Review Article

Nanotechnology: The future

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ABSTRACT

The challenge to our profession today is to improve the quality of oral health while overcoming both extrinsic and intrinsic factors which may adversely affect our progress toward achieving this goal. Nanotechnology which is fast developing, its name reverberating in almost every field, is also making and is set to transform dentistry in a huge way. This article tries to give an insight of the application of nanotechnology in dentistry using both top down and bottom up approach, recent development of nano products with superior quality, helical rosette nanotubes as a bone substitute, surface treatment of implant, dentifrobot, improved diagnostic instruments, (biomarkers, stem cell imaging in MRI) precise drug delivery system, controlled radiation therapy and bio nano sensors for cancer treatment, the near to achieve future ground breaking realities of development of bionic mandible, nanorobots, respirocytes, microbiovore, cytorobots, karyorobots, their effect on dentistry and medicine, and the possible risk factors and the ethical concerns to be looked into for application of nanotechnology in dentistry.

Key words: Bionic mandible, green nano, biosensors, cytorobot, dentifrobot, karyorobot, microbiovore, nanotechnology, respirocytes

INTRODUCTION

To believe in the things you can see and touch is no belief at all. But to believe in the unseen is both a triumph and a blessing. - Bob Proctor

Witnessing the beginning of truly ground breaking advances in technology is a rare opportunity.[1] Skepticism is a natural reaction where we are presented with a radically new method and its potential use, skepticism helps us filter the valuable from the worthless, the permanent from the ephemeral and the rational from the preposterous. In a race toward limits set by natural law, the finish line is predictable even if the path and the pace of the runner are not. So however futuristic, they may seem sound projection of technological possibilities are quite distinct from prediction.

NANOTECHNOLOGY

Nano is derived from the Greek word for dwarf.

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Nanotechnology is distinguished primarily by the scale at which it acts, one billionth of a meter or one ten thousand the width of human hair. In simple terms, it is engineering at the atomic or molecular scale.

How new is nanotechnology?

In 1959, physicist and future Nobel Prize winner Richard Feynman [Figure 1] gave a lecture to the American Physical Society called "There's Plenty of Room at the Bottom.[2]" The focus of his speech was about the field of miniaturization and how he believed man would create increasingly smaller, powerful devices. Feynman's idea remained largely undiscussed until the mid-1980s, when the MIT educated engineer K. Eric Drexler [Figure 1] published "Engines *of Creation*", a book to popularize the potential of molecular nanotechnology in 1986 and introduced the term nanotechnology.[3] In a lecture called "Small Wonders: The World of Nanoscience," Nobel Prize winner Dr. Horst Störmer said that the nanoscale is more interesting than the atomic scale because the nanoscale is the first point where we can assemble something.[4] It is not until we start putting atoms together that we can make anything useful. Many scientists around the world are engineering their thoughts for the creation, application of nanotechnology. Dr. Robert A. Fretias Jr is one among the pioneer scientist who has written about nanomedicine, nanodentistry and its future changes.

What made nanotechnology possible?

Two achievements developed nanotechnology through the scientific method rather than conceptual. First, the invention of scanning tunneling microscope (STM) by Binnig and Rohrer in 1981, by which the individual atoms were easily identified for the first time. Some of the limitations of this microscopy were eliminated through the invention of the atomic force microscope [Figure 2], which could image non-conducting materials such as organic molecules. This invention was integral for the study of carbon buckyballs[5], discovered at Rice University in 1985-1986 and carbon nanotubes few years later.

Man's desire to create materials with better improved properties is ever lasting and still persuing. Nanotechnology has immense potential in fullfilling this desire; the properties of materials change very drastically by just manipulating the way atoms or molecules are arranged, considering a simple example graphite *vs.* diamond [Figure 3].

What is the difference between graphite and diamonds? Both materials are made of carbon, but both have vastly different properties. Graphite is soft; diamonds are hard. Graphite conducts electricity, but diamonds are insulators and can not conduct electricity. Graphite is opaque; diamonds are usually transparent. Graphite and diamonds have these properties because of the way the carbon atoms bond together at the nanoscale.

