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REVIEW ARTICLE

Nanorobot: A Revolutionary Tool in Dentistry for Next Generation

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ABSTRACT

Nanorobotics is the technology of creating machines or robots at or close to the microscopic scale of a nanometer (10^{-9} meters). These nanorobots allow precision interactions with nanoscale objects or can manipulate with nanoscale resolution. Treatment opportunities in dentistry may include local anesthesia, dentition renaturalization, and permanent hypersensitivity cure, complete orthodontic realignments during single office visit, and continuous oral health maintenance using mechanical dentifrobots. Dental nanorobots could be constructed to destroy caries-causing bacteria or to repair tooth blemishes where decay has set in, by using a computer to direct these tiny workers in their tasks. Recent advances in the field of nanorobots prove that nanodentistry has strong potential to revolutionarize dentistry to diagnose and treat diseases. Although research into nanorobots is still in its primary stage, the promise of such technology for its use in future generation is endless!

Keywords: Nanotechnology, Nanorobots, Dentistry.

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INTRODUCTION

It is rightly said 'Great things are not done by impulse, but by a series of small things brought together.' The word nano is derived from Greek word 'dwarf'. The term nano describes a length of measurement equal to one billionth of a meter which is about the width of 10 atoms. Nanomaterials are those with parts less than 100 nm in at least one dimension, including clusters of atoms, grains less than 100 nm in size, fibers less than 100 nm diameter, films less than 100 nm in thickness.[1]

The growing interest in the application of nanotechnology in dentistry is leading to the emergence of a new field called nanodentistry. An emerging branch of technological research, involving the use of nanotechnology for designing and constructing nanorobot, will indeed play an indispensible role in medical science and dentistry. Nanorobot induces oral analgesia, desensitize tooth, and manipulate the tissue to realign and straighten irregular set of teeth and to improve durability of teeth. Further, it is explained that how nanorobot are used for preventive, restorative, curative procedures.

These devices are in the development phase, and only hypothetical nanorobot has been produced.

NANOROBOTS

The nanorobots are known as nanites or nanomachines. Nanorobots are theoretical microscopic devices measured on the scale of nanometers (1 nm equals one millionth of 1 mm). Presently, the nanorobots are at the hypothetical stage, and they would work at the atomic, molecular and cellular level to perform tasks in both the medical and industrial fields that have made them stuffs of science fiction.[2] Nanorobotics deals with manipulation of nanoscale objects by the usage of micro or macro devices, and construction and programming of robots with overall dimensions that of the nanoscale (or with microscopic dimensions but nanoscopic components) level. Scientists provide the information that the exterior of a nanorobot will likely be built of carbon atoms in a diamonded structure because diamond particles are chemically inert and have strength. Ultra smooth surface of nanorobot will provide streamlined path for them as these won't trigger the immune system. Glucose or natural body sugars and oxygen might be a source for propulsion and the nanorobot will have other biochemical or molecular parts depending on its task.

The typical size of a blood born medical nanorobot will be 0.5 to 3 μm as it is the maximum size that can be permitted due to capillary passage requirement. These nanorobots would be fabricated in desktop nanofactories specialized for this purpose. The capacity to design, build, and deploy large numbers of medical nanorobots into the

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human body would make possible the rapid elimination of disease and the effective and relatively painless recovery from physical trauma. Medical nanorobots can be of great importance in easy and accurate correction of genetic defects, and help to ensure a greatly expanded health span. More controversially, medical nanorobots might be used to enhance natural human capabilities. However, mechanical medical nanodevices would not be allowed to self-replicate inside the human body, nor would there be any need for self-replication or repair inside the human body since these nanobugs are manufactured exclusively in carefully regulated nanofactories with outmost precision.

