Nanotechnology in Dentistry Today

OE Ogle, N Byles

ABSTRACT

A review was done of nanotechnology as it applies to dentistry today. Information was gathered from literature search, research data and material inserts in products. Nanotechnology deals with the physical, chemical and biological properties of structures and their components at nanoscale dimensions. One of the biggest contributions to restorative and aesthetic dentistry has been nanocomposites. These composites are characterized by filler-particle sizes ≤ 100 nm and offer aesthetic and strength advantages over the current microfilled and hybrid resin-based composites. Nanoparticles for coating implant surfaces and the nanopatterning of dental implants are leading to better osseointegration and improved physiologic functions of implants, while nanophase hydroxyapatite has improved its adaptation into bone graft sites. Nano-biochips are now making oral cancer screening and diagnosis of diseases by saliva easier and more affordable.

Keywords: Dental composites, dental implants, dentistry, hydroxyapatite, nano-biochip oral biopsy, nanophase, nanotechnology

La Nanotecnología en la Odontología Actual

OE Ogle, N Byles

RESUMEN

Se realizó un examen de la nanotecnología, tal cual se aplica en la odontología hoy día. Se recopiló información a partir de búsquedas bibliográficas, datos de investigación, e inserciones materiales en los productos. La nanotecnología se ocupa de las propiedades físicas, químicas y biológicas de las estructuras, y sus componentes a dimensiones de nanoescala. Una de las contribuciones mayores a la odontología restauradora y estética ha sido la de los nanocompuestos. Estos compuestos se caracterizan por dimensiones de partículas de relleno ≤ 100 nm, y ofrecen ventajas en cuanto a fortaleza y estética por encima de los compuestos actuales de microrelleno y los compuestos híbridos de resina. Las nanopartículas para el revestimiento de las superficies de implantes, y la nanoestructuración de los implantes dentales están llevando a una mejor osteointegración, y al mejoramiento de las funciones fisiológicas de los implantes, mientras que la hidroxiapatita en nanofase ha mejorado su adaptación a los sitios de injerto óseo. Las nano-bio-chips están haciendo ahora la detección del cáncer oral y el diagnóstico de enfermedades mediante saliva más fácil y más asequible.

Palabras claves: dental, implantes dentales, odontología, hidroxiapatita, biopsia oral, nano-bio-chips, nanofase, nanotecnología

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From: Faculty of Medical Sciences – Dentistry Programme, The University of the West Indies, Kingston 7, Jamaica.

Correspondence: Dr OE Ogle, 4974 Golf Valley Court, Douglasville, GA 30135, USA. E-mail: oeogle@aol.com

INTRODUCTION

Nanotechnology deals with the physical, chemical and biological properties of structures and their components at nanoscale dimensions. The United States National Nanotech-

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nology Initiative defines nanotechnology as the manipulation of matter with at least one dimension sized from one to 100 nanometres. A nanometre (nm) is a unit of length that is equal to one billionth of a metre (10^{-9} metre) and is often used to express dimensions on an atomic scale. The diameter of the hydrogen atom, for example, is approximately 0.1 nm [actually 0.074 nm] (1). The use of this technology has led to developments in material science and biotechnology which is now proving to be very beneficial to the field of dentistry. These developments in material science and biotechnology are leading to the production of better dental materials and improved oral health-related diagnostic methods.

COMPOSITES

Dental composite materials are types of synthetic resins which are used in dentistry to restore teeth. These resins are most commonly composed of bisphenol-glycidyl methacrylate monomers (an ester of methacrylic acid), a filler material such as silica and in most current applications, a photo-initiator (a chemical compound that decomposes into free radicals when exposed to light). These composite restorations involve dentin and enamel bonding techniques.

Prior to the early 1970s, amalgam restoration was the work-horse of restorative dentistry. Placing amalgam restorations took quite a bit of operative skills, requiring the operator to place strategic undercuts to retain the restoration and enamel rod bevels to provide a marginal seal. Since the beginning of the era of microfills in 1973, resin-based composites have been increasingly used instead of amalgam as the filler-matrix technologies have improved. The original microfills lacked strength and they could only be used to restore anterior teeth, which do not have great biting forces and it took years to develop these composites to the state that they could be used in applications traditionally served by amalgam. Today, posterior teeth with bite forces averaging 392 N are restored with composites that have overcome most of the strength issue by using hybrids of microfills and nanofills (nanohybrids). These materials use filler particles ranging from < 100 nm to 600+ nm.

