Nanotechnology in Dentistry - Hope or Hype

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Abstract

A new revolution in the field of dentistry is the use of nanotechnology. This technology has got remarkable potential that can bring considerable improvements to human health in the form of nanomaterials, nano diagnostics and nano robotics. Nano dentistry will make possible the maintenance of comprehensive oral health by employing nano tissue devices which will allow precisely controlled oral analgesia, dentine replacement therapy, permanent hypersensitivity cure and complete orthodontic realignment etc., all in single office visit. However, like two sides of a coin, though nanotechnology possesses tremendous potential, it has its share of limitations including social issues of public acceptance, ethics, regulation, and human safety. The present article focuses on the current status and the future applications of nanotechnology in dentistry, assessing whether it is a hope or just hype.

Key Words: Nanomaterials, Nanodentistry, Nanocomposites, Nanorobots

Introduction

Man's quest to create new technology and materials which are better and more efficient led to the introduction of 'Nanotechnology', a technology that deals with structures ranging in the size of 100 nanometers or smaller in at least one dimension and developing materials or devices within that size. The term 'nano' is derived from a greek word meaning 'dwarf'. The late Nobel Prize winning physicist Richard P. Feynman contemplated the potential of nanosize devices as early as 1959. In his historic lecture, "There's plenty of room at the bottom" he concluded by saying, "this is a development which I think cannot be avoided" [1]. Feynman's idea was revived in the mid-1980s, when an engineer K. Eric Drexler published "Engines of Creation", a book to popularize the potential of molecular nanotechnology and introduced the term nanotechnology [2].

The basic idea of nanotechnology is to employ individual atoms and molecules to construct functional structures. Nanotechnology has revolutionized all fields from health care to engineering into a new archetype beyond traditional and dentistry is no exception. The speed at which progress has been made in science has introduced nanotechnology to dentistry from its theoretical basics instantly into the actual world. Nanodentistry is expected to make it possible to maintain near-perfect oral health through the use of nanomaterials, bioengineering and nanorobotics [3-8]. Nanotechnology possesses tremendous potential but social issues of public acceptance, ethics, regulation, and human safety must be addressed before nanotechnology can be looked upon as the hope for the future.

The purpose of this article is to review current status of nanotechnology in dentistry and to provide an insight into the future highlighting the various possible applications as well as concerns associated with the use of this technology.

Approaches in nanotechnology [9,10]

The fabrication techniques of the nanoscale structures can be divided into the following three approaches:

Top-down approach: Top-down fabrication reduces large pieces of materials all the way down to the nanoscale, This approach requires larger amounts of materials and can lead to waste if excess material is discarded. Here, larger materials are patterned and carved down to make nanoscale structures in precise patterns. Materials reduced to the nanoscale can suddenly show very different properties, enabling unique applications.

Bottom-up approach: The bottom-up approach to nano manufacturing creates products by building them up from atomic- and molecular-scale components, which can be time-consuming. This begins by designing and synthesizing custom made molecules that have the ability to self-assemble or self-organize into higher order structures.

Functional approach: In this approach, components of a desired functionality are developed without regard to how they might be assembled.

Self-assembly: It is an autonomous organization of components into patterns or structures without human intervention.

Nanomaterials

Siegel has classified nanomaterials as zero dimensional, one dimensional, two dimensional and three dimensional nanostructures [11]. Various nanostructures include:

Nano particles, Nano pores, Nano tubes, Nano rods, Nano spheres, Nano fibres, Nano shells, Dendrimers & dendritic copolymers.

Nano dentistry – A Hope

The applications of nanotechnology in dentistry can be studied under:

- Nano diagnostics
- Nano materials
- Nano robotics

Nano diagnostics

The following nanostructures can be used in the detection of oral cancer and other diseases:-

Nanoscale Cantilevers: These are flexible beams built using semiconductor lithographic techniques that can be engineered to bind to molecules associated with cancer.

Nano pores: These are tiny holes that allow DNA to pass through one strand at a time. They will make DNA sequencing more efficient.