PARTS OF NANOROBOTS

Parts constitute of camera, pay load, capacitor (energy storage unit), swimming tail. They will have a diameter of 0.5 to 3 microns and will be constructed out of parts with dimensions of range of 1 to 100 nm. Carbon will be primarily the principal element in the buld of medical nanorobot because of its inert properties and strength, basically in the form of diamond or fullerene. Many other light elements, such as sulfur, hydrogen, nitrogen, oxygen, fluorine, etc. will be used for special purposes in nanoscale gears and other components.[3] The chemical inertness of diamond is proved by several experimental studies. One such experiment conducted on mouse peritoneal macrophages cultured on DLC showed no significant excess release of lactate dehydrogenase or of the lysosomal enzyme β, N-acetyl-β-D-glucosaminidase (an enzyme known to be released from macrophages during inflammation). Building nanorobots involve sensors, actuators, control, power, communications and interfacing across spatial scales and between organic/inorganic as well as biotic/abiotic systems.

MECHANISM OF ACTION

The powering of nanorobots can be done by metabolising local glucose, oxygen and externally supplied acoustic energy. Other sources of energy within the body can also be used to supply the necessary energy for the devices. They can be controlled by onboard computers capable of performing around 1,000 or more computations per second. Communication with the device can be achieved by broadcast type acoustic signalling. A navigational network installed in the body provide high positional accuracy to all passing nanorobots and keep track of various devices in the body. These nanorobots will be able to distinguish between different cell types by checking their surface antigens. They are accomplished by the use of chemotactic sensors keyed to the specific antigens on the target cells. When the task of the nanorobots is completed, they can be retrieved by allowing them to exfuse themselves via the usual human excretory channels. These can also be removed by active scavenger systems.[4]

NANOROBOTS IN DENTISTRY

The growing interest in the future of dental applications of nanotechnology is leading to the emergence of a new field called nanodentistry. Nanorobots induce oral analgesia, desensitize tooth, manipulate the tissue to realign and straighten irregular set of teeth and to improve durability of teeth. Further, nanorobots are used to do preventive, restorative, curative procedures.[5]

DEVELOPMENTS OF NANOTECHNOLOGY IN THE FIELD OF DENTISTRY

1. *Nanocomposites:* Composite with nanofillers has two types of nanofillers—nanomeric and nanocluster type.

   Trade name: Filtek Supreme universal restorative pure nano.[6,7]

   Advantages
   - High filler loading
   - Desirable handling characteristics
   - Superior physical properties like modulus of elasticity and flexural strength, etc
   - High polish retention because of nanosize fillers which even if get plucked away by tooth brush abrasion, leave the surface with defects smaller than the wavelength of light
   - Higher translucency giving it more lifelike appearance
   - Fifty percent reduction in curing shrinkage.
2. *Nanoimpression:* The introduction of nanofillers into polyvinylsiloxanes yields a siloxane impression material with properties superior to conventional impression materials.

   Trade name: Nanotech Elite H-D

   Advantages
   - Better flow
   - Improved hydrophilic properties leading to fewer voids at margin and better model pouring
   - Enhanced detail precision.
3. *Nanosolutions:* Unique, dispersible nanoparticles with superior properties can be produced from nanosolutions which forms a uniform mixture after being mixed with solvents, polymers and paints. This can be made use of dentin bonding agents (Adper^{TM}) as these materials have better dentin bond strength and better performance.
4. *Nanoencapsulation:* Controlled drug release has been best experimented in nanomaterials with hollow spheres, nanotubes, core-shell structure and nanocomposite.

In order to achieve a novel drug delivery system apt for the treatment of periodontal diseases, studies were conducted on triclosan-loaded nanoparticles with dimension of 500 nm by Pinon-Segundo E et al.[8]

These particles proved to be anti-inflammatory at experimental sites. Best example of the development of this technological advancement is the production of ARESTIN, where minocycline is introduced into microspheres for drug delivery to periodontal pocket.[9]

Target delivery system has been developed successfully by SWRI (South West Research Institute) that encompass nanocapsules including antibiotics, vaccines and drug delivery.

