IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 3 Ser.1 (March. 2020), PP 18-22
www.iosrjournals.org

Nanotechnology in Cancer – Theragnostics

Dr Divya Uppala M.D.S[1], Dr AnupamaBonam B.D.S[2], Dr B.Alekhya B.D.S (M.D.S)[3], Dr Sudharshan M.D.S[4], Dr B.sucharitha MS[5]

[1]Associate professor, Dept of Oral Pathology & Microbiology, GITAM Dental College & Hospital, Visakhapatnam -45.
[2]Graduate Student GITAM Dental College & Hospital,
[3]Postgraduate Student Dept of Oral Pathology & Microbiology,GITAM Dental College & Hospital,Visakhapatnam -45
[4]Senior lecturer, Dept. of Oral Pathology & Microbiology, Ragas Dental College & Hospital, Chennai 600119.
[5]Obstructive and gynaecology, Andhra Medical College, Visakhapatnam -45
***Corresponding Author:** Dr B.Alekhya B.D.S (M.D.S)*

Abstract: *Nanotechnology is rapidly evolving domain, has changed the very foundation of cancer diagnosis, treatment and prevention. Since everything is made up of atoms and molecular matter, nanotechnology has provided a way to rearrange and restructure matter on the atomic scale thus allowing us to reach down to the very roots of any problem. This emerging field is multidiscipline science, essential for Electronic Engineering,Drug-delivery, Optical Computer Tomography Photo-Thermal Therapy, Imaging, Sensing, Catalysis etc.*

Nanotechnology had improved cancer detection and diagnosis in inceptive stage. The present article gives the information on use of nanotechnology to solve the enigma in the field of oncology.

Date of Submission: 19-02-2020 Date of Acceptance: 03-03-2020

I. Introduction:

Nano: It is one-billionth of a meter. The concept of nanotechnology was first initiated by Richard P Feynman in 1959. The term nanotechnology by itself is defined by Norio Taniguchi of the Tokyo Science University in a scientific paper termed “Nanotechnology” in the year 1974. It was defined as **the processing of, separation, consolidation and deformation of materials by one atom or one molecule.[1]** More than 1000 nanostructures have been reported, many with potential medical applications.[2] A plethora of nanostructures have been in fact described according to the size, morphology shapes including solid nanoparticles (eg, spheres, rods, triangles, cubes), nanoshells (within inner and outer cores), nanocages and various physical and chemical properties, with varying compositions (eg, gold, iron oxide, carbon, dielectric materials, molecular, liposomal) and nanowires, nanotubes, branched dendrimers, and polymeric and organic lipid nanoparticles.[2]

Nanoparticles range from the 1 to 100 nm, whereas nanomaterials have unique materials with size ranging up to 100 nm. Nanomaterials can be broadly classified as **naturally occurring and artificially occurring**. Naturally occurring biological substances like viruses to materials which make up the bone are all-inclusive under the spectrum of nanoparticles. Artificial nanoparticles range from carbon, metal, dendrimers and composites. The carbon-based are mostly in the form of hollow tubes, spheres, ellipsoids and tubes.[3] Basically, the one dimensional, two dimensional and three dimensional are called sheets, nano wires.[4] The cylindrical ones are called as the nanotubes. The metal-based includes quantum dots, nanogold, nanosilver and metal oxides, such as titanium dioxide.[5]

Nanoparticles can be broadly divided according to the varying compositions. The compositions range from gold, carbon, dielectric materials, iron oxide, molecular or liposomal. Nanoparticles can be evenly divided according to the numerous shapes available. They would be spheres, rods, triangles and cubes. Among other nanoshells are mentioned, they are thin dielectric spherical structures with an outer gold covering. This is widely used in medical imaging and cancer diagnosis. The detailed features of each imaging structures are as mentioned below.

Liposomes:

Though the term nanoparticles and liposomes are used interchangeably. They mostly deal with the controlled and systematic delivery of medicine to the target area. The major advantage of this system is its low toxicity. Specific combinations of various lipid and lipid bilayers are used to process this system. Because of its similarity to the naturally occurring liposomes, the bioavailability of such structures is immense and are used as a major mode of drug delivery system.

Polymer micelles:

Polymer micelles are again structures which provide an efficient mode of delivery of cancer-targeted drugs which are poorly water-soluble. A micelle can be described as an aggregate of an electrically charged molecule. Thus based on such composition polymer micelles can be categorized as amphophilic micelles, polyion complex micelles and micelles derived from various metal complexes

Polyacid nanoparticles:

Dendrimers: These are especially branched, nano-sized, artificial macromolecules which are highly defined with functional groups. They have also been termed as cascade molecules.[6] Dendrimers generally increase in diameter in subsequent generations, which basically provides for effective drug delivery mechanisms.