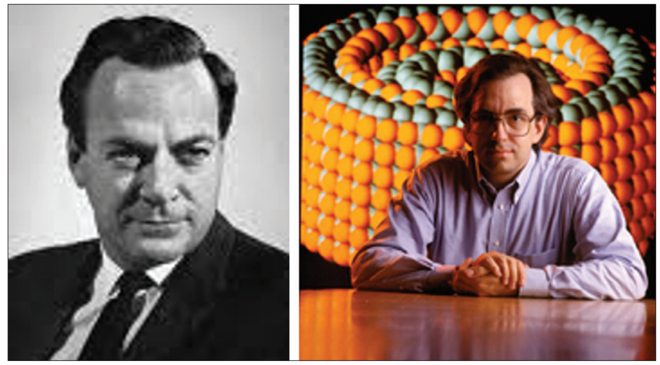

Figure 1: Richard Feynman and K. Eric Drexler

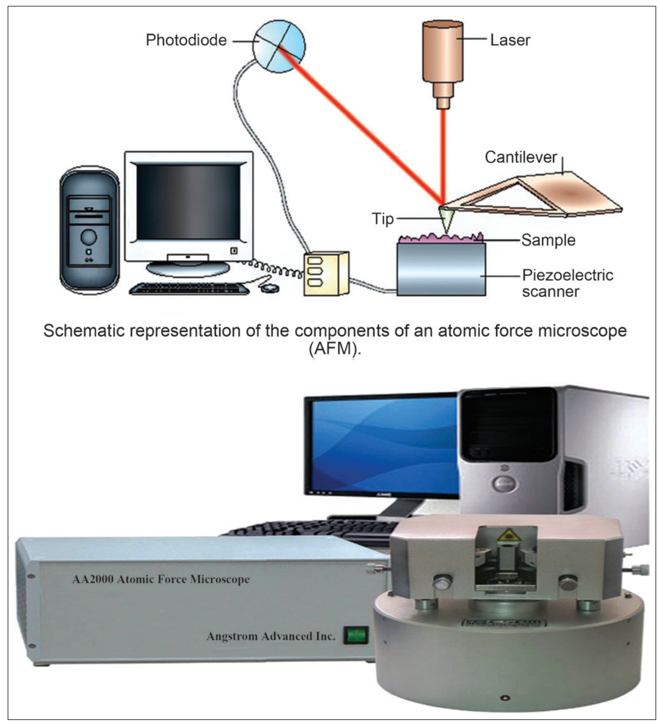

Figure 2: Atomic force microscope

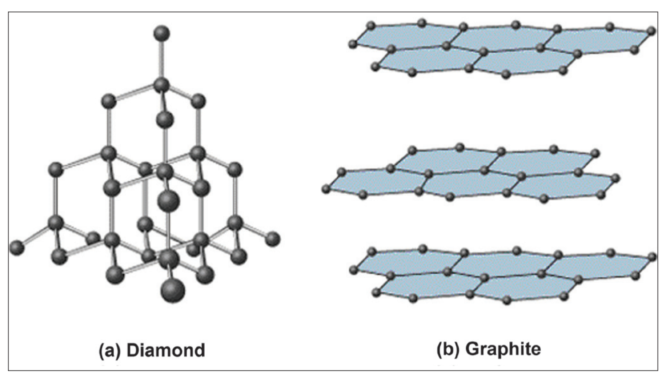

Figure 3: Graphite vs diamond

APPROACHES IN NANOTECHNOLOGY

There are many different approaches followed for creation of nanoproducts; the most common approaches are bottom up, top down, and functional.

Bottom up

Methods used for producing nanoscale structure, through this method nanoparticles are produced directly.[6] Various nanoparticles produced through bottom up method and used in dentistry are nanopores, nanotubes, quantum dots, nanoshells, dendrimers liposomes, nanorods, fullerenes, nanospheres, nanowires, nanobelts, nanorings, nanocapsules.

Top down

Used to manufacture nanoscale structures. Mostly extension of method already employed in small scale (at micron size), this is further miniaturization.

Functional approach

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

Other approaches followed at Rice University[7] are given as follows:

Wet nanotechnology

Study of biological system that exist mainly in water environment, which include genetic material, membranes, enzymes, and nano-sized cellular components.

Dry nanotechnology

It derives from surface science and physical chemistry focuses on fabrication of structure in carbon, silicon and other organic materials.