Nano tubes: These are carbon rods about half the diameter of

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a molecule of DNA that not only can detect the presence of altered genes but also may help researchers pinpoint the exact location of those changes.

Quantum Dots: These are nanomaterials that glow very brightly when illuminated by ultraviolet light. They can be coated with a material that makes the dots attach specifically to the molecules to be tracked. Quantum dots bind themselves to proteins unique to cancer cells.

Lab-on-a-chip: Lab-On-a-Chip (LOC) is a device which integrates several laboratory functions on a single chip. Assays are performed on chemically sensitized beads populated into etched silicon wafers with embedded fluid handling and optical detection capabilities. This device has been used to assess the levels of interleukin-1beta (IL-1beta), C-Reactive Protein (CRP), and Matrix Metallo Proteinase-8 (MMP-8) and other molecules in whole saliva, which are potential use of these biomarkers for diagnosing and categorizing the severity and extent of periodontitis [12,13].

Nano Electromechanical Systems (NEMS) [14]: These are a class of devices integrating electrical and mechanical functionality on the nanoscale. NEMS form the logical next miniaturization step from so-called microelectromechanical systems, or MEMS devices. Nanotechnology based NEMS biosensors that exhibit exquisite sensitivity and specificity for analyte detection, down to single molecule level are being developed.

Oral Fluid Nano Sensor Test (OFNASET): The Oral Fluid Nano Sensor Test (OFNASET) technology platform combines cutting-edge technologies, such as self-assembled monolayers (SAM), bio nano technology, cyclic enzymatic amplification, and microfluidics, with several well-established techniques including microinjection molding, hybridization-based detection, and molecular purification. This technology is used for multiplex detection of salivary biomarkers for oral cancer. It has been demonstrated that the combination of two salivary proteomic biomarkers (thioredoxin and IL-8) and four salivary mRNA biomarkers (SAT, ODZ, IL-8, and IL-1b) can detect oral cancer with high specificity and sensitivity [15].

Optical Nano biosensor: The nano biosensor is a unique fiber optics-based tool which allows the minimally invasive analysis of intracellular components such as cytochrome c, which is a very important protein for the production of cellular energy and is involved in apoptosis, or programmed cell death [16].

Nano materials

Nano composites: Non agglomerated discrete nanoparticles are homogeneously distributed in resins or coatings to produce nano composites which are either of nano hybrid or nano filled types, usually in the context of particle size. Characterized by filler-particle sizes of ≤100 nm, these materials can offer many advantages over conventional micro filled and hybrid resin-based composite systems, primarily in terms of smoothness, polishability and precision of shade characterization, moreover flexural strength and micro hardness provided is similar to those of the newer posterior resin-based composites. Andrade et al tested fragments of nano filler containing alumino silicate (1:4 M ratio of alumina to silica) powder. These fragment nano fillers had a mean particle size of 80 nm and 1.508 refractive index [17]. Nano composites show better hardness, superior flexural strength, modulus of elasticity and translucency, superior handling properties, and display a 50% decrease in filling shrinkage.

Nano Light-curing glass ionomer restorative: This combines nanotechnology with Fluoro Alumino Silicate (FAS) technology. Advantages offered are excellent esthetics, improved wear resistance and superior polish.

Impression materials: Nanofillers are incorporated in vinylpolysiloxanes, creating an exclusive addition of siloxane impression materials. The material has improved flow, enhanced hydrophilic properties and better feature accuracy. Commercially available as Nanotech Elite H-D, these offer following additional advantages: high tear resistance, resistance to distortion and heat resistance, instant set that reduces errors caused by micro movements [18].

Nano solutions: Nano solutions produce unique and dispersible nanoparticles, which can be added to various solvents, paints & polymers in which they are dispersed homogenously. Nanotechnology ensures homogeneity in bonding agents and makes adhesive mix perfectly every time [19,20].

Nano capsules: The South West Research Institute (SWRI) Texas, United States, has developed targeted release systems that cover nano capsules together with novel vaccines, antibiotics, and drug delivery with reduced side effects. Nanoparticles could be engineered to target oral tissues as well as cells derived from the periodontium. Engineered Hepatitis B virus envelope L particles were allowed to form hollow nanoparticles displaying a peptide that is crucial for liver-specific entry by the virus in humans [21].