Advantages of using nanotechnology in the diagnosis/treatment of cancer:

The mainstay of this type of technology is that it is multifunctional and different approaches can be integrated into this towards a holistic treatment of cancer.[7]The imaging and treatment modalities go hand in hand in this type of technology integrated into cancer treatment modality.

PROPERTIES OF NANOPARTICLES/NANOMATERIALS

3.0 Properties of nanoparticles

Size: The unique properties of nanoparticles are because of their small size and large surface area, as such they act as a proper bridge between the main bulk materials and the smaller atoms.

Their small size, which runs to billionths of a cm, are being proven to be of high value in the area of medical imaging, especially for angiogenesis imaging.

Melting Point: As the size reaches 100nm, the melting point of the particles also reduces.

Optical properties: The size of such nanoparticles also defy laws such as the quantum effect. According to this law, as the size of the nanoparticle is too small, it doesn't follow the quantum laws as these laws are obeyed by electrons and nanoparticles have their sizes lesser than an electron.

In quantum size effect, as the size of the particle decreases, the quantum bandwidth increases, in turn, increasing the frequency which would not be present in bulk material. For example, as the size of gold decreases the colour of the particle changes from yellow to red. Hence, nanoparticles follow this principle and contain high energy capacity.

Plasmon Resonance Property:

Application of SPR in Gold Nanotechnology in Head and Neck Cancer: The other eminent optical property of nanoparticles is the SPR or surface **plasmon resonance property** of nanomaterials. When materials are stimulated by light, a specific set of electrons start to resonate coherently producing a resonance. In this, the accurate localization of the point on the nanoparticle where resonance has occurred can be found. The resonance at which the electrons get excited on a nanomaterial and then calibrated is called as the SPR. This property is used in various imaging modalities as this principle provides better resolution and better resolution, which results in better visualization during the various phases of malignancy. Generally, gold nanoparticles are coated with antibody, and the shift in the resonance is observed, which is interpreted in colour. This property of nanoparticles is also used in calculating the ligand and analyte molecule bonding.

Kah et al. have shown that gold NPs can provide an optical contrast to discriminate between cancerous and normal cells and their conjugation with antibodies also allows them to map the expression of relevant biomarkers for molecular imaging.[8]

Nanoparticles seem to increase Raman scattering of saliva samples of oral cancer patients.[9]

Biocompatibility:

Inorganic nanoparticles as already discussed above have unique properties in electronic, photothermal, catalytic, and optical areas [2]

Of special mention are the plasmonic gold nanoparticles because of their simplicity in their fabrication, multifunctional nature, facile surface chemistry, biodistribution properties, and relatively low toxicity,[2] further these particles greatly enhance the signals which in turn tend to lower the background noise of the cells and tissues.

Application:

Nanoparticles can be used in various theragnostic areas such as follows:

Super**p**aramagnetic **i**ron **n**anoparticles or SPION are iron-oxide nanoparticles which are coated with biocompatible materials such as dextran. These particles are further conjugated with a cancer-targeting ligand for targeting cancer.

Hence, such ligand-bound particles are visualized using MRI, which eventually drain into the lymph nodes. The limitation of such particles is toxicity, chances of embolization and the risk of uptake by phagocytic cells. **Q**uantum **D**ots or QD are frequently used in imaging, and when compared with other fluorescent particles, these exhibit sharper images and enhanced visualization with photostability.

One dimensional nanostructure like the **nanotubes** has also shown to have a great potential in medical imaging as they consist of high optical absorption in the near-infrared and photoluminescence and strong resonance Raman scattering.

Facile Surface Chemistry:

Toxicity:

Nanotechnology In Diagnostic Imaging In Oral Cancers

Magnetic Resonance Imaging

The frequently used contrast agents which have been complexed with diethyltri – amine – Penta acetic acid (Gd- DTPA) or tetra azocycloodo – decane 1,4,7,10 – tetraacetic acid (Gd- DOTA) are used.[10] Though these contrast agents distribute throughout the entire body and provide good contrast. They are not specifically found in any organ as the contrast is flushed out due to blood circulation. In addition, the half-lives of such agents are very short ranging from 1 – 1.5 hours leading to the less usable time period for various diagnostic applications.[11] In contrast to such materials have been used by coating specific nanoparticles on its surface. The most frequently used nanoparticles used are a superparamagnetic iron oxide (SPIO), and ultra-small super magnetic iron oxide (USPIO) are being used for liver and spleen associated disorders as negative contrast agents.[12]

Nanoparticles are being also used in oral cancers with amazing results. As reported by Asifkhan et al. used a combination of chitosan and magnetic polyglycolide to create an MRI contrast and a treatment modality, in its use in oral cancers.[9] They have been reported to be having no adverse reactions in this study.

