

SMALL WONDERS, PAVING A GREAT FUTURE - NANOTECHNOLOGY

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ABSTRACT:

The future trend in dentistry is nanotechnology, aptly named as, Nanodentistry. Nanotechnology is a technology which manipulates matter at a nanometer level, and is increasingly finding its application in treatment of cancer, ranging from early detection, accurate staging at a microtumour level and therapy. This technology offers a shift from non specific, highly toxic and expensive drugs to highly specific, less toxic and inexpensive drugs. Nanomedicine breaches the walls of conventional medicine, by being more soluble, site specific and with a longer duration of action. Thus, this review aims to summarize in a nutshell the future of nanotechnology in dentistry with key emphasis on its role as an anticancer modality.

KEYWORDS: Nanotechnology, Nanodentistry, Nanomedicine, Oral Cancer

INTRODUCTION

The concept of Nanotechnology was visualized as early as 1959 by the late Nobel Prize winning Physicist, Richard P. Feynman, who had concluded in his lecture saying "this is a development which I think cannot be avoided."¹ The word 'Nano' is derived from the Greek word 'nannos', meaning dwarf.^{1,2} Nanotechnology as defined by the National Nanotechnology Initiative, is the understanding and control of matter at dimensions of roughly 1 to 100 nanometers, where unique phenomena enable novel applications.² The novelty of Nanotechnology lies, not only in its size but also in certain properties that are manifested due to its nanoscale.

Nanodentistry

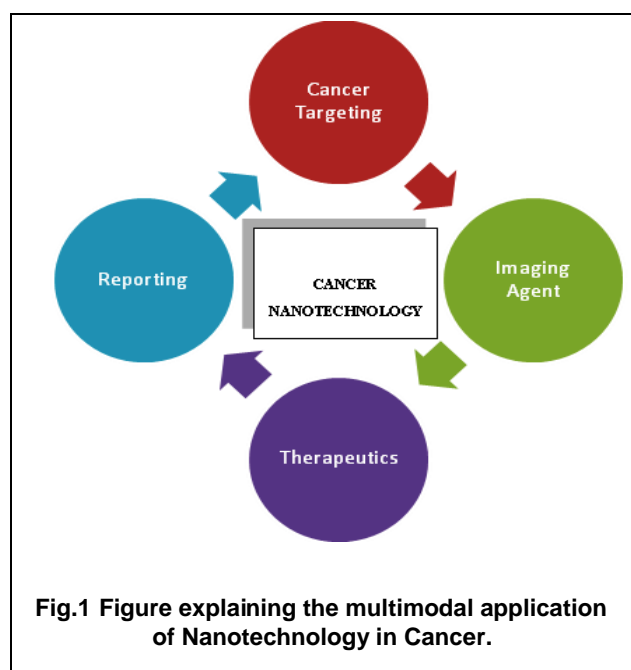
Nanotechnology will ring in the era of dental nanorobots which find their application in the relief from hypersensitive teeth, identification and destruction of pathogenic bacteria residing in the plaque, nanocomposites with nanofillers for enhanced durability and aesthetics and impression materials with nanofillers for precise tissue detail. Ongoing research presents a future wherein a dentist can instill a colloidal suspension containing millions of active analgesic micrometer-sized dental nanorobots on the patient's gingivae, which after contacting the surface of the crown, reach the pulp, where the nanorobot establishes control over the nerve-impulse traffic in the tooth, and after subsequent treatment, the control can be relinquished as and when commanded by the dentist. Under development are the Nano-sized stainless steel crystals incorporated in suture needles called as Nanoneedles and Nanotweezers, which will make cell surgeries possible in near future, with the

emergence of the field of 'Nanosurgeries'.¹ In the offing is the instant orthodontic treatment by painless manipulation of the periodontal ligament and alveolar bone, to reposition the tooth. Soon the dentition renaturalization procedure and major tooth repair can be conceptualized by the combination of nanotechnology, genetic engineering, tissue engineering and tissue regeneration.³

Nanomedicine

Nanomedicine is the preservation and improvement of human health, using molecular tools and molecular knowledge of the human body.⁴ It is also described as 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.³ It utilizes Nanopores, Nanotubes, Quantum Dots, Nanoshells and dendrimers to name a few.¹ These particles are made up of natural and synthetic polymers including albumin, fibrinogen, alginate, chitosan and collagen, with lactic-glycolic acid copolymers being the most frequently employed materials due to their biocompatibility and biodegradability.⁵ These nanoparticles get classified in the size domain of proteins and cells as they are smaller than 50nm, while those smaller than 20nm can transit out of blood vessels, and hence enable itself to be used as biological tags. The shape and dimensions of these particles play a critical role in cellular membrane penetration, optical absorbance and fluorescence.⁶

Oral squamous cell carcinoma is the sixth most common cancer for both sexes worldwide with a five year survival rate of about 5%.⁷ Most current anticancer drugs do not greatly differentiate between cancerous and normal cells, leading to systemic toxicity and adverse effects. Treatment requires large amount of drug administration limited by the maximum allowable dose owing to toxic side effects and is uneconomical. Therefore the need of the hour is the fabrication of nanodevices for early detection, with prompt location of the cancer at a microtumour level, delivering anticancer drugs to the specific site and simultaneously determining their efficacy in reducing cancer load. (Fig.1)



