to selectively encourage hard tissue growth on implants while discouraging the formation of soft tissue growth that can result in non-optimal performance. Nano-structured metaloceramic coatings are still in the early stage of development and in vitro testing.<sup>27,24,29,33</sup>

#### **Nanoporous ceramic implant coatings**

A different approach to improve implant properties is anodisation of aluminium. Anodisation is widely used for producing corrosion resistant aluminium parts (Thompson, 1997). It has the effect of covering metallic aluminium with a strongly adherent surface layer principally composed of ceramic alumina (Al<sub>2</sub>O<sub>3</sub>). This technique was used to create a nanoporous alumina layer on top of a titanium alloy implant. The pores in the layer are roughly cylindrical and parallel to each other running perpendicular to the layer surface. At the base of each nanopore is a thin barrier layer of oxide separating the pore from the metallic aluminum underneath.

Human osteoblast cell response *in vitro* showed normal osteoblast adhesion, morphology, and proliferation indicating that nanoporous alumina coatings could improve implant designs. It should be noted that nanoporous alumina has the potential of being rendered bioactive by loading the porous structure with appropriate bioactive agents improving cell response and facilitate osseointegrative activity.

#### **Novel nanomaterials for implant coatings**

Titanium and titanium alloys have been successfully used as dental implants because these materials osseointegrate, i.e. direct chemical or physical bonding with adjacent bone surface without forming a fibrous tissue interface. For the optimisation of bone growth surface treatments have been applied, such as surface roughening by sandblasting, hydroxyapatite coating formation of titanium dioxide or titania and recently novel nanomaterials such as helical rosette nanotubes and titania nanotubes. Helical rosette nanotubes are a new class of organic nanomaterial featuring two basic DNA components, i.e. guanine and cytosine

(Fenniriet *et al.*, 2001). The results of this study showed that functionalised helical rosette nanotubes enhanced osteoblast function and could improve the next generation of orthopaedic implants.

### Implant surface roughness modification

Another way to improve the performance of dental implants can be achieved by modification of the surface roughness, specifically by creating nanometre-scale roughness. Cell responses might be triggered by changes in surface roughness, i.e. in horizontal as well as vertical direction, in the nanometre domain (<100 nm) rather than on submicron scale (>100 nm). Increased *in vitro* osteoblast function and osteoclastic (bone-resorbing cells) response was correlated with nanometre surface roughness (ranging from ~20-300 nm) for nanophase alumina and poly-lactic-co-glycolic acid (PLGA) cast of carbon nanofibres. More research is needed to determine optimal topographical parameters affecting a wide range of cell functions.

The performance of surgical blades can be enhanced significantly when micro structured hard metal is coated with diamond and processed. Major advantages of the diamond nano-layers in this application are low physical adhesion to materials or tissues and chemical/biological inertness. In addition, diamond has a low friction coefficient decreasing the penetration force necessary.

### Conclusion

Nanotechnology is at a crossroads. The emergence of consensus concerning the direction, safety, desirability and funding of nanotechnology will depend on how it is defined, and on who will be included as a result. It is safe to say that, as our world comes to depend more and more on science and technology, and as public awareness of the dangers and possibilities continues to increase, the involvement of all manner of participants will move further 'upstream' – into the heart of scientific work itself.

Although the achievement of the goal of complete regeneration of the periodontal tissues (cementum, periodontal ligament and bone) for periodontal management may not be possible for many years, recent developments in nanomaterials and nanotechnology have provided a promising insight into the commercial applications of nanomaterials in the management of periodontal diseases.

Nanotechnology offers great potential for benefit to humankind, and also brings severe dangers. While it is appropriate to examine carefully the risks and possible toxicity of nanoparticles and other products nanoscale technology, the greatest hazards are posed by malicious or unwise use of molecular manufacturing.

