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NANODENTISTRY

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ABSTRACT

Background. Nanodentistry will make possible the maintenance of comprehensive oral health by involving the use of nanomaterials, biotechnology (including tissue engineering) and, ultimately, dental nanorobotics (nanomedicine).

Results. When the first micrometer-sized dental nanorobots can be constructed within 10 to 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.

Clinical Implications. New treatment opportunities may include dentition renaturalization, permanent hypersensitivity cure, complete orthodontic realignments during a single office visit, covalently bonded diamondized enamel and continuous oral health maintenance through the use of mechanical dentifrobots.

NANODENTISTRY

In 1959, the late Nobel Prize–winning physicist Richard P. Feynman presented a talk entitled "There's Plenty of Room at the Bottom"[1] at the annual meeting of the American Physical Society. Feynman proposed using machine tools to make smaller machine tools, which, in turn, would be used to make still smaller machine tools, and so on all the way down to the molecular level. He suggested that such nanomachines, nanorobots and nanodevices ultimately could be used to develop a wide range of atomically precise microscopic instrumentation and manufacturing tools. Feynman[1] argued that these tools could be applied to produce vast quantities of ultrasmall computers and various microscale and nanoscale robots. He concluded that this is "a development which I think cannot be avoided." The vision of nanotechnology was born.

Forty years ago, this talk was greeted with astonishment and skepticism. However, since then, we have made remarkable progress toward realizing Feynman's vision. From the dawn of the microcomputer era several decades ago, we have witnessed a significant increase in the speed and power of computers. This is due, in large measure, to the ever-decreasing size of the electronic components that can be packed at ever-increasing densities onto a single silicon chip. Transistor density has doubled every 18 months, an observation that has come to be known as Moore's law.[2] The size of features on computer chips has shrunk from a fraction of a millimeter in the first microprocessor chip to 0.1 to 0.2 micrometers (1 µm = 10^{-6} meter) in the latest chips. Recently, two new companies have been formed[3,4] with the explicit goal of producing molecular computer components[4,5] using molecular parts at the nanometer (10^{-9} meter, or one-billionth of a meter) scale, within just a few years.

Similar progress is under way in the related field of robotic miniaturization. The burgeoning field of microelectromechanical systems was made possible by the fabrication of the first micromotors in the late 1980s and early 1990s.[6] By 1994, engineers at Nippondenso Ltd.[7] had constructed a working electric car smaller than a grain of rice, a 1/1,000th-scale replica of a 1936 Model AA Toyota sedan that incorporated 24 parts, including a motor, wheels, body, spare tire, bumpers and even a 10-µm-thick license plate. In 1997, researchers at Cornell's Nanofabrication Facility[8] produced a silicon guitar that was 10 µm in length and 2 µm wide, with six individual "strings" that were only 50 nanometers (approximately 200 atoms) thick.

Even Feynman had notions of how nanotechnology could be applied to medicine. After discussing his ideas with a colleague, Feynman[1] offered the first known proposal for a nanomedical procedure to cure heart disease: "A friend of mine [Albert R. Hibbs] suggests an interesting possibility for relatively small machines. He says that, although it is a very wild idea, it would be interesting in surgery if you could swallow the surgeon. You put the mechanical surgeon inside the blood vessel and it goes into the heart and looks around. (Of course, the information has to be fed out.) It finds out which valve is the faulty one and takes a little knife and slices it out. Other small machines might be permanently incorporated in the body to assist some inadequately functioning organ."

Development of nanodentistry will make possible the maintenance of near-perfect oral health.

Once one considers other potential applications of nanotechnology to medicine, it is not difficult to imagine what nanodentistry would look like. The main purpose of this report, therefore, is to provide an early glimpse of nanodental applications and to illustrate their potentially far-reaching impact on clinical dental practice. In this article, I briefly survey the field of nanomedicine and present some potential applications to dentistry, such as local anesthesia, reconstruction of dental hard tissues, orthodontic treatment and disease prevention. I conclude by placing the expected development of nanodentistry, which may see its earliest practical uses within the next 10 to 20 years, in the context of today's trends in dental science and practice.