In 2003, Osaka University of Japan developed targeted delivery of genes and drugs to human liver. Future specialized nanoparticles could be engineered to target oral tissues, including cells derived from the periodontium of effects. Nanoparticles with peptide feature were formed from engineered hepatitis B virus enveloped L particles that proved vital for liver specific entry by the virus in humans.

5. *Nonsurgical devices:* A surgical knife from microstructured silicon with a diamond-layered tip has been developed. Diamond is a material that is chemically rigid, and silicon is non-magnetic and biocompatible.

   Trade name: Sandvik Bioline, RK 91™ needles (AB Sandvik, Sweden).

   Advantages
   - Sharper incisions
   - Lower penetration pressure.

   Nanosized stainless steel crystals incorporated in suture needles have been developed. Nanotweezers are also under development which aims in making cell-surgery possible in the near future.

6. *Nanorobotic dentifrices:* Nanorobotic dentifrices provided by mouthwash or toothpaste can cover the subgingival surfaces that would metabolize trapped organic matter into harmless and odorless vapors. Properly configured dentifbots can identify and destroy pathogenic bacteria existing in the plaque and elsewhere that will eventually provide a barrier to halitosis.

   Nanorobots provided by mouthwash or toothpaste could perform continuous calculus debridement and metabolize trapped oraganic matter into odorless and inert vapors by hovering on supragingival and subgingival surfaces. These mechanical devices crawling at 1 to 10 microns/sec would be inexpensive and would be programmed in such a manner that they would deactivate themselves if swallowed.[10]

7. *Nanoadhesives:* These are unique and dispersible nanoparticles which prevent agglomerations and these are produced from nanosolutions.

   Advantages:
   - Higher dentin and enamel bond strength
   - High stress absorption
   - Longer shelf life
   - Durable marginal seal
   - No separate etching required
   - Fluoride release.

8. *Nanosterilizing solution:* Gandly Enterprises Inc, Florida, has introduced a new disinfectant based on super science of nanoemulsion technology which uses nanosized emulsifier droplets of oil that bombard the pathogens, e.g. EcoTru disinfectant.

   Advantages:
   - Broad spectrum
   - Hypoallergic
   - Noncorroding
   - Does not stain fabric
   - Require no protective clothing
   - Environment friendly
   - Compatible with various impressions
   - Materials.

9. *Nanodiagnostics:* It involves the use of nanodevices or machines for early diagnosis of disease or predisposition at cellular and molecular level. In *in vitro* diagnostics, nanomedicine could increase the efficiency and reliability of the diagnostics using human fluids or tissues sample by using selective nanodevices, to make multiple analyses at subcellular scale, etc. In *in vivo* diagnostics, nanomedicine could develop devices able to work inside the human body in order to identify the early presence of a disease, to identify and quantify toxic molecules, tumor cells.

10. *Orthodontic wires:* Sandvik Nanoflex is a new and advanced stainless steel wire which has the following properties:
    - Ultra-high strength combined
    - Good deformability
    - Corrosion resistance
    - Good surface finish.

11. *New electrochemical process for coating implants:* Prof Noam Eliaz the one who developed an electrochemical process for coating implants. The new implant after coating improves function and longevity. This process involves an electrochemical deposition of synthetic hydroxyapatite over the implant surface. These new implants are more acceptable to human body as these are able to enhance the integration of the nanocoatings

to the human tissues. These nanocoatings resembled with the biological materials.

12. *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 and thus will be lethal to the target cell.
13. *Protective clothing and filtration masks:* These clothing use antipathogenic nanoemulsions and nanoparticles.
14. *Medical appendages for instantaneous healing:* They involve biodegradable nanofibers which provide a delivery platform for hemostatic. Wound dressings with silk nanofibers are under development. Nanocrystalline silver particles provide antimicrobial properties on wound dressings, e.g. Acticoat.
15. *Bone targeting nanocarriers:* A biomaterial composing primarily calcium phosphate has been developed. It has the following features:

    This bone biomaterial is an easily flowable, moldable paste that conforms to and interdigitates with host bone. It supports growth of cartilage and bone cells.