### References

- [1] **Sumita B. Mitra, Dong Wu, BRIAN N. HOLMES, Ph.D.** An application of nanotechnology in advanced dental materials. *J.Am.dent.assoc*, 2003;134:1382-90.
- [2] **Cecilia P. Turssi A,B, Jack L, Ferracane, Monica C. Serra.** Abrasive wear of resin composites as related to finishing and polishing procedures. *Dent Materials*;2005(21):641–648.
- [3] **Otilia M, Koo, Israel Rubinstein, HayatOnyuksel.** Role of nanotechnology in targeted drug delivery and imaging: a concise review. *NANOMED-NANOTECHNOL*: 1 (2005) 193–212.
- [4] **Robert A. Freitas, Jr.** Current Status of Nanomedicine and Medical Nanorobotics. *J. Comput. Theor. Nanosci.* 2005; 2:1–25.
- [5] **Robert A. Freitas Jr.** Nanotechnology, nanomedicine and nanosurgery. *Int.J.Surg.* 2005;10:1-4.
- [6] **Xuejun W, Donglu S, Ning Z.** Applications of Nanotechnology in Tissue Engineering.
- [7] **David T. Wong.** Salivary diagnostics powered by nanotechnologies, proteomics and genomics. *J.Am.dent.asso*, 2006;137:313-21.
- [8] **Ling X, Zhengpeng, Si-Dongli & P. Markbartold.** Nanotechnology and its role in the management of periodontal diseases. *Periodontol* 2000, 2006;40: 184–196.
- [9] **Sarvanakumar R, Vijayalashmi R.** Nanotechnology indentistry. *Ind J Dent Res*, 2006;17(2):62-65.
- [10] **Mallanagouda P, Dhoom S. M, and Sowjanya G.** Future impact of nanotechnology on medicine and dentistry. *J Indian Soc Periodontol*. 2008;12(2).
- [11] **Yves F. Dufrêne.** Towards nanomicrobiology using atomic force microscopy. *Microbiology*, 2008;6:674-80.
- [12] **Singla G, Vasudev K and Puri N .** Nanodentistry the future ahead. *BFUDJ*, 2008;1(1):43-45.
- [13] **V. Sujatha, Malathi S, S. Mahalaxmi.** Nanorobotics- A futuristic approach. *J Dent Sci*, 2010;1(1):86-90.
- [14] **Giovanna O, mauriziop et al.** A double-blind randomized-controlled trial comparing the desensitizing efficacy of a new dentifrice containing carbonate/hydroxyapatite nanocrystals and a sodium fluoride/potassium nitrate dentifrice. *J Clin Periodontol* 2010; 37: 510–517.
- [15] **Ana-Maria D, Cristina.** Dental nanorobots small instruments with large potential. *J.Oral Rehabil.* 2011;3(4):77-83.
- [16] **Rita C, M.Kala, Kiran.KN. Biji.B, Priyank B and Ruchi.B.** NANODENTISTRY: Exploring the beauty of miniature. *J Clin Exp Dent*. 2012; 4(2):119-24.
- [17] **Akhil J, Sameer M, Tamanpreet K and Sunpreet K.** Nanotechnology – The New Era of Dentistry. *J Dent Med Sci*. 2016;15( 5) : 47-49.
- [18] **Saranya G.** Nanotechnology in Dentistry- A Review. *J Dent Med Sci*. 2017;16( 1) : 90-95.
- [19] **Dayanand C. Irshad K, Shashank K, Srinivas B, Neha G and Rucha D.** Nanotechnology: Conservative Dentistry and Endodontics. *J Dent Med Sci* 2017;16(4):102-107.
- [20] **Shaesta K. B, Smiti B and M.L.V. Prabhuj.** Current applications of nanotechnology in dentistry: a review. *Microbiology*;72-77.
- [21] **Shweta D, Chandra D.D, Akhilesh C, Naresh S.** Nanotechnology boon or bane for restorative dentistry; A review. *Int J Eng Sci*. 2013; 2 ( 11):01-05.
- [22] **Aishwarya D, Iffat N.** Nanotechnology in dentistry: A review. *J Adv Pham Educ Res* 2017;7(2):43-45.
- [23] **Ira G, Shankar T.G, Rohit G and Sweta.** Nanorobots in periodontics. *J Dent Sci Res* 2013;4(2):6-9.