NANOMEDICINE

Molecular manufacturing[9,10] promises precise control of matter at the atomic and molecular level. One major implication of this is that, within the next 10 to 20 years, it should become possible to construct machines on the micrometer scale made up of parts on the nanometer scale. Subassemblies of such devices may include such useful robotic components as 100-nm manipulator arms, 10-nm sorting rotors for molecule-by-molecule reagent purification, and smooth superhard surfaces made of atomically flawless diamond (a durable, well-characterized material, composed of abundant carbon atoms, that should be relatively easy to manufacture).[10]

Nanocomputers would assume the important task of activating, controlling and deactivating such nanomechanical devices. Nanocomputers would store and execute mission plans, receive and process external signals and stimuli, communicate with other nanocomputers or external control and monitoring devices, and possess contextual knowledge to ensure safe functioning of the nanomechanical devices.

Such technology has enormous medical implications.[11] Programmable nanorobotic devices would allow physicians to perform precise interventions at the cellular and molecular level. Medical nanorobots have been proposed for gerontological applications,[12] in pharmaceutical research[13] and clinical diagnosis,[11,14] and in dentistry.[15,16] Other applications include mechanically reversing atherosclerosis,[17] improving respiratory capacity,[18] enabling near-instantaneous hemostasis,[19] supplementing the immune system,[15,20] rewriting[21] or replacing[22] DNA sequences in cells, repairing brain damage[23] and resolving gross cellular insults,[21] whether caused by "irreversible" processes[24] or by cryogenic storage of biological tissues.[9,25]

Growing interest in the future medical applications of nanotechnology is leading to the emergence of a new field called nanomedicine.[11] This is the science and technology of diagnosing, treating and preventing disease and traumatic injury; of relieving pain; and of preserving and improving human health, through the use of nanoscale-structured materials, biotechnology and genetic engineering, and eventually complex molecular machine systems and nanorobots. Similarly, development of nanodentistry will make possible the maintenance of near-perfect oral health through the use of nanomaterials[26,27]; biotechnology,[27-31] including tissue engineering[32,33]; and nanorobotics. The first two of these approaches have been discussed extensively elsewhere. This report offers a first look at the third—and most exciting (although somewhat more technologically remote)—approach to nanodentistry: dental nanorobotics.

APPLICATIONS OF NANOROBOTICS TO DENTISTRY

When the first micrometer-sized dental nanorobots are constructed, perhaps 10 to 20 years from today, how might they be applied to dentistry? I[11] have described how medical nanorobots might use specific motility mechanisms to crawl or swim through human tissues with navigational precision; acquire energy, and sense and manipulate their surroundings; achieve safe cytopenetration (for example, pass through plasma membranes such as the odontoblastic process without disrupting the cell, while maintaining clinical biocompatibility[11]); and use any of a multitude of techniques to monitor, interrupt or alter nerve-impulse traffic in individual nerve cells.

These nanorobotic functions may be controlled by an onboard nanocomputer that executes preprogrammed instructions in response to local sensor stimuli. Alternatively, the dentist may issue strategic instructions by transmitting orders directly to in vivo nanorobots via acoustic signals (as are used in ultrasonography) or other means—similar to an admiral commanding a fleet.

Tubule branching patterns may present a significant challenge to navigation of nanorobots.

Inducing anesthesia. One of the most common procedures in dentistry is the injection of local anesthetic, which can involve long waits and varying degrees of efficacy, patient discomfort and complications.[34] Well-known alternatives, such as transcutaneous electronic nerve stimulation,[35,36] cell demodulated electronic targeted anesthesia[37] and other transmucosal,[36] intraosseous[36] or topical[38] techniques, are of limited clinical effectiveness.

To induce oral anesthesia in the era of nanodentistry, dental professionals will instill a colloidal suspension containing millions of active analgesic micrometer-sized dental nanorobot "particles" on the patient's gingivae. 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[39] or the 1- to 3-µm–thick layer of loose tissue at the cemento-dentinal junction.[40] On reaching the dentin, the nanorobots enter dentinal tubule holes that are 1 to 4 µm in diameter [41-43] and proceed toward the pulp, guided by a combination of chemical gradients, temperature differentials and even positional navigation,[11] all under the control of the onboard nanocomputer, as directed by the dentist.