To date, one of the biggest contribution to restorative and aesthetic dentistry has been nanocomposites for the restoration of tooth structure. These composites are characterized by filler-particle sizes ≤ 100 nm and offer aesthetic and strength advantages over the current microfilled and hybrid resin-based composites. They have better polish-ability properties which produce a smoother surface with better shade characteristics and their microhardness is greater than currently used posterior resin-based composites. However, to date, comparative clinical performance among the various types of nanocomposites with older hybrids does not yet show a distinct advantage for nanofills.

Composites using nanotechnology (such as Filtek™ Supreme Plus [3M ESPE] and Estelite® Sigma [Tokuyama America, Inc., Encinitas, CA, USA]) consistently use fillers less than 100 nm. Using progressively decreasing filler particle sizes should result in better dispersion and increased interfacial area between matrix and filler. This would translate into increased flexural strength, surface microhardness, and thus polish-ability of the finished restoration (2). Nanocluster particles as small as 2–20 nm are currently being used as nanofilled restoratives (3). By creating these smaller particles, properties such as optical properties − with a potential bearing on aesthetic dentistry − can be maximized (3) [translucent shades have fillers of 5–20 nm]. Polishing and abrasions caused by function can separate particles from the composite matrix. Polishing and functional abrasions, however, would only allow poorly attached nanoclusters to separate from the nanocomposites and a well-polished restoration surface would therefore retain its smoothness for a long time. Further, the particles that are separated from the surface of the nanocomposites and form defects on the surface during abrasion are nano size and are smaller than the wavelength of light. Since particles in the wavelength of visible light (0.4 to 0.8 µm) do not reflect light, nanocomposites have superior optical character (3). The fillers in nanocomposites have higher translucence since they are smaller than the wavelength of light, allowing the generation of more aesthetic restorations with a vast range of color options (4).

A key challenge to using nanofillers is the ability to manufacture non-agglomerated discrete nanoparticles that can be homogeneously distributed in resins or coatings to produce the nanocomposites. Agglomeration of nanoparticles will become micro-sized particles. Titanium dioxide (TiO_2) nanoparticles, for example, are very fine and agglomerate easily in practical applications and are especially difficult to disperse in organic solvents. To decreasing agglomeration, inorganic fillers in dental resin-based composites are typically coated with organosilane in order to enhance their bond to the resin matrix and increase the service life of the composite (5). Changing the surface characteristics of the nanofiller means that it can be incorporated in higher concentrations, and are better polymerized into the resin system, thus maintaining their nano-size. The particle size of conventional composites are so dissimilar to the structural sizes of hydroxyapatite (HA) crystal, dentinal tubule and enamel rods that there is a potential for compromise in adhesion between the relative "macroscopic" (40 nm–100 nm) restorative material and the nanoscopic (1 nm–10 nm) tooth structure (6). As the nanofillers become smaller, nanocomposite systems will have the potential to improve the continuity between the tooth structure and the nanosized filler particle and provide a more stable and natural interface between the mineralized hard tissues of the tooth and these advanced restorative biomaterials (6).

Another advancement in nanocomposite is the remineralization of teeth. In May 2012, researchers at the University of Maryland School of Dentistry announced that they have patents pending on a new nanocomposite and that they were in negotiations with manufacturers about the potential for bringing the product to market. This new composite comprised nano-size particles of silver and calcium, along with an antibacterial primer and antibacterial adhesive that treat cavities while also destroying bacteria in the cavity and re-grow tooth structure lost to bacterial decay. The product features a primer that is applied to the surface of a drilled tooth, an adhesive to bond the filling to the tooth, and the filling material, which has a high pH that has been shown to kill bacteria (7). The implication is that dentists will be able to maintain much more of a tooth structure and need not remove all the bacteria. This will lead to the ability to maintain more natural tooth structure and stronger restorations. Tackling residual bacteria may be able to reduce acid formation between the filling and tooth structure which could lead to remineralization of the tooth lost to decay by odontoblasts.

Research is also being done with a fluoride (F^-) releasing nanocomposite. This material contains calcium fluoride (CaF_2) nanoparticles in a whisker-reinforced resin matrix that has sustained F^- release (8). This should decrease the incidence of caries.