Optical Computer Tomography

OCT is another non-invasive, real-time measure between normal and abnormal. It works in a similar principle to that of ultrasound but works with infrared light hence gives a good resolution up to 10 micrometre, which remains higher than the other mainstream non-invasive diagnostic techniques.[13] But the major disadvantage remains in the fact that the contrast offered is still low, especially to diagnose between normal and neoplastic. Meanwhile, Kim et al., have gold-coated nanoparticles to enhance the contrast to up to 150 per cent of the images of oral dysplasia in hamster models.[14]

Gold nanoparticles have also been used in the concept of photoacoustic imaging, especially in the areas of brain, breast and prostate cancer diagnosis. They have provided increased and better contrast imaging.

Diffusion Reflection Imaging

Diffusion reflection imaging is a process where the light remnant after absorbing and transmitting gets reflected, and this property is utilized to visualize an image. The image is smooth when the reflecting object is smooth and sharp, for example, a mirror; if the reflecting object is slightly bumpy, then the reflected image would not be clear. This property of the reflected light is used to visualize normal, OMPD and oral cancer.

Gold Nano Rods or GNRs have proven to differentiate between the surgical margins with high specificity and sensitivity of 97% and 87% respectively with the help of Diffusion Reflection Imaging process which by itself has a huge margin of accuracy.

Quantum Dot Imaging

Quantum dots are unique nanomaterials with properties intermediate between bulk semiconductors and discrete molecules.[15] Their size range from 2 to 10 nanometers and possess special characters in producing specific colours depending on the size of the particle. As discussed in the above section, quantum dots are basically classified as Core Type, Core Alloyed Type and Alloyed Type Quantum dots.

Quantum dots work on the Bohr principle where it states that electrons occupy certain and fixed positions in orbit. Therefore, the colour of the emitted light can be altered by just changing the size of the quantum dot.

Studies have proven the quantum dots with 800 nm emission spectrum when conjugated with EGFR antibodies.[9] This technique has been proven to have potential in the treatment of OSCC.

Sensitive Biomarker Detection

Compared to the routine biomarkers available nowadays like the ELISA, western blot and polymerase chain reaction, nanotechnology has proven to have a higher detection sensitivity rate which can be useful for detecting minute quantities in tissue samples or other body fluids.

Routine biomarkers such as EGFR, TNF Alfa, IL 6, VEGF and the likes of these have been used in for cancer detection.[9] Nano based biotechnology has been successfully used in further detection of lower or minute quantities of such markers using MALDI – TOF – MS.

Besides this method, a gold protein chip method also was used for TNF alfa detection in oral cancer.[9] Such studies have given a positive take on the usefulness of nanoparticles in cancer diagnosis. Further, oral cancer detection rates could be markedly improved if saliva is used as an alternative method to improve cancer detection rates as shown in table 1.

NANOPARTICLES	PROPERTIES	THERAGNOSTICS
Liposomes	Specific combinations of various lipid and lipid bilayers similarity to liposomes	Systematic delivery of medicine to the target area
Polymer micelles	Aggregate of an electrically charged molecule	Efficient mode of delivery of cancer-targeted drugs which are poorly water-soluble
Dendrimer	Artificial macromolecules which are highly defined with functional groups	Basically provides for effective drug delivery mechanisms
Nano gold particles	Small gold particles with a diameter of 1 to 100 nm which once dispersed in water are known as colloidal gold	Drug-delivery, Optical Computer Tomography photo-thermal therapy, imaging, sensing, catalysis
Super paramagnetic iron nanoparticles (SPION)	Iron-oxide nanoparticles which are coated with biocompatible materials such as dextran	Targeting cancer
Quantum Dots	Tiny semiconductor particles a few nanometres in size.	Laser, medical imaging
Nanotubes	A tubular molecule composed of a large number of carbon atoms	Imaging

Why an alternate is required?

