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The role of Nanotechnology in the diagnosis and management of Prostate cancer

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Abstract

The quick development of nanoscience in the last few years has given an abundance of information into the biological performance and physicochemical properties of nanoscale materials that can be considered while utilizing nanotechnology for medicinal applications. Nanotechnology enabled medicine is defined as the comprehensive examination, control, development, repair, resistance, and enhancement of all human natural frameworks, working from the atomic dimension, utilizing designed nano-devices and nanostructures. Nanomedicine is also known as the science and innovation of diagnosis, therapeutics, and anticipating infection and awful damage. Prostate cancer is one of the major causes of morbidity and mortality in developing and under-developed countries. The most frequent non-skin cancer causing second largest number of deaths in men as compared to other cancers. In this short review, we demonstrated the application of nanotechnology in diagnosis and management of prostate cancer.

Keywords: Nanotechnology, prostate cancer

Introduction

Nanomedicine is a relatively new field of science and technology. It looks sometimes ill defined and interpretations of that term may vary, especially between Europe and the United States. There is no nanomedicine, there is nanotechnology in medicine. Even if the expression "nanomedicine" has been widely used for a couple of years, it is more proper to refer to "nanotechnology enabled medicine" in different sub-areas of medicine such as diagnostics, therapy or monitoring [1].

"Nanotechnology is the investigation and utilization of structures between 1 nanometer (nm) and 100 nanometers in size" [2]. One billionth of a meter is defined as a nanometer which is too microscopic to be seen by any usual optical microscope. Nanotechnology has the potential to transform the way the medical and healthcare solutions are developed and delivered through its application toward the diagnosis, treatments, or prevention of diseases at the cellular level [2].

The quick development of nanoscience in the last few years has given an abundance of information into the biological performance and physicochemical properties of nanoscale materials that can be considered while utilizing nanotechnology for medicinal applications, for example, in atomic imaging applications (diagnostics), thermal initiated annihilation of tumors (therapy), and, furthermore, disintegration of ineffectively soluble medications generally utilized inside the pharmaceutical businesses [3].

Nanotechnology enabled medicine is defined as the comprehensive examination, control, development, repair, resistance, and enhancement of all human natural frameworks, working from the atomic dimension, utilizing designed nano-devices and nanostructures. Nanomedicine is also known as the science and innovation of diagnosis, therapeutics, and anticipating infection and awful damage, of assuaging torment, and of safeguarding and enhancing human well-being, utilizing subatomic instruments and subatomic learning of the human body [4].