IMPLANT DENTISTRY

Titanium dental implants have been used successfully for the last thirty years, but they still have shortcomings related to their total osseointegration and the fact that their mechanical properties do not match those of bone. Advances in the fabrication of nanoparticles for coating the implant surface and the nanopatterning of dental implants is leading to better osseointegration and improved physiologic functions of implants. The improvement of the bone-forming activity at the bone-implant interface is committed to nanoscale features that have the ability to induce the differentiation of stem cells along the osteogenic pathway. Various reports support the concept that nanotopography enhances osteoblastic differentiation which promotes stability and favourably alter the biomechanical environment for healing. The nanoscale modification of an implant surface contributes to the mimicry of a cellular environment that favours the process of rapid bone accrual. Nanoscale modification also affects the chemical reactivity of the endosseous implant surface and alters its ionic and biomolecular interactions with the surface that leads to enhanced osseointegration.

Nanophase HA − the main component present in the hard tissues of the body − represents a promising class of maxillofacial implant formulations with improved osseointegrative properties. For one, synthesized nanophase HA has similar properties with natural HA which will permit better incorporation of implants and possible regeneration of bone material. Coating titanium dental implant surface with nanocrystalline HA powders will improve overall dental implant performance. Osteointegration of dental implants is better achieved because adhesion and proliferation of osteoblasts are significantly greater on nanophase HA. Also, apart from nanostructured HA, both nanophase alumina and titania demonstrate the same improved osseointegrative properties with dental implants.

These new coating technologies for applying nanoparticles of HA and related calcium phosphates (CaP) onto the surface of implants have been shown to provide titanium implants with an osteoconductive surface (9). The cell-substratum interface presents primary signals which allow for cellular adhesion and subsequent induction and tissue neogenesis. The regulation of cellular adhesion or selective adhesion of specific cellular phenotypes is crucial to regulating optimal tissue-specific integration while preventing inflammatory cell recruitment and scar tissue formation at the implant site. Several investigators have demonstrated the relative diminution of fibroblast adhesion compared to osteoblast adhesion when nano- and micron-structured surfaces were evaluated (10). Stem cells are extremely sensitive to their nanoenvironment, and topography is important for tissue-specific differentiation (11). It is known that the macrophage is the dominant cell in the foreign body response. Once it attaches to an implanted material, single macrophage cells fuse to form multinucleated giant cells. This response is accompanied by the recruitment of fibroblasts and thus fibrous tissue formation at the implant-bone interface. The adherence of giant cells to the implant surface is also associated with the release of enzymes and other bioreactive intermediates that can degrade and cause a loss of implant osseointegration.

Nanofeatures of dental implant surfaces are therefore critical in the achievement of osseointegration beyond what is possible with conventional titanium implants. A great variety of techniques using chemical and physical processes are used to create nanofeatures on dental implant surfaces. Chemical processes involve anodic oxidation or titanium etching with a solution of strong acids, *eg* sulfuric acid (H_2SO_4) − hydrogen peroxide (H_2O_2), at a constant temperature and for a specific duration. The etching with H_2SO_4-H_2O_2 of titanium screw-shaped implants creates a nanopattern that has been demonstrated *in vivo* to be associated with an enhanced osteogenesis (12). Physical modifications involve plasma spraying to coat the implants with nanoparticles or blasting with microscopic particles to create a porous layer on the implant surface.

NANOPHASE HYDROXYAPATITE

Hydroxyapatite − $Ca_{10}(PO_4)_6(OH)_2$ − is one of the most stable forms of the calcium phosphates and is the major inorganic component of human bone and teeth. Nanophase HA represents a promising class of bone graft substitutes in the fields of maxillofacial surgery and periodontics due to its dimensional similarity with bone crystals and its improved osseointegrative properties. Nanophase crystals of HA can bind to bone and stimulate bone healing by the stimulation of osteoblastic activity. These materials could be used for sinus lift procedures, to fill large cystic cavities, periodontal and craniofacial defects and in alveolar augmentation. A synthetic nano-crystalline hydroxyapatite (ncHA) bone substitution material has been successfully used in maxillofacial surgery for the augmentative treatment of bone defects after defect fractures and cystectomies without having any negative side effects (13, 14).

The structure of bone differs in different locations of the skeleton but the basic nanoscale structure remains the same throughout. The structure of the 206 bones in the adult human skeleton is dependent on their location and function. Bones that support teeth are unique in their structure and vary with age, gender and the presence or absence of teeth. Replacing lost jaw bone tissue is very complex. The use of synthetic nano-HA as a bone graft substitute should improve the quality and quantity of dental bone since it exhibits good properties as a biomaterial, such as bio-compatibility, bioactivity, osteoconductivity and direct bonding to bone.