Computational nanotechnology

It permits the modeling and stimulation of complex nanometer scale structure, the predictive and analytical power of computation is critical to success in nanotechnology.

Nanotechnology has a wide range of application involving various fields. It is multidisciplinary, just looking into the potential benefits as applied in medicine and dentistry.

NANOMEDICINE

Drug delivery

Liposomes and polymer-based nanoparticles are the widely used nanoparticles[8] as drug-delivery system.

5 fluorouracil, doxorubicin, paclitaxl are some of the anti cancer drugs[9] used.

Biodegradable nanoparticles based vaccines are used for oral vaccination[10] VivaGel™ [Figure 4], a microbicide intended to be applied to prevent the spread of HIV and other sexually transmitted diseases (STDs), is a combination drug and dendrimer-based drug-delivery system is proven to be effective in preventing the transmission of STDs (Starpharma).

New drugs for male pattern baldness are developed through the use of nanoparticles that stimulate the regrowth of hair (Hosokawa Powder Technology Research).[11]

A type of long-acting insulin, Basulin, is developed as a product of its Medusa nanoparticulate system (Flamel Technologies).[12]

Diagnostic aids

As biomarkers

Nanoparticles help in increasing the concentration, amplification and protection of a biomarker from degradation. For example, streptavidin-coated fluorescent polystyrene nanospheres fluospheres (green fluorescence) and transfluospheres (red fluorescence)[12] are applied in single color flow cytometry to detect the epidermal growth factor receptor (EGFR) on A431 cells (human epidermoid carcinoma cells). The results have shown that the sensitivity of fluorescent nanospheres is 25 times more than that of the conjugate streptavidin-fluorescein. (http://www.azonano.com/details.aspArticleID=1242#_Nanoparticles_as_Biomarkers)

Figure 4: SPL7013, the active dendrimer that binds to surface proteins on HIV, preventing the virus from infecting human T-cells

Stem cell imaging in MRI

Firstly, *in vitro* stem cells are treated with supra magnetic nanoparticles. Like iron oxide,gadolinium complex,quantum dots are nanoparticles used. *In vivo*-treated stem cells are injected into specific location in body, intracellular accumulation of these nanoparticles exerts a local effect for detection by endocytosis.

Microbivore

These are nanorobotic phagocytes that each measuring 2-3 micron. Act 1000 times faster than normal phagocytes.[13] Microbivores will be the ultimate defense against biological weapons of mass distraction or biological warfare agents, as well as against any influenza pandemic or other potential pathogens. They have no drug resistance.

Genes

99.9% of DNA sequencing is same in entire human population.[14]

Sequencing of pathogen streptococcus pyogens and others will broaden our understanding of how the organism and their products cause diseases. This will lead to the development of measures to counter or mitigate their untoward effect. First major impact will likely be modification of bacteria that causes dental diseases. 15 bacterial genomes were produced each in just 11/2 working days. Nanopores facilitate sequencing.

Cytobots and karyobots

Gorden's group at the University of Manitoba have also proposed magnetically controlled 'cytobots' and 'karyobots' for performing wireless intracellular and intranuclear surgery, respectively.

Respirocytes

The respirocyte is a blood borne, spherical, 1μm, diamondoid, 1000 atmosphere pressure vessel, with reversible molecule selective surface pumps powered by endogenous serum glucose. This nanorobot would deliver 236 times more oxygen to body tissues per unit volume than natural red cells.[15] An injection of respirocytes administered by emergency medical personnel would allow the patient's brain and other vital organs to be perfused with oxygen for several hours.

Nanorobotic surgeon

A surgical nanorobot, programed or guided by a human surgeon, could act as a semiautonomous on site surgeon inside the human body, when introduced into the body through vascular system or cavities.[16] Axotomy of roundworm neurons was performed by femtosecond laser surgery, after which the axons are functionally regenerated.[17] Femtolaser acts like a pair of nanoscissors by vaporizing tissue locally while leaving adjacent tissue unharmed.