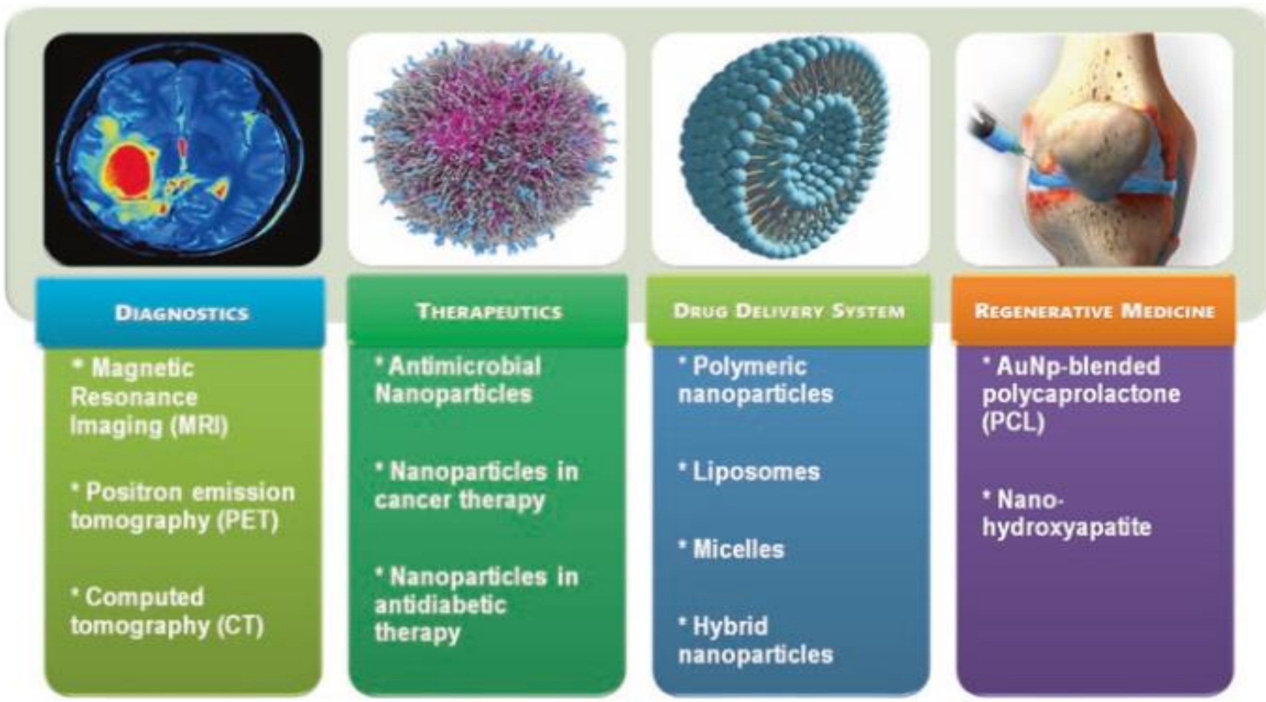

Figure 1. Application of nanotechnology in medicine

Principles of nanotechnology

A number of important properties of these nanoparticles make them ideal as targeted delivery vehicles [5]:

- Increased adherence to damaged vasculature and endothelium.
- Ability to noncovalently bind to carriers.
- Potentiation of selective carrier uptake by cells or tissue.

Several biological agents like albumin/dextran/perfluorobutane gas microcarriers (PGMCs) nanoparticles can be utilized for cardiac applications. Albumin-coated gas microbubbles have an interesting property, that is, they do not adhere to normally functioning endothelium but can attach to dysfunctional endothelial cells or to extracellular matrix of the disrupted vascular wall, an interaction that could be used not only as a marker of endothelial damage but even drug delivery. The cardiovascular drugs can be incorporated into the microbubbles in a number of different ways, including binding of the drug to the microbubble shell and attachment of site-specific ligands. Perfluorocarbon as a component makes microbubbles sufficiently stable, so that they can circulate in the vasculature as blood pool agents, acting as a carrier of the drug until the site of interest is reached, in this case, damaged/dysfunctional vasculature. The mechanism of this selective adherence involves destruction of the negatively charged glycocalyx protecting the healthy endothelium and binding of microbubbles to activated leukocytes slowly rolling over the damaged endothelial surface [6].

Mechanism of nanoparticles

These materials and devices can be designed to interact with cells and tissues at a molecular (i.e., subcellular) level, for applications in medicine and physiology, with a high degree of functional specificity, thus allowing a degree of integration between technology and biological systems not previously attainable. It should be appreciated that nanotechnology is not in itself a single emerging scientific discipline, but rather, a meeting of different traditional sciences, such as, chemistry, physics, materials science and biology, to bring together the required collective expertise needed to develop these novel technologies. The promise that nanotechnology brings is multifaceted, offering not only improvements to the current techniques, but also providing entirely new tools and capabilities [7].

By manipulating drugs and other materials at the nanometer scale, the fundamental properties and bioactivity of the materials can be altered. These tools can permit a control over the different characteristics of drugs or agents such as:[8]

a. alteration in solubility and blood pool retention time.

b. controlled release over short or long durations.

c. environmentally triggered controlled release or highly specific site-targeted delivery.

Applications of nanotechnology in medicine

These applications include fluorescent biological labels, drug and gene delivery, bio-detection of pathogens, detection of protein, probing of DNA structure, tissue engineering, tumor detection, separation and purification of biological molecules and cells, MRI contrast enhancement and phagokinetic studies. The long-term goal of nanomedicine research is to characterize the quantitative molecular-scale components known as nanomachinery. Precise control and manipulation of nanomachinery in cells can lead to better understanding of the cellular mechanisms in living cells, and to the development of advanced technologies, for the early diagnosis and treatment of various diseases [9].