Nano-composite denture teeth*:* Nano composite denture teeth comprise of Polymethylmethacrylate (PMMA) and uniformly dispersed nano - sized filler particles. These have superior polish, stain and impact resistance, active surface structure as well as improved surface hardness and wear resistance [22].

Nanomaterials for Periodontal Drug Delivery: Drugs can be incorporated into nanospheres composed of a biodegradable polymer thus allowing for timed release of the drug as the nanospheres degrade. Recently triclosan-loaded nanoparticles were found to be effective in achieving reduction of inflammation [23-26]. Tetracycline incorporated into microspheres is available as Arestin for local drug delivery into periodontal pocket [27]. A nanostructured 8.5% doxycycline gel was observed to exhibit favorable results following experimental periodontal disease in rats [28].

Nano needles: Suture needles incorporating nano-sized stainless steel crystals have been developed. Nano tweezers, which are expected to make cell-surgery possible in the near future, are also under development. Trade name: Sandvik Bioline, RK 91TM needles [AB Sandvik, Sweden] [21].

Bone graft materials: Hydroxyapatite nanoparticles used to treat bone defects are: Ostium (Osartis GmbH, Germany) HA, VITOSSO (Orthovita, Inc, USA) HA + TCP, Nano SSTM (Angstrom Medica, USA) HA. Recently developed nano-bioactive glass in concentration less than 4mg/ml. was found to be biocompatible with gingival fibroblasts in an in vitro study [29].

Laser Plasma Application for periodontics: When nanoscale (20-50 nm) TiO_2 particle sizes are presented on human skin in the form of a gel-like emulsion, these exhibit some interesting properties such that when irradiated with laser pulses, these particles can be optically broken down with accompanying effects like shock wave, micro-abrasion of hard tissue and stimulation of collagen production [22]. Its clinical applications include periodontal treatment, depigmentation, incision of soft tissue without anesthesia and caries preparation.

Implants: Nanoscale alteration of titanium implant surfaces can alter cellular and tissue responses that may promote osseointegration. Three nano-structured implant coatings have been developed:

- **Nanostructured diamond:** It has ultrahigh hardness, improved toughness, low friction and good adhesion to titanium alloys.
- **Nanostructured hydroxyapatite coatings:** This is used to achieve the desired mechanical characteristics and enhanced surface reactivity and has been found to increase osteoblast adhesion, proliferation, and mineralization [29].
- **Nanostructured metallo ceramic coatings:** These provide continuous variation from a nano crystalline metallic bond at the interface to the hard ceramic bond on the surface [30].

Tooth durability and appearance: The durability and appearance of teeth may be improved by substituting upper enamel layers with covalently bonded artificial materials such as sapphire or diamond, which have 20-100 times the hardness and strength of natural enamel and good biocompatibility. However, sapphire and diamond are brittle and prone to fracture; this drawback can be overcome by the addition of carbon nanotubes [17].

Wound healing:

- Biodegradable nano fibres - delivery platform for haemostatic
- Wound dressings with silk nano fibres in development.
- Nano crystalline silver particles with antimicrobial properties on wound dressings [21].

Nano Vectors: Application of nanotechnology in human gene therapy has been reviewed widely by Davis, who described non-viral vectors based on nanoparticles (usually 50-500 nm in size) that were already tested to transport plasmid DNA. He emphasized that nanotechnology in gene therapy would be applied to replace the currently used viral vectors with potentially less immunogenic nano size gene carriers [31].

Biofilm management: These include liquids and pastes that contain nano-apatites for biofilm management at the tooth surface, and products that contain nanomaterials for the remineralization of early sub–micrometer–sized enamel lesions.

Easy–to–clean, wear–resistant and biocompatible nanocomposite surface coatings for biofilm management are close to being used in dental practice [32,33].