DENTAL APPLICATIONS

1. *Inducing anesthesia:* After instillation of colloidal suspension containing millions of active analgesic nanorobots into the patients gingiva, the ambulating nanorobots reach dentin by migrating into the gingival sulcus and pass painlessly through the lamina propria. Upon reaching the dentin, they enter the dentinal tubules and proceed toward the pulp guided by a combination of chemical gradient, temperature differentials and positional navigation under nanocomputer control. Thus, the migration of nanorobots from tooth surface to the pulp occurs in l00 s. Once installed in the pulp, they establish control over nerve impulse, analgesic nanorobots commanded by the dentist shut down all sensitivity in any particular tooth requiring treatment. When the dentist presses the handheld control, the selected tooth is immediately anesthetized. After the procedure is completed, the dentist orders the nanorobots to restore all sensation and egress from the tooth.

    Nanorobot analgesia offers greater patient comfort, reduces anxiety, no needles, greater selectivity, controllability of analgesic effect, fast and completely reversible action, avoidance of side effects and complications.[11-13]
2. *Tooth repair:* Involves manufacturing and installation of a biologically autologous whole replacement teeth by using genetic engineering, tissue engineering, that includes both mineral and cellular components, i.e. 'complete dentition replacement therapy' should become feasible within the time and economic constraints of a typical office visit through the use of an affordable desktop manufacturing facility, which would fabricate the new tooth in the dentist's office.

    Chen et al took advantage of these latest developments in the area of nanotechnology to simulate 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.
3. *Hypersensitivity cure:* It is a pathological phenomenon. It is caused by pressure transmitted hydrodynamically to the pulp. Natural hypersensitive teeth have eight times higher surface density of dentinal tubules and diameter with twice as larger than nanosensitive teeth. Reconstructive dental robots using native biological materials could selectively and precisely occlude specific tubules within minutes, offering a quick and permanent cure.[14,15]

    On reaching the dentin, the nanorobots enter dentinal tubular holes that are 1 to 4 µm in diameter and proceed toward the pulp, guided by a combination of chemical gradients, temperature differentials and even position of navigation, all under the control of the onboard nanocomputer as directed by the dentist. There are many pathways to travel nanorobots from dentin to pulp. Because of different tubular branching patterns, tubular density may present significant challenge to navigation. Assuming a total path of length of about 10 mm from the tooth surface to the pulp and a modest travel speed of about 100 µm/second. Nanorobots can complete the journey into the pulp chamber in approximately 100 s. The presence of natural cells that are constantly in motion around and inside the teeth, including human gingival, pulpal fibroblasts, cementoblasts, odontoblasts and bacteria inside dentinal tubules, lymphocytes within the pulp or lamina propria suggests that such journey be feasible by cell-sized nanorobots of similar mobility.[16]
4. *Tooth durability and appearance:* Nanodentistry has given material that is nanostructured composite material, sapphire which increases tooth durability and appearance. Upper enamel layers are replaced by covalently bonded artificial material, such as sapphire. This material has 100 to 200 times hardness and failure strength than ceramic. Like enamel, sapphire is a some what susceptible to acid corrosion. Sapphire has best standard whitening sealant, cosmetic alternative. New restorative nanomaterial to increase tooth durability is nanocomposites. This is manufactured by nanoagglomerated

discrete nanoparticles that are homogeneously distributed in resins or coatings to produce nanocomposites. The nanofiller includes an aluminosilicate powder having a mean particle size of about 80 nm and a 1:4 ratio of alumina to silica. The nanofiller has a refractive index of 1.503, it has superior hardness, modulous of elasticity, translucency, esthetic appeal, excellent color density, high polish and 50% reduction in filling shrinkage. They are superior to conventional composites and blend with a natural tooth structure much better.