Molecular imaging has emerged as a powerful tool to visualize molecular events of an underlying disease, sometimes prior to its downstream manifestation. The merging of nanotechnology with molecular imaging provides a versatile platform for the novel design of nanoprobes that will have tremendous potential to enhance the sensitivity, specificity and signaling capabilities of various biomarkers in human diseases [10].

Nanoparticle probes can endow imaging techniques with enhanced signal sensitivity, better spatial resolution and the ability to relay information on biological systems at molecular and cellular levels. Simple magnetic nanoparticles can function as magnetic resonance imaging (MRI) contrast enhancement probes. These magnetic nanoparticles can then serve as a core platform for the addition of other functional moieties including fluorescence tags, radionuclides and other biomolecules, for multimodal imaging, gene delivery and cellular trafficking. An (MRI) with hybrid probes of magnetic nanoparticles and adenovirus can detect target cells and monitor gene delivery and expression of green fluorescent proteins optically [11].

Nuclear techniques such as positron-emission tomography (PET) potentially provide detection sensitivities of higher magnitude, enabling the use of nanoparticles at lower concentrations than permitted by routine MRI. Furthermore, a combination of the high sensitivity of PET with the anatomical detail provided by computed tomography (CT) in hybrid imaging, has the potential to map signals to atherosclerotic vascular territories [12].

For imaging modalities with low sensitivity, nanoparticles bearing multiple contrast groups provide signal amplification. The same nanoparticles can, in principle, deliver both the contrast medium and the drug, allowing monitoring of the bio-distribution and therapeutic activity simultaneously (referred to as theranostics) [13].

Recent Advancement of Nano-Based Molecular Diagnostics

Gold nanoparticles have got much attention because of its physiochemical properties. Gold nanoparticles play a crucial role in the identification of genetic diseases based on biomarkers, SNP genotyping, and detection of nucleic acids in infectious conditions. Noble metal nanoparticles have been used extensively as tags for nucleic acid probes, and such AuNps can bind to small pieces of DNA of size not larger than 13 nm in diameter. Several FDA-approved products use AuNps as probes for diagnostic purposes [14].

Quantum dots (QDs) are inorganic semiconductor nanocrystals with a typical diameter of 2–10 nm. QDs are capable of emitting at very well-defined wavelength upon excitation and have been successfully used for imaging tumor target cells in animal models. Studies have unfolded great relevance of quantum dots in the field of early diagnosis and, also, in the field of locating the cancer tumors in patients and for carrying diagnostic tests in samples. The recent studies in quantum dots are on its composition of cadmium which is considered to be ounce of toxic, the reason behind the limitations on its use in vivo, and hence, study has been proposed to manufacture quantum dots of silicon as it's considered to be less toxic [15].

The magnetic properties and ease of derivatization of magnetic nanoparticles (MNPs) have been crucial for separation of analytes or to potentiate immobilization prior to recognition step. Detection of trace levels of prostate-specific antigen (PSA) and amyloid-beta derived diffusible ligands (ADDLS) in clinical samples by biobarcode assay are the prominent applications of MNPs. Within the blood stream, the MNPs attach to form microvesicles that help to identify the target cells. The early diagnosis can be then achieved by using NMR which discovers the microvesicles/magnetic nanoparticle clusters [16].

Role of nanotechnology in diagnosis and management of prostate cancer

Prostate cancer is one of the major causes of morbidity and mortality in developing and under-developed countries. The most frequent non-skin cancer causing second largest number of deaths in men as compared to other cancers. Prostate cancer can be localized and advanced depending upon its severity. Prostate cancer can metastasize via the lymphatic system and invade into bones. Various factors like age, genetics, environmental toxins, chemical hazards and radiations seem to be involved in the pathogenesis of prostate cancer but the exact mechanism is still unknown. Androgens are involved in the normal developmental phase of prostate and their functions, but, in that phase, they can still steep towards carcinogenesis [17].