In general, nano-HA has been designed for use in nonloaded areas, due to its inadequate mechanical properties and its use would therefore be limited to sinus lifts, periodontal pockets or other two or three-wall bony cavities. NanOssR bone void filler from Angstrom Medica (Woburn, MA, USA) was the first such product to receive clearance by the US Food and Drug Administration (FDA) in 2005. Other products now on the market are: Ostim® (Osartis GmbH, Germany) – HA and VITOSSO (Orthovita, Inc, USA) – HA +TCP. According to Angstrom Medica, NanOss duplicates the microstructure, composition and performance of human bone and possesses high osteoconductivity.

Systematic studies on synthetic carbonate-substituted hydroxyapatites and biologic hydroxyapatites led to the conclusion that they should both be considered as carbonate-hydroxyapatite (15). Detailed studies indicated that carbonate ions could be located in the two anionic sites of the apatite structure: in phosphate ion ($PO_4{}^{3-}$) sites (type B carbonated apatite) and OH^- sites (type A carbonated apatite). Carbonated calcium-deficient hydroxylapatite is the main mineral of which dental enamells have been utilized as active ingredients in toothpastes and mouthwashes and were demonstrated to be able to remineralize the surfaces of enamel and exposed dentine. This remineralization effect of carbonate-hydroxyapatite nanocrystals has encouraged the preparation of toothpastes exhibiting remineralizing effect with the capability of reversing dentine hypersensitivity (16).

ENDODONTICS

Conventional root canal therapy is used to salvage and restore millions of teeth per year. Nanotechnology may be able to produce regenerative approaches in which diseased or necrotic pulp tissues are removed and replaced with healthy pulp tissue to revitalize teeth. Recent published studies have indicated that melanocortin peptides (α-MSH) covalently coupled to poly-l-glutamic acid (PGA-α-MSH) were able to reduce the inflammatory state in inflamed dental pulp, increased the viability of cells and promoted human pulp fibroblast adhesion and cell proliferation. Nanostructured and functionalized multilayered polyelectrolyte films were used as a reservoir for PGA-α-MSH (17).

ORAL CANCER DIAGNOSIS

Oral cancer is the sixth most common cancer worldwide. The incidence of oral cancer in Jamaica was reported to be 3.5/100 000 population (World Health Organization, 2010) with a death rate of 2.17/100 000 (18). If detected early, the prognosis for patients with oral cancer is excellent, with a five-year survival rate of about 90%. Unfortunately, many oral cancers are not diagnosed early and the overall survival rate is only about 50%, among the lowest rates for all major cancers.

The current procedure used to diagnose oral cancer in a suspicious lesion involves an incisional biopsy and off-site histopathologic examination by a pathologist. The biopsy procedure is painful to the patient and the histopathologic diagnosis can be time consuming. New technology using the latest techniques in microchip design, nanotechnology, microfluids, image analysis, pattern recognition and biotechnology will allow dentists to have a diagnosis of a suspicious lesion in eight to ten minutes rather than days or even weeks. The new test will involve removing cells with a brush, placing them on a nano-biochip the size of a credit card, and inserting the chip into the analyser, where they will be analysed within minutes in the presence of the patient, so that the patient would know the result before leaving the clinic. This will have a number of benefits such as decreasing waiting time and the number of visits, and will also be beneficial to Caribbean countries that may not have many pathologists. There will also be cost savings to the patient and the national healthcare system.

The nano-biochips are disposable and slotted like a credit card into a battery-powered analyser. A brush-biopsy sample is placed on the card and microfluidic circuits wash cells from the sample into the reaction chamber. The cells pass through mini-fluidic channels about the size of small veins and come in contact with "biomarkers" that react only with specific types of diseased cells. The machine uses two LEDs to light up various regions of the cells and cell compartments. Healthy and diseased cells can be distinguished from one another by the way they glow in response to the LEDs. The device has just entered the more extensive trial that will involve 500 patients in Houston, San Antonio in the United States of America and in England. This could lead to an application for FDA approval between 2013 and 2015. In preliminary test, Rice's diagnostic nano-biochip was found to be 97% "sensitive" and 93% specific in detecting biopsies (19–21).

CONCLUSION

The field of nanotechnology holds a bright future for developments in medicine and dentistry. Many innovative materials and treatment modalities are being researched and should be available to clinicians within the next decade. With progress in nanorobotics, medicine and dentistry will be transformed. Nanorobots will operate at microscopic level to perform tasks such as providing local anaesthesia, cleaning teeth and doing precision orthodontics. This paper presented what is now available to dentists and what will soon be available.

Authors note

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