The main reasons why the cancer therapeutics now requires an alternate platform for drug delivery can be attributed to a myriad of causes. The most fundamental question of disorderedly pharmacokinetics which ultimately leads to increased toxicity and the other reason owing to the repeated IV routes which eventually become problematic. It has been seen that the traditional mode of drug delivery has always come with a price tag. The healthy cell being killed as well as the cancerous cell. Thus, various alternatives are a keen interest to scientists.

Drug Delivery: Drug delivery can be broadly classified into passive targeting and active targeting of cancer cells. Passive targeting can include drug delivery through a) vascularity, b) Tumor Microenvironment, c) Local Drug application[16].
Active targeting includes a) carbohydrate targeted, mostly lectin carbohydrate binding, b) Receptor targeted, c) Antibody targeted.[16]

Future Directions:

Conclusion:

This review aimed to highlight the, the various types and efficiency, and the progress of nanotechnology towards cancer detection with a special focus on oral cancer. This review hopes to cover the recent developments of nanotechnology and the strides made so far in the field of cancer detection and treatment.

References

[1]. N. Taniguchi, "On the Basic Concept of 'Nano-Technology'," Proc. Intl. Conf. Prod.Eng. Tokyo, Part II, Japan Society of Precision Engineering, 1974.
[2]. El-Sayed IH. Nanotechnology in head and neck cancer: the race is on. CurrOncol Rep. 2010; 12(2):121–128.
[3]. Parappurath N, S., Kirubanandam, S., Kumar, V. and Ahmed, B. (2018). Emerging Applications of Nanoparticles and Architectural Nanostructures. [online] Google Books.
[4]. Gracco, A., Siviero, L., Dandrea, M. and Crivellin, G. (2016). Nanobiomaterials in Dentistry. [Online] Google Books
[5]. U.S Environmental Protection Agency (2007). Classification of Nanomaterials, The Four Main Types of Intentionally Produced Nanomaterials. [Online] AZoNano.com
[6]. Abbasi E, Aval SF, Akbarzadeh A, et al. Dendrimers: synthesis, applications, and properties. Nanoscale Res Lett. 2014;9(1):247. Published 2014 May 21.
[7]. Chen-Yang Zhao, Rui Cheng, Zhe Yang, Zhong-Min Tian Molecules. 2018 Apr; 23(4): 826. Published online 2018 Apr 4.
[8]. Poonia M, Ramalingam K, Goyal S, Sidhu SK. Nanotechnology in oral cancer: A comprehensive review. J Oral MaxillofacPathol. 2017;21(3):407–414.

[9]. Chen XJ, Zhang XQ, Liu Q, Zhang J, Zhou G. Nanotechnology: a promising method for oral cancer detection and diagnosis. J Nanobiotechnology. 2018;16(1):52
[10]. Cheng W, Ping Y, Zhang Y, Chuang KH, Liu Y. Magnetic resonance imaging (MRI) contrast agents for tumor diagnosis. J Healthc Eng. 2013; 4:23–45.
[11]. Bennett KM, Jo J, Cabral H, Bakalova R, Aoki I. MR imaging techniques for nano-pathophysiology and theranostics. Adv Drug Deliv Rev. 2014;74:75–94
[12]. Brigger I, Dubernet C, Couvreur P. Nanoparticles in cancer therapy and diagnosis. Adv Drug Deliv Rev. 2002; 54:631–651.
[13]. Pande P, Shrestha S, Park J, Gimenez-Conti I, Brandon J, Applegate BE, et al. Automated analysis of multimodal fluorescence lifetime imaging and optical coherence tomography data for the diagnosis of oral cancer in the hamster cheek pouch model. Biomed Opt Express. 2016; 7:2000–2015.
[14]. Kim CS, Wilder-Smith P, Ahn YC, Liaw LH, Chen Z, Kwon YJ. Enhanced detection of early-stage oral cancer in vivo by optical coherence tomography using multimodal delivery of gold nanoparticles. J Biomed Opt. 2009; 14:034008.
[15]. Wikipedia contributors. Quantum dot. Wikipedia, The Free Encyclopedia. November 7, 2019, 21:00 UTC.
[16]. Arun Sharma, Nitin Jain, and RashmiSareen, "Nanocarriers for Diagnosis and Targeting of Breast Cancer," BioMed Research International, vol. 2013, Article ID 960821, 10 pages, 2013.

Dr B.Alekhya B.D.S (M.D.S), etal. "Nanotechnology in Cancer – Theragnostics." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(3), 2020, pp. 18-22.