Nano Robotics

Dentin hypersensitivity: Dentin hypersensitivity may be caused by changes in pressure transmitted hydrodynamically to the pulp. Dental nano robots could selectively and precisely occlude selected tubules in minutes offering patients a quick and permanent cure [22].

Local anesthesia: Micron sized active analgesic dental robots suspended in a colloidal solution instilled on the patient's gingiva reach the pulp via the gingival sulcus, lamina propria and dentinal tubules. This is guided by a combination of chemical gradients, temperature differentials and even positional navigation which are all under the control of on board nano computer as directed by the dentist [34-36]. Once installed in the pulp and having established control over nerve-impulse traffic, the analgesic dental nano robots may be commanded by the dentist to shut down all sensitivity in any tooth that requires treatment. After the oral procedures are completed, the dentist orders the nano robots to restore all sensation, to renounce control of nerve traffic and to exit from the tooth via similar pathways used for entry; following this, they are aspirated. Nano robotic analgesics offer greater patient comfort and reduced anxiety without the use of needles, greater selectivity and controllability of the analgesic effect, fast and completely reversible action, and avoidance of most side effects and complications [22].

Dentif robots: Nano robotic dentifrice delivered by mouthwash or toothpaste could patrol all supra gingival and sub gingival surfaces atleast once a day, metabolizing trapped organic matter into harmless and odorless vapors and performing continuous calculus debridement [34-37]. Properly configured dentif robots could identify and destroy pathogenic bacteria residing in the plaque and elsewhere, while allowing species of harmless oral microflora to flourish in a healthy ecosystem. Dentif robots would also be a useful means to treat halitosis, since bacterial putrefication is the central metabolic process involved in oral malodor [22].

Orthodontic treatment: Orthodontic nano robots could openly influence the periodontal tissues, including gingivae, periodontal ligament, cementum, and alveolar bone, allowing rapid and painless tooth straightening, rotating, and vertical repositioning within minutes to hours. This offers an advantage over the molar uprighting techniques in current use, which require weeks or months to complete [23].

Complete dentition replacement therapy: Fabrication of a new tooth in the dentist's office, within the time frame of a typical dental office visit through a desktop manufacturing facility, i.e., complete dentition replacement therapy will become possible soon. Chen et al. utilizing nanotechnology simulated the natural bio mineralization process to create the dental enamel, using highly organized micro architectural units of nano rod-like calcium hydroxyapatite crystals arranged roughly parallel to each other [38]. Whether, dentin, cementum and alveolar bone can be simulated in a similar fashion remains to be seen.

Nano Technology-only a Hype?

Though nanotechnology offers several promises in the field of dentistry, it still faces many significant challenges in realizing its tremendous potential. The problems range from basic engineering problems like precise positioning and assembly of molecular-scale parts, economical mass production techniques to biocompatibility and the simultaneous coordination of the activities of large number of independent micrometer-scale robots. In addition, there are larger social issues of public acceptance, ethics, regulation and human safety that must be addressed before we may call nanotechnology as a hope for the future.

Regulation issues

Food and Drug Administration (FDA) regulations for the control of nanotechnology-based materials are still lacking. There is a serious requirement to standardize these nanotechnology-based products and delivery devices.

The three main elements of nanomaterials that need to be regulated are characterization, safety, and environmental impact [39]. However, regulatory agencies like the FDA, the Environment Protection Agency (EPA), and the Nuclear Protection Agency are regulating the major health risks associated with nanomaterials. Workers may be exposed to nanosized particles in the manufacturing or industrial use; the National Institute for Occupational Safety and Health is performing research on nanoparticle interaction with body systems [11]. The organic food sector has been the first to act with the regulated exclusion of engineered nanoparticles from certified organic produce. So far, neither engineered nanoparticles nor the products and materials that contain them are subject to any special regulation regarding production, handling or labeling. Limited nanotechnology labeling and regulation may exacerbate potential human and environmental health and safety issues associated with nanotechnology. It has been argued that the development of comprehensive regulation of nanotechnology will be vital to ensure that the potential risks associated with the research and commercial application of nanotechnology do not overshadow its potential benefits.