Nanomaterials have been in use for a number of applications, especially for treatment and targeting diseases in the last decade. A carrier system must be biocompatible, inert and can carry a high concentration of drug efficiently. According to present knowledge, most of carrier systems are not able to deliver drug at high concentrations due to their increase cytotoxicity at targeting site. Therefore, many present treatment strategies cannot be used for treatment of cancers specifically breast tumor in females and prostate cancer in males. Prostate cancer (PCa) is one of the most common diseases and its targeting needs greater concentration of active to the organ and tissues affected by malignancy. Both organic (nanoemulsions, liposomes, niosomes, and polymeric nanocapsule) and inorganic (carbon nanotubes, gold nanoparticles, magnetic nanoparticles, silica mesoporous nanoparticles, quantum dots, selenium nanoparticles) are types of nanocarrier that have shown greater efficacy as drug delivery systems for greater number of active pharmaceutical agent (API) for targeting prostate tumor [18].

Prostate cancer is fifth cause of cancer death in the world and the second abundant cancer among men. Currently, imaging techniques, MRI, ultrasonography, digital rectal examination (DRE), computed tomography (CT), and cancer protein assay are various clinical diagnostic strategies for PCa detection . While all of these methods are powerful and highly successful in detecting of PCa, most of these approaches still complain about lack of precision, sensitivity and specificity for clinical purposes. Evidence strongly indicate that the tracking of PCa at the first development stage can help maximize the effectiveness for medical approaches and improve cancer survival from 10% to 90%. Nano-medicine can represent new interventions for the early detection of cancer based on PCa biomarkers, and resultantly, many attempts have been undertaken to develop novel nanotechnology-based diagnostics for early detection of cancers [19].