5. *Orthodontic treatment:* The treatment generally involves a frictional type of force which provides the desired movement. In a study published by Katz, a reduction in friction has been reported by coating the orthodontic wire with inorganic fullerene-like tungsten disulfide nanoparticles which are known for their dry lubrication properties. It has been reported that orthodontic nanorobots could directly manipulate the periodontal tissues, allowing rapid and painless tooth straightening, rotating and vertical repositioning within minutes to hours.
6. *Diagnosis of oral cancer*
   - *Nanoelectromechanical systems (NEMS):* Nanotechnology-based NEMS biosensors that exhibit exquisite sensitivity and specificity for analyte detection, down to single molecule level are being developed. They convert (bio) chemical to electrical signal.[17]
   - *Oral fluid nanosensor test (OFNASET):* The oral fluid nanosensor test 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.[18]
   - *Optical nanobiosensor:* The nanobiosensor is a unique fiberoptics-based tool which allows the minimally invasive analysis of intracellular components, such as cytochrome C, which is a very important protein to the process which produces cellular energy and is well-known as the protein involved in apoptosis, or programmed cell death.[19]
7. *Treatment of oral cancer:* Nanotechnology in field of cancer therapeutics has offered highly specific tools in the form of multifunctional dendrimers and nanoshells. The unique property of dendrimers, such as their high degree of branching, multivalence, globular structure and well-defined molecular weight make them promising in cancer therapeutics. Nanoshells are miniscule beads with metallic outer layers designed to produce intense heat by absorbing specific wavelengths of radiations that can be used for selective destruction of cancer cells leaving aside intact and adjacent normal cells.[20,21]
   - *Nanomaterials for brachytherapy:* BrachySil™ (Sivida, Australia) delivers 32P, clinical trial.
   - *Photodynamic therapy:* Hydrophobic porphyrins are potentially interesting molecules for the photodynamic therapy (PDT) of solid cancers or ocular diseases.[22,23]
8. *Oral hygiene and halitosis:* 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 micro flora to flourish in a healthy ecosystem. Dentifrobots also would provide a continuous barrier to halitosis, since bacterial putrefaction is the central metabolic process involved in oral malodor.
9. *Periodontal tissue engineering:* Tissue engineering concepts for periodontal regeneration are focused on the utilization of synthetic scaffolds for cell delivery purposes. Nonbiologic self-assembling nanosystems will automatically undergo prespecified assemblies much in line with known biologic systems associated with cells and tissues.
10. *Surgical nanorobotics:* A surgical nanorobot, programmed or guided by a dentist, could act as a semi-autonomous onsite surgeon inside the human body. Such a device could perform various functions, such as searching for pathology and then diagnosing and correcting lesions by nanomanipulation, coordinated by an onboard computer, while maintaining contact with the supervising surgeon via coded ultrasound signals.[24]

    The earliest forms of cellular nanosurgery are already being explored today. For example, a rapidly vibrating (100 Hz) micropipette with a <1 micron tip diameter has been used to completely cut dendrites from single neurons without damaging cell viability. Axotomy of roundworm neurons was performed by femtosecond laser surgery, after which the axons functionally regenerated. A femtolaser acts like a pair of 'nanoscissors' by vaporizing tissue locally while leaving adjacent tissue unharmed.
11. *Bone replacement materials:* These can be used in maxillofacial injuries requiring bone graft, cleft patient and osseous defect in periodontal surgeries.
    - Hydroxyapatite nanoparticles used to treat bone defects are Ostim® (Osartis GmbH & Co KG, Obernburg, Germany) HA.
    - VITOSSO (Orthovita, Inc., Great Valley Parkway Malvern, PA 19355, USA) HA and TCP.
    - NanOSS™ (Angstrom Medica, USA) HA.