Nanosensors

Molecule detector containing nanowire transistors that allows only certain molecules to bond with its connection points, thereby altering the wire's conductance signals in the presence of a particular molecule (Cornell). Ion channel switching (ICS) technology allows its biosensors to potentially detect a variety of disease-causing agents. Multiple tests can be performed on a single disposable chip. The hand held reader helps determine a prognosis after reading the results of the tests. This technology has potential application in diagnosis, bacterial detection, and food safety inspection (Ambri).

NANODENTISTRY

Nanodentistry as bottom up approach

Local anesthesia

In the era of nanodentistry, a colloidal suspension containing active analgesic of micron sized dental robot will be instilled on the patients' gingival, travelling to the pulp. Once installed in pulp, analgesic dental robot will be commanded by the dentist to shut down all sensitivity in any particular tooth that require treatment. After all the oral procedures are completed, the dentist orders the nanorobot to restore all sensation.[18]

Hypersensitivity cure

Hypersensitivity tooth have eight times higher surface density of dentinal tubules and tubules with diameter twice as large as normal tooth. Dental robots could selectively and precisely occlude selected tubules using native biological materials offering patients a quick and permanent cure.

Nanorobotic dentifrice [dentifrobots]

Subocclusal dwelling nanorobotic dentrifice delivered by mouthwash or tooth paste 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[19].

Dental durability and cosmetics

Tooth durability and appearance can be improved by replacing outer enamel layers with pure sapphire and diamonds. These are more fracture resistant with high strength, possibly by embedding carbon nanotubes.

Orthodontic treatment

Orthodontic nanorobots could directly manipulate the periodontal tissues allowing rapid and painless tooth straightening, rotating and vertical repositioning within minutes to hours.

Photosensitizers and carriers

Quantum dots can be used as photosensitizers and carriers. They can bind to the antibody present on the surface of the target cell and when stimulated by UV light, they can give rise to reactive oxygen species, lethal to target cell.[20]

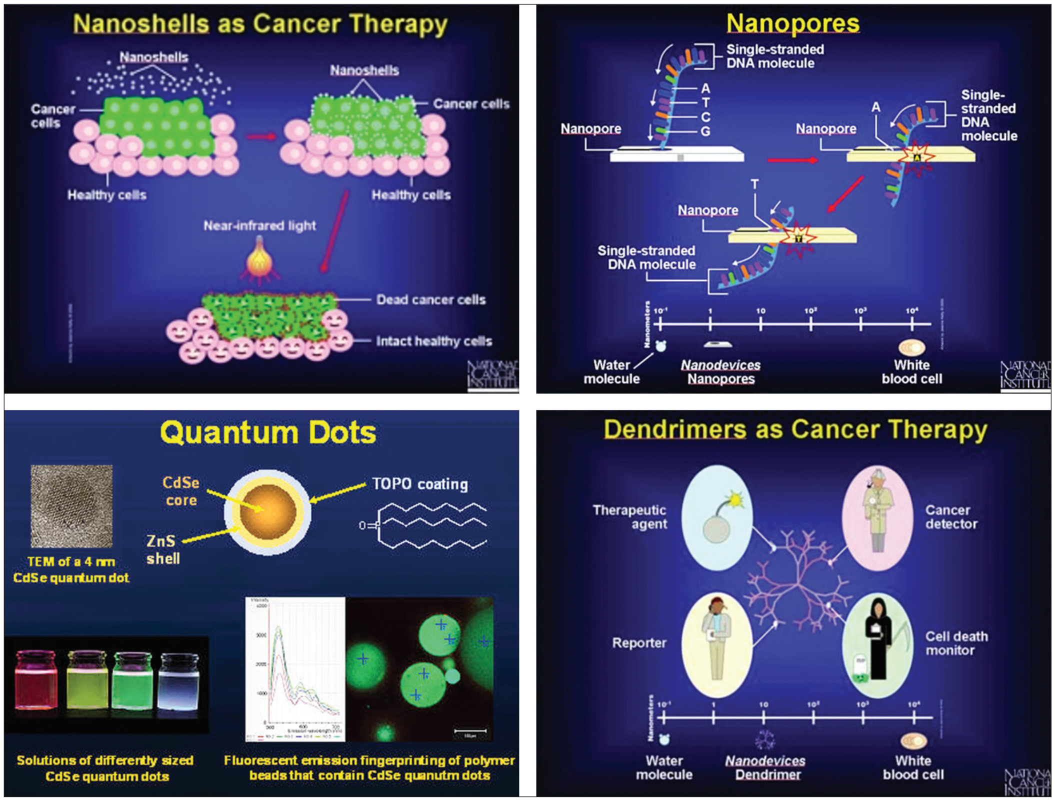

Figure 5: Detection of oral cancer and treatment of oral cancer

Major tooth repair

Nanodental techniques involve many tissue engineering procedures for major tooth repair. Mainly, nanorobots manufacture and install a biologically autologous whole replacement tooth that includes both mineral and cellular components which leads to complete dentition replacement therapy.[21]