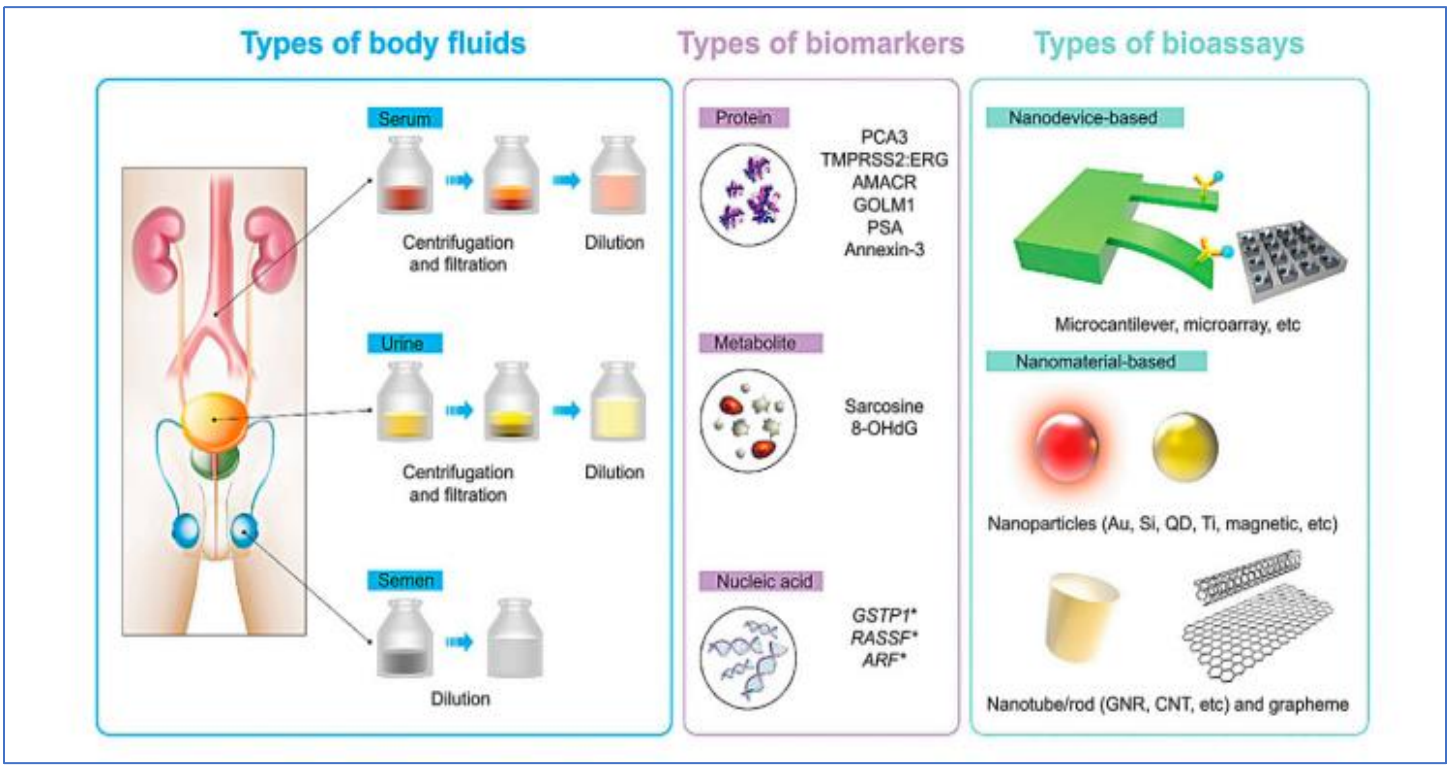

Figure 2. Nanotechnology-based diagnostic approach.

Magnetic nanoparticles (MNPs) were widely utilized due to their unique properties such as magnetic susceptibility, physical characteristics, stability, biocompatibility, ease of mechanism and many more important outcomes. MNPs are used to isolate and purify some molecular compounds, like proteins or nucleic acids, before diagnosis. This development was indicated for the detection of various biomarkers of prostate cancer proteins in the urine and bloodstream. *Yamkamon et al.* developed Fe3O4 magnetic nanoparticles-combined with streptavidin-horseradish peroxidase based on PCR method for detecting of urinary PCA3 (a gene specific to prostate cancer). This technique was able to detect PCA3 at femto-gram concentration which was around 1000-fold more effective than traditional RT-PCR. In real sample analysis, PCa patients' PCA3 expression measured by the prepared nano-platform was greatly higher than that of patients with benign prostatic hyperplasia (BPH) and healthy controls [20].

Gold nanoparticles (AuNPs) exhibited excellent flexibility in medical application, including diagnostic imaging, drug delivery, radiation and photo-therapy. Innovations in nano-chemistry and surface chemistry have promoted the creation of AuNPs as nano-biosensors. AuNPs coated with certain hydrophilic polymers exhibit excellent in vivo circulation and high tumor aggregation through the improved permeability and retention effect (EPR). Lue et al. conjugated PSMA-1 (PCa targeting antigen) to AuNPs for X-ray radiotherapy improvement and observed that the targeting ligand improved gold absorption by PSMA-expressing PC3 pip cells compared to PC3flu cells that lack PSMA receptors [21].

Quantum dots (QDs) are semiconducting structures of a nanometer scale with better fluorescence emissions than traditional organic fluorophores due to the quantum confining effect of electron energy bands. QDs have ultra-high porous structure, wide surface area, lower electrochemical behavior (higher analytical signal), flexible structure, high electrical and chemical function, etc. The design of developed electrochemical biosensors can be using QDs with such special characteristics [22].

Ehzari et al. documented an enzyme-free sandwich immuno-sensor (magnetic structure Fe3O4@TMU-10 and nickel-cadmium quantum dots) for the PSA biomarker detection. The second antibody, as an electro-active non-enzymatic probe, is cross-linked to a nickel-cadmium quantum dot. The designed immuno-sensor showed a consistent range between 1 pg/mL and 100,000 pg/mL and the 0.45 pg/mL detection limit with appropriate repeatability [23].

Graphene plays a significant role in the field of biosensors with extraordinary electrochemical, electrical, magnetic and optical properties. Graphene features, such as functionalization, high flexibility and optical transmittance, have made possible the recent rise of graphene application in nanosensors. Numerous studies indicated the possibility for sensitive detection of PCa biomarkers with graphene structures [24].

Conclusion and recommendations

The nanotechnology can be of great benefit in medicine especially in the diagnosis and management of tumors and other medical disorders. MNPs are used to isolate and purify some molecular compounds, like proteins or nucleic acids, before diagnosis. This development was indicated for the detection of various biomarkers of prostate cancer proteins in the urine and bloodstream, which can be very beneficial in the early stages.

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