There are many pathways to choose from. Dentinal tubule number density is typically 22,000 mm^{-2} near the dentino-enamel junction, 37,000 mm^{-2} midway between the junction and the pulpal wall, and 48,000 mm^{-2} close to the pulp[41] in coronal dentin,[41] with the number density slightly lower in the root (for example, 13,000 mm^{-2} near the cementum[44]). Tubule diameter increases nearer the pulp,[43,45] which may facilitate nanorobot movement, although circumpulpal tubule openings vary in number and size.[46]

Tubule branching patterns may present a significant challenge to navigation, because they exhibit an intricate and profuse canalicular anastomosing system that crisscrosses the intertubular dentin, with dentinal branching density most abundant in locations where tubule density is low.[47] Dentinal tubules are continuous between primary dentin and regular secondary dentin in young and old teeth, but not between primary and irregular secondary dentin.[48] Regular secondary dentin becomes highly sclerosed in older teeth,[48] and many tubule openings on the outer dentin surface can become completely occluded in some circumstances,[49] probably requiring significant detouring by the dental nanorobots. (On the other hand, a small number of microcanals,[50,51] large tubules[52] or giant tubules[51,53] with diameters of 10 to 50 µm or even larger[54] may exist in some cases, possibly affording easier transit.)

Assuming a total path length of about 10 mm from the tooth surface to the pulp and a modest travel speed[11] of 100 µm/s, nanorobots can complete the journey into the pulp chamber in approximately 100 seconds. The presence of natural cells that are constantly in motion around and inside the teeth—including human gingival and pulpal fibroblasts,[55] cementoblasts at the cementodentinal junction,[56] bacteria inside dentinal tubules,[57] odontoblasts near the pulpal/dentin border[43,46,58,59] and lymphocytes within the pulp or lamina propria[60]—suggests that such journeys should be feasible by cell-sized nanorobots of similar mobility.

Once installed in the pulp and having established control over nerve-impulse traffic,[11] the analgesic dental nanorobots may be commanded by the dentist to shut down all sensitivity in any tooth that requires treatment. When the dentist presses the icon for the desired tooth on the hand-held controller display, the selected tooth immediately numbs (or later, on 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 via similar pathways used for ingress; following this, they are aspirated. Nanorobotic analgesics offer greater patient comfort and reduced anxiety, no needles,[61,62] greater selectivity and controllability of the analgesic effect, fast and completely reversible action, and avoidance of most side effects and complications.[34]

New treatment opportunities abound in nanodentistry, as illustrated by these examples:

Major tooth repair. Nanodental techniques for major tooth repair may evolve through several stages of technological development, first using genetic engineering, tissue engineering[32,33,63-67] and tissue regeneration,[33,63-68] and later involving the growth of whole new teeth in vitro[69,70] and their installation. Ultimately, the nanorobotic manufacture and installation of a biologically autologous whole-replacement tooth that includes both mineral and cellular[71-73] components—that is, 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.

Renaturalization procedures. Dentition renaturalization procedures may become a popular addition to the typical dental practice, providing perfect treatment methods for esthetic dentistry. This trend may begin with patients who desire to have their old dental amalgams[74] excavated and their teeth remanufactured with native biological materials. However, demand will grow for full coronal renaturalization procedures in which all fillings, crowns and other 20th-century modifications to the visible dentition are removed, with the affected teeth remanufactured to beome indistinguishable from the original teeth.

Dentin hypersensitivity. Dentin hypersensitivity is another pathological phenomenon that may be amenable to nanodental treatment. Dentin hypersensitivity may be caused by changes in pressure transmitted hydrodynamically to the pulp. This etiology is suggested by the finding that hypersensitive teeth have dentinal tubules with surface number densities that are eight times higher than those of nonsensitive teeth, as well as tubules with diameters that are twice as large.[75] Many therapeutic agents provide temporary relief for this common painful condition,[76] but reconstructive dental nanorobots, using native biological materials, could selectively and precisely occlude specific tubules within minutes, offering patients a quick and permanent cure.