Bionic mandible

The bionic mandible is helpful to reconstruct the entire mandible similar to normal mandible in function and sensation. It is not far from achieving, just like the first bionic arm constructed on Sullivan by Todd Kuiken and his team using nanotech-enabled robotic myeoelectric prosthetic limb.[22]

Skin grafts

Skin tissue application from an improved sticking plaster to complete thickness skin graft and 3d synthetic scaffolds are being investigated.

Detection and treatment of oral cancer

Nanoparticles play a key role in developing new methods for detecting cancer [Figure 5]. Detection of cancer in an early stage is a critical step in improving cancer treatment. Various nanoparticles used are cantilever, nanopore, nanotubes, and quantum dot.

As cancer cells secrete its molecular products, the antibodies coated on the cantilever fingers selectively bind to these secreted proteins. The physical properties of the cantilever change in real time and provide information about the presence and also the concentration of different molecular expressions. Luke lee, Ph.D, university of California at Berkeley, has developed a simple device for studying single molecule interaction called nanomechanical force gauge. It consists of nanocantilevers fabricated from single crystal silicon, an etched nanometer reading scale and a light microscope to read cantilever deflection along reading scale.

Another interesting nanodevice is nanopore. Improved methods of reading genetic code will help researchers in detecting errors in genes that may contribute to cancer. Nanopores contain a tiny hole that allows DNA to pass through one stand at a time making DNA sequencing more efficient.

Nanotubes-carbon rods about half the diameter of a molecule of DNA will not only detect the presence of altered genes but also pinpoint the exact location of those changes. A multidisciplinary team at the Massachusetts institute of technology (MIT) has developed carbon nanotubes that can be used as sensors for cancer drugs and other DNA damaging agents inside living cells. Carbon nanotubes fluoresce near infrared light takes advantage whereas human tissue does not. The