- [24] **Saloni c.** Nanotechnology and its Application. *International J Agr Food Sci Tech* 2013;4(10) :1011-1018.
- [25] **R. Hemalatha, A. Sivachandran, R. Kalaivani.** Nanotechnology - A Novel Strategy in Periodontal Regeneration? *Int J Med Biosci.* 2014; 3(1): 26 – 28.
- [26] **Abiodun-S, Ajayi ,Arigbede .** Nanotechnology and its Application in Dentistry. *Ann Med Health Sci Res* 2014 ; 4( 3 ):171-77.
- [27] **Ritika A, Himanshu K.** Nanotechnology in Dentistry - Hope or Hype. *Ora Health Dent M* 2014;13 ( 4):928-33.
- [28] **Mayuresh J B, Nandlal GT.** Nanotechnology: A Boon to Dentistry. *J Dent Sci Oral Rehab* 2014; 5(2):78-88.
- [29] **Shilpa S. , Sathyajith N. Naik, K. K, Shashibhushan, P. Poornima, Shivayogi M. Hugar, N. M. Roshan.** Nanodentistry: The next big thing is small. *Int J Contemp Dent Med Rev* 2014;1-6.
- [30] **Suhail M. J , Reyaz A M, Roobal B, Munaza S, Mehraj K, Muzafar A.B.** Role of Nanotechnology in Dentistry. *Sch. J. App. Med. Sci.,* 2014; 2(2D):785-789.
- [31] **Ali A ,LaurentB,RomanA,Hae-won K, Jonathan C K.** Nanotechnology in dentistry: prevention, diagnosis, and therapy. *Int J Nanomed* 2015;10 6371–94.
- [32] **Jayashree. A M, Pradnya P W, Veena A P, Jignesh P, B. Bhargavi.** Small Things Have a Big Impact- Nanotechnology in Periodontics. *Int J Sci Res* 2017;6 (2): 1840-48.
- [33] **Yancong Z, Hanwen S, Xinfeng S, Xiangling G And Chunyan S.** Biomaterials for periodontal tissue regeneration. *Rev Adv Mater Sci* 2015;40:209-14.
- [34] **Anna P. N.** Nanotechnology and its Applications in Medicine. *Med Chem* 2015;5(2):81-89.
- [35] **Deeksha J, Tarun G, Amit K. G & Goutam R.** Advanced drug delivery approaches against periodontitis. *Drug Delivery,* 23(2), 363-377.
- [36] **Lakshmi S, Balasubramanian D.** Nanotechnology in Dentistry. *Int J Dent Sci Res* 2013;1(2) 40-44.
- [37] **Maria J. R, Daniela .M et al.** Organic nanomaterials and their applications in the treatment of oral diseases. *Molecules* 2016;21(207):1-23.
- [38] **Siddharth T, Anukrit R et al.** Nanotechnology: The Beginning of New Era. *Int J En Res Med Dent Care* 2016; 3 (4):1-14.
- [39] **Chintan R, Komal V.** Nanotechnology in dentistry. *J Adv Med Dent Sci Res* 2016;4(3):51-53.
- [40] **Kiran R, JayaShree M et al.** Biosynthesis, Characterization and Antibacterial Efficacy of Silver Nanoparticles Derived from Endophytic Fungi against *P. gingivalis*. *J Clin Diag Res.* 2017 ;11(9):92-96.
- [41] **Neha Y, Probal S et al.** Role of nanotechnology in advancement of periodontology. *J Dent Med Sci* 2017;16( 8):38-41.
- [42] **Mohammad A, Masoud B, Sirous R.** Periodontal diseases and recently applied
- [43] nano-technology: a review article. *Health* 2017;345-51.
- [44] **Afiu A, Siok-Y ,Seok-Ming T.** Roles of nanotechnological approaches in periodontal disease therapy. *J App Pharm Sci* 2017;7 (07): 234-242.