Tooth repositioning. Orthodontic nanorobots could directly manipulate the periodontal tissues, including gingivae, periodontal ligament, cementum and alveolar bone, allowing rapid and painless

Orthodontic nanorobots could directly manipulate the periodontal tissues.

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.[77]

Durability and appearance. Tooth durability and appearance may be improved by replacing upper enamel layers with covalently bonded artificial materials such as sapphire[78] or diamond,[16] which have 20 to 100 times the hardness and failure strength (that is, the pressure that must be applied to cause a solid material to fail catastrophically) of natural enamel[11] or contemporary ceramic veneers,[79] as well as good biocompatibility.[80] Like enamel, sapphire is somewhat susceptible to acid corrosion,[81] but sapphire can be manufactured in virtually any color of the rainbow,[11] offering interesting cosmetic alternatives (for example, iridescence) to standard whitening[82] and sealant[83] procedures. Pure sapphire and diamond are brittle and prone to fracture if sufficient shear forces are imposed,[84] but they can be made more fracture-resistant as part of a nanostructured composite material[85] that possibly includes embedded carbon nanotubes.[86]

Effective prevention has reduced the incidence of caries in children[87] and a caries vaccine may soon be available.[88] However, a 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 débridement. These almost-invisible (1 to 10 μm) dentifrobots, perhaps numbering 10^3 to 10^5 per mouth and crawling at 1 to 10 μm/second, might have the mobility of tooth amoebas,[89] but would be inexpensive, purely mechanical devices that safely deactivate themselves if swallowed. Moreover, they would be programmed with strict protocols to avoid occlusal surfaces. (Even diamondoid nanorobots can be crushed by dental grinding unless the thickness of their outer shells is at least 10 percent of the device's radius.[11])

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. Dentifrobots also would provide a continuous barrier to halitosis, since bacterial putrefaction is the central metabolic process involved in oral malodor.[90] With this kind of daily dental care available from an early age, conventional tooth decay and gingival disease will disappear.

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THE PATH TO NANODENTISTRY

The visions described thus far may sound unlikely, implausible or even heretic. Yet, the theoretical and applied research needed to turn them into reality is progressing rapidly. Nanotechnological developments are expected to accelerate significantly through new governmental[91] and private-sector[92] initiatives.

Nanotechnological advances should be viewed in the context of other expected developments relevant to oral health in the coming decades. Biological approaches such as tissue and genetic engineering[32,33,63-67] will yield new diagnostic and therapeutic approaches much sooner than will nanotechnology. At the same time, continual refinement of traditional methods, development of advanced restorative materials, and new medications and pharmacological approaches will continue to improve dental care.

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 curative or restorative interventions, as has already happened with dental caries. Deeper understanding of the causes and pathogenesis of other disease processes—such as periodontal disease, developmental craniofacial defects and malignant neoplasms—should make prevention a viable approach for most of them.

The role of the dentist will continue to evolve along the lines of currently visible trends. In the United States, for example, cases involving simple self-care neglect will become fewer, while cases involving cosmetic procedures, acute trauma or rare disease conditions will become relatively more commonplace. Diagnosis and treatment will be customized to match the preferences and genetics of each patient. Treatment options will become more numerous and exacting. All this will demand, even more so than today, the best technical abilities, professional judgment and strong interpersonal skills that are the hallmark of the contemporary dentist.

CONCLUSION

Nanodentistry still faces many significant challenges[11] in realizing its tremendous potential. Basic engineering problems run the gamut from precise positioning and assembly of molecular-scale parts, to economical mass-production techniques, to biocompatibility and the simultaneous coordination of the activities of large numbers 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 molecular nanotechnology can enter the modern medical armamentarium. However, there are equally powerful motivations to surmount these various challenges, such as the possibility of providing high-quality dental care to the 80 percent of the world's population that currently receives no significant dental care. Time, specific advances, financial and scientific resources, and human needs will determine which of the applications described in this article are realized first. ■

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