Ethical issues

A common misconception regarding nanotechnology that the nanotechnology revolution is inevitably good, results from a preoccupation with the crucial contributions that technology makes to the comfort, security, health and longevity of people's lives in industrialized nations. If one takes a more encompassing historical, global and ecological view of technology's development and impacts, it is clear that emerging technologies (including emerging nanotechnologies) are not inevitably good. Another misconception, that the point of the social and ethical issues is to secure public acceptance, arises from the desire for smooth commercialization of emerging nanotechnologies coupled with the view that public opposition to them is primarily the result of misunderstandings or baseless concerns regarding them. In fact, people's concerns regarding emerging technologies are often neither the result of ignorance nor baseless. Moreover, as indicated above, there are robust roles for ethics in responsible development of nanotechnology other than securing public acceptance.

The goal for any emerging technology is to contribute to the flourishing of human race in socially just and environmentally sustainable ways.

The role of ethics in responsible development of nanotechnology includes:

- Elucidating what constitutes justice, human flourishing and sustainability;
- Identifying opportunities for nanotechnology to accomplish the goal and anticipating impediments to its doing so;
- Developing standards for assessing prospective nanotechnologies;
- Providing ethical capacity to enable society to adapt effectively to emerging nanotechnologies
- Identifying limits on how the goal should be pursued.

Environmental and health issues

Nanomaterials released in the environment can be further modified by temperature, pH, different biological conditions and presence of other pollutants, altering atmosphere, soil and water and proving to be harmful to human health and the environment.

There are four portals of entry for nanoparticles into the body: they can be inhaled, swallowed, absorbed through skin or be deliberately injected during medical procedures. Once within the body they are highly mobile and in some instances can even cross the blood-brain barrier. One of the big issues that needs to be resolved is how these nanoparticles behave inside the organism. Basically, the behavior of nanoparticles is a function of their size, shape and surface reactivity with the surrounding tissue. They could cause overload on phagocytes, thereby triggering stress reactions that lead to inflammation and weaken the body's defense against other pathogens. Another concern is their potential interaction with biological processes inside the body: because of their large surface, nanoparticles on exposure to tissue and fluids will immediately adsorb some of the macromolecules that they encounter, onto their surface. They can also produce nervous and cardiovascular adverse effects. Nanoparticles can be absorbed from the gastrointestinal tract and enter the circulatory system. Nanoparticles are readily taken up by many types of cells in vitro and are expected to cross the blood-brain barrier. Carbon black nanoparticles have been implicated in interfering with cell signaling. It could also have unwanted effects on the DNA of cells, which could potentially cause genetic defects [40,41].

As long–term effects of nanotechnology are unknown, therefore, potential hazards caused by the nanotechnology might not show for many years.

A particular problem with nanotechnology lies in the huge gap between the public perception of what the hype promises and the scientific and commercial reality of what the technology actually delivers today and in the near future. There is a need for developing systemic solutions, monitoring, and recording of the potential hazard as well as finding timely responses in order to achieve safety for human health and the environment. The benefits of nanotechnology are enormous, therefore studies that examine the health, environmental, ethical, and safety issues should improve our understanding of how to exploit the benefits and diminish the risks [42,43].

Support for the continued advancement of nanotechnology research, and eventual integration of nanotechnology into consumer products and useful applications, will depend heavily on the public's acceptance of nanotechnology. Governments around the world must take a proactive stance to ensure that environmental, health and safety concerns are addressed as nanotechnology research and development moves forward in order to assure the public that nanotechnology products will be safe.

Once nano mechanics are available, the ultimate dream of dentists throughout the world will, at last, become a reality. Programmable and controllable micro scale robots comprising nanoscale parts fabricated to nanometer precision will allow dentists to execute therapeutic and reconstructive procedures at the cellular and molecular levels after having fulfilled all the safety norms. The current materials available from nanotechnology through green nanotechnology have fulfilled the safety norms and possess improved qualities than their previous ones. Thus, in spite of all the limitations and problems that nanotechnology faces at present, it certainly promises to be a hope for the future and not merely a hype.

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