12. *Personalized treatment:* Dentists will perform routine examinations that will include use of high-resolution imaging devices to better visualize the subsurface tomography of each tooth. Dentists will possess additional predictive tools to characterize bacteria underlying infections and the specific nature of the immune response will be developed, and they will be able to personalize treatments using nanoparticle drug delivery systems, that most effectively target and eliminate both the bacteria and the infection.

CHALLENGES FACED BY NANODENTISTRY

- Precise positioning and assembly of molecular scale part
- Economical nanorobot mass production technique
- Biocompatibility
- Simultaneous coordination of activities of large numbers of independent micronscale robots
- Social issues of public acceptance, ethics, regulation and human safety
- Design cost very high
- Electrical systems can create stray fields which may activate bioelectric-based molecular recognition systems in biology
- Hard to interface, customize and design, complex
- Nanorobots can cause a brutal risk in the field of terrorism. The terrorism and antigroups can make use of nanorobots as a new form of torturing the communities as nanotechnology also has the capability of destructing the human body at the molecular level.

PROBLEMS FOR RESEARCH IN NANOTECHNOLOGY IN INDIA[25]

- Painfully slow strategic decisions
- Suboptimal funding
- Lack of engagement of private enterprises
- Problem of retention of trained manpower.

ARE NANOROBOTS SAFE?

The nonpyrogenic nanorobots used *in vivo* are bulk, carbon powder and monocrystal sapphire. Pyrogenic nanorobots are alumina, silica and trace elements like copper and zinc.

If inherent nanodevice surface pyrogenicity cannot be avoided, the pyrogenic pathway is controlled by *in vivo* medical nanorobots.

Nanorobots may release inhibitors, antagonists or dowmegulators for the pyrogenic pathway in a targeted fashion to selectively absorb the endogenous pyrogens, chemically modify them, then release them back into the body in a harmless inactivated form.[26]

NANODIAGNOSIS

It is the use of nanodevices for the early disease identification or predisposition at cellular and molecular level. In *in vitro* diagnostics, nanomedicine could increase the efficiency and reliability of the diagnostics using human fluids or tissues sample by using selective nanodevices, to make multiple analyses at subcellular scale, etc. *In vivo* diagnostics, nanomedicine could develop devices able to work inside the human body in order to identify the early presence of a disease, to identify and quantify toxic molecules, tumor cells.[27-29]

CONCLUSION

Nanotechnology is part of a predicted future in which dentistry and periodontal practice may become more high-tech and more effective looking to manage individual dental health on a microscopic level by enabling us to battle decay where it begins with bacteria. Construction of a comprehensive research facility is crucial to meet the rigorous requirements for the development of nanotechnologies.

Researchers are looking at ways to use microscopic entities to perform tasks that are now done by hand or with equipment. This concept is known as nanotechnology. Tiny machines, known as nanoassemblers, could be controlled by computer to perform specialized jobs. The nanoassemblers could be smaller than a cell nucleus so that they could fit into places that are hard to reach by hand or with other technology. Used to destroy bacteria in the mouth that cause dental caries or even repair spots on the teeth where decay has set in, by use of computer to direct these tiny workers in their tasks. Role of periodontitis will continue to evolve along the lines of currently visible trends. For example, simple self-care neglect will become fewer, while cases involving cosmetic procedures, acute trauma, or rare disease conditions will become relatively more commonplace. Trends in oral health and disease also may change the focus on specific diagnostic and treatment modalities. Increasingly, preventive approaches will reduce the need for cure prevention a viable approach for the most of them. Diagnosis and treatment will be customized to match the preferences and genetics of each patient. Treatment options will become more nume-rous and exciting. All this will demand, even more so than today, the best technical abilities, professional skills that is the hallmark of the contemporary dentist and periodontist. Developments are expected to accelerate significantly. Nanometer and nanotube technologies could be used to administer drugs more precisely. Technology should be able to target specific cells in a patient suffering from cancer or other life-threatening conditions.

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