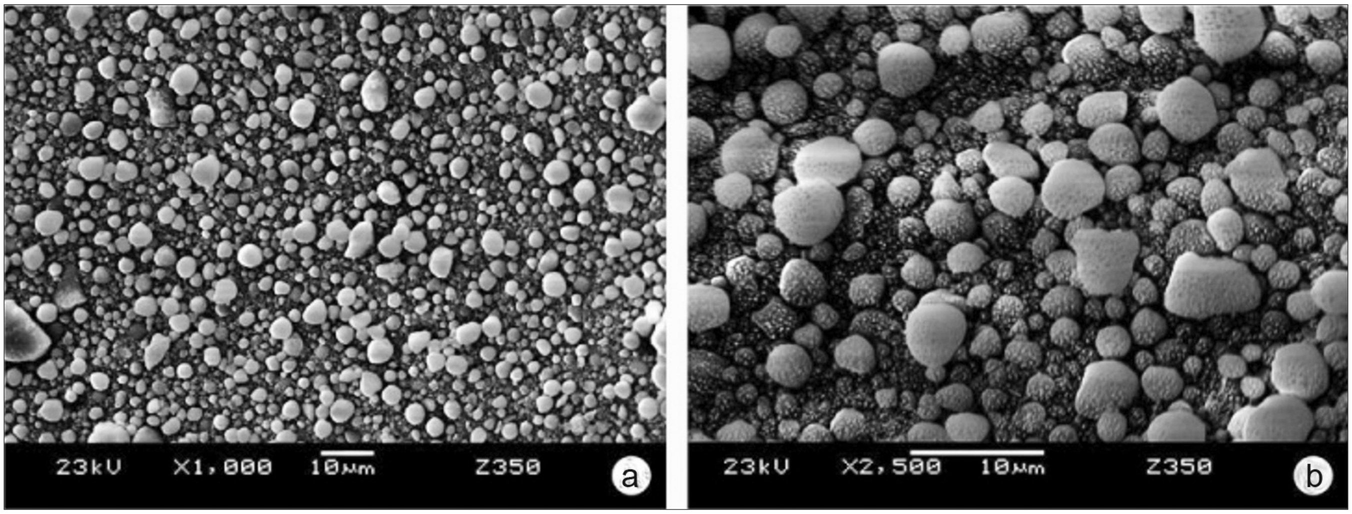

Figure 6: Sem micrograph of filtek supreme [a=x1,000 b=x2,500 magnification] spherical nanocluster of 1 to 4 um

interaction between DNA and the DNA disruptor changes the intensity or wavelength of the fluorescent light emitted by nanotubes.

QUANTUM DOTS

These are tiny crystals that glow when they are stimulated by ultraviolet light. When injected into the body, they would drift around until encountering cancerous tissue. The deadly cells would latch onto a special coating on the glowing dots. The light particles would serve as a beacon to show doctors where the disease has spread.

TREATMENT OF ORAL CANCER

Most common use of dendrimer and nanoshells Dendrimer nanoparticles will facilitate drug delivery. A single dendrimer can carry a molecule that recognizes cancer cell, a therapeutic agent to kill those cells, a molecule that recognizes the signal of cell death. Dendrimer nanoparticles have shown promise as drug delivery vehicles capable of targeting tumors with large doses of anti cancer drugs.

Nanoshells have a core of silica and a metallic outer layer. By manipulating the thickness of the layer, scientist can design beads to absorb near infra red light, creating an intense heat that is lethal to cancer cells. The physical selectivity to cancer lesion site occurs through a phenomenon called enhanced permeation retention (EPR).

NANODENTISTRY AS TOP-DOWN APPROACH

Nanocomposites

Nanoproducts' corporation has successfully manufactured nonagglomerated discrete nanoparticles that are homogeneously distributed in resins or coating to produce nanocomposites.

Trade name – filtek O supreme universal restorative pure nano [Figure 6].

Nanosolutions

Nanosolutions produce unique and dispersible nanoparticles which can be used in bonding agents. This ensures homogeneity, and is perfectly mixed every time. 10% 5 nm spherical silica is used as the filler.

Trade name –adper O single bond plus adhesive single bond [Figure 7].

Impression material

Nanofillers are integrated in vinyl polysiloxanes producing a unique addition silicone impression material. The material has better flow, improved hydrophilic properties, and enhanced detail precision.

Trade name – nanotech elite H-D plus [Figure 8].

Bone substitute

Biologically inspired rosette nanotubes and nanocrystalline hydroapatite hydrogel nanocomposites can be used as improved bone. HRN–helical rosette nanotubes are formed by chemically immobilizing 2 DNA base pairs, creating a novel type of soft nanomaterial that biomimics natural nanostructural component of bone. They are 3.5nm in diameter and are self assembled.

Nanocrystalline hydroxyl apatite of 2 and 10%wt was well dispersed into helical rosette nanotubes. It demonstrated[23] improved mechanical properties, increased osteoblast adhesion up to 236% compared to hydroxyapatite, Stimulated hydroxyapatite showed nucleation and mineralization along their main axis in a

Figure 7: Adper O single bond plus adhesive single bond

Figure 8: Nanotech elite H-D plus

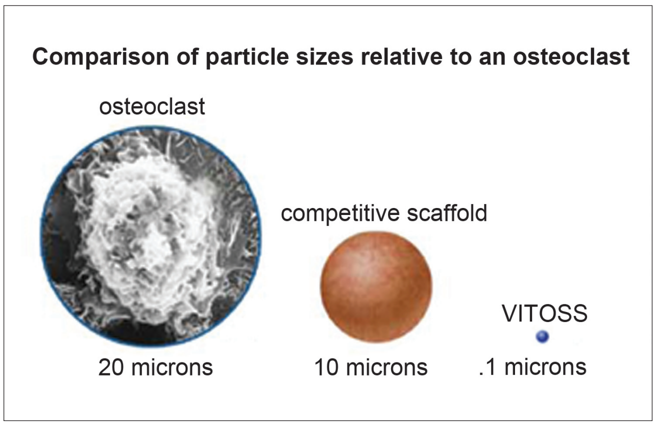

Figure 9: Vitoss made of β-TCP and composed of nanoparticle (100 nm particle)