(i) Role in the study of carcinogenesis

The ability of nanoparticles, to simultaneously interact with multiple critical proteins and nucleic acids at the molecular scale should provide better understanding of the complex regulatory and signalling networks that govern the behaviour of cells in their normal state and as they undergo malignant transformation. Nanotechnology integrates proteomics with other scientific investigations to simultaneously measure gene and protein expression, recognize specific protein structures and structural domains, and follow protein transport among different cellular compartments.⁶

(ii) Role in cancer diagnostics

Screening Tests: Nanotechnology allows the reduction of screening time in detecting cancer by running many screening tests in a single device. The nanoscale devices operate on the principles of selectively capturing cancer cells or target proteins. The sensors are often coated with a cancer-specific antibody or other biorecognition ligands so that the capture of a cancer cell or target protein yields

an electrical, mechanical, or optical signal for detection. Nanowires, Nanocantilever, DNA Nanotube biosensors and Nanobarcodes are some such devices.⁸

Imaging of Cancer: One of the molecular imaging strategies is to improve the specificity of cancer detection in target specific imaging of biomarker molecules specifically produced by cancer cells, coupled with imaging probes guided by ligands that can recognize and interact with target molecules. Nanoparticles with sizes between 10 to 100 nm have a prolonged circulation time since they are usually not taken up by the Mononuclear Phagocytic system within the liver or excreted by the kidney. Such nanoparticles can navigate the vasculature and cross barriers through small capillaries into tumour cells and accumulate preferentially at the tumour site through the Enhanced Permeability and Retention (EPR) effect.^{9,10}

Nanoparticles of specific sizes can be synthesized under controlled conditions to obtain the desired optical and magnetic properties and levels of therapeutic agents attached to the particle. One such application is the Quantum Dots (QD), made up of semiconductor material such as cadmium selenide, which harvest solar energy and act as molecular light sources whose color depends solely on particle size and when they bind with substance of interest they light up like beacon.^{11,12} Near Infrared Fluorescence Reflectance imaging (NIRF) light penetrates much more deeply into tissues compared with visible fluorescence and allows for the detection of signals which can pass through several millimeters in the tissues. The advantage of QD NIRF is that their emission is well beyond the spectral range of the fluorescence signal produced by blood and tissues (auto fluorescence), resulting in imaging with a high signal-to-background ratio and hence aid in sentinel lymph nodes imaging.¹¹

One of the promising avenues is the utilization of super paramagnetic iron oxide or iron oxide nanoparticles as the precursor for the development of a target-specific MRI contrast agent, owing to the property of internalization of these particles by the cells which allows for magnetic labeling of the cell.^{11,13}

(iii) Multifunctional therapeutic

The conventional methods of delivery of anticancer drugs via the oral route undergoes metabolism forming active or inactive metabolites and those delivered via the IV routes are limited by low specificity, and damage to the healthy tissue. In contrast the advantage of nanoparticles is their longer duration of circulation time and sustained drug release. The delivery of the drug to the target tissue can be achieved in the following two ways:-

(a) *Passive targeting* relies on the properties of the drug delivery system and disease pathology to preferentially accumulate the drug at the specific site, avoiding non-specific distribution. Angiogenic blood vessels in tumour

tissue, unlike in normal tissue, have gaps as large as 600 – 800u between endothelial cells. The defective vascular architecture along with poor lymphatic drainage induces the EPR effect whereby nanoparticles are allowed to extravasate through the gaps into extravascular spaces and a 10 to 100 fold higher concentration of drug is achieved.^{8,14}

(b) *Active targeting* relies on use of nanocarriers to enhance circulation time and achieve passive targeting coupling of a specific ligand on the surface that will be recognized by cells at diseased sites. If the surface of polyethylene glycol nanocarriers is modified with folic acid, they can be targeted to tumour cells that over express folate receptors. Once the nanocarrier drugs reach the diseased organ, they need to enter the cells and deliver the drugs to intracellular organelles.^{8,14}

Reduction/Reversion of multi drug resistance

Chemoresistance is defined as either a lack of tumour size reduction or the occurrence of clinical relapse after an initial positive response to anti-tumour treatment. Drug resistance can be caused by physiological barriers or alterations in biochemistry of cancer cell. Nanoparticles based drug delivery systems aim to overcome both non cellular and cellular-based drug resistance, to increase selectivity of drugs.¹¹

Nanorobotics and cancer

Adriano Cavalcanti and co workers are developing a nanorobot to diagnose cancer before metastasis. They plan to incorporate a higher gradient of signal intensity of E-Cadherin for chemical parameter identification in guiding nanorobots to identify malignant tissue.¹² It is also envisaged that biocompatible surgical nanorobots would be made which could find and eliminate isolated cancer cells, remove microvascular obstruction, perform non invasive tissue transplants, conduct molecular repairs on extracellular and intra cellular structures and even exchange new whole chromosomes for the old ones living inside living human cells.

Future implications

By incorporating multidisciplinary engineering innovations, an avenue for development of enhanced, miniaturized and low cost diagnostic and treatment nanodevices has opened. But its clinical and environmental safety aspects should be established. Nanomedicine has the potential to increase the life span of humans. This will create populations with a large proportion of elderly people – an ageing society. With any new powerful invention comes the power to misusing it, hence ethical issues should also be discussed. Hence as quoted by someone “Nanotechnology is a promissory note on the future. As a discipline, it provokes our creativity in uniquely interdisciplinary ways. It asks us to imagine, to dream, and to dare”

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