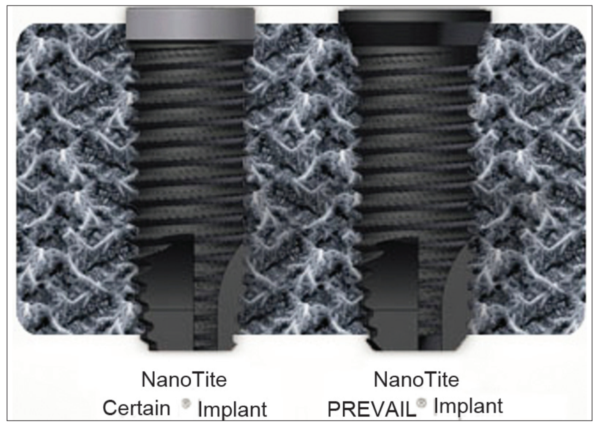

Figure 10: Nanotite implants

way similar to hydroxyapatite/collagen assembly pattern in natural bone.

Trade name – OSTIM, NANOSS, VITOSS [Figure 9].

Implants

Current trends in clinical dental implant therapy include use of endosseous implant surfaces embellished with nanoscale topography. Nanoscale modification of titanium endosseous implant surface can alter cellular and tissue response that benefit dental implant therapy.

Three nanostructured implant coatings in use are- diamond, which possess improved hardness, toughness, low friction, hydroxyapatite, which possessincreased osteoblast adhesion proliferation and mineralization, graded metalloceramics, which possesshave ability to overcome adhesion problems.

Trade name – nanotite [Figure 10].

Decay resistant tooth

Researchers at the Clarkson advanced materials center have found a way to use nanotech to help protect almost any teeth or surface from caries.[24] These are done by polishing teeth with silica that is made from nanoparticles. This material is 90,000 times smaller than a tiny grain of sand.

Surface disinfectant

Eco-True is a surface disinfectant that safely kills 100% of HIV and other particles. It has been used to sterilize tools and incisions to prevent post-operative infections (EnviroSystems).

RISKS

Crosses blood brain barrier

Some doctors worry that nanoparticles are so small that they could easily cross the blood brain barrier, a membrane that protects the brain.

Gray goo

Scenario where synthetic nanosize devices replace all organic matters.

Green goo

Scenario where nanodevices made of organic material wipe out the earth.

Black goo

Scenario in which destructive nanomachines are developed and used for war fare or terrorist purpose.

Trans humans

Nanotechnology makes it possible for us to enhance ourselves physically and mentally making us smarter, stronger. The threat is could we continue calling ourself as humans or trans humans, creating two races wealthy trans humans and poorer unaltered people.

ETHICS

The dominance of the drastic opposition of utopian dreams and apocalyptic nightmares in the debate on the future perspectives of nanotechnology holds the risk of undesirable conflicts and unnecessary backlashes. Hence, the present state of debate on nanotechnology calls for the development of more balanced ethical views. In response to this important challenge, a six-step method is followed:[25]

Steps 1: what specific field of nanotechnology is to be assessed?

Step 2: what are the objective of that specific field of nanotechnology?

Step 3: are these objectives ethically desirable?

Step 4: will further development of the field of research contribute to the realization of these objectives?

Step 5: what are the ethical problems connected with further development of the field of research?

Step 6: are these ethical problems surmountable?

CONCLUSION

Nanotechnology will change dentistry, healthcare, and human life more profoundly than many developments of the past. Once nanomechanics are available, the ultimate dream of physician throughout the world will, at last, become a reality. Programmable and controllable micro scale robots comprising nanoscale parts fabricated to nanometer precision will allow dentist and doctors to execute curative and reconstructive procedures at the cellular and molecular levels. Before that, they have to fulfill all the safety norms. The current materials available from nanotechnology through green nanotechnology[26] have fulfilled the safety norms, and improved qualities than their previous ones. Therefore, don't let just wait for things to happen, start believing and let's contribute our part all for a healthier you.

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