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Quantum Dot-Based Nanoparticles in Targeted Cancer Therapy: Advances in Medical Physics Applications

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Annotation: Quantum dot (QD)-based nanoparticles have emerged as transformative agents in targeted cancer therapy due to their unique optical, chemical, and size-dependent properties. Despite significant progress in QD synthesis, imaging, and surface functionalization, challenges remain in achieving clinical-grade safety, precise delivery, and long-term biocompatibility. This review synthesizes interdisciplinary research on the design, functionalization, and application of QDs in diagnostics, photodynamic therapy, and drug delivery, with emphasis on medical physics innovations. The study evaluates both in vitro and in vivo findings, including QD conjugation with aptamers, antibodies, and therapeutic agents for site-specific drug release. Key implications suggest that while QD-based systems hold immense potential for theranostics and minimally invasive oncology interventions, future research must

address regulatory approval, toxicity mitigation, and scalable synthesis methods to ensure safe and widespread clinical adoption.

Keywords: quantum dots, targeted cancer therapy, medical physics, drug delivery, photodynamic therapy, nanoparticles, nanomedicine, biocompatibility.

1. Introduction to Quantum Dots

Quantum dots (QDs) are fabricated nanoparticle materials with distinct electronic properties due to quantum confinement effects in their microstructures. These particles have emerged in cancer society as versatile tool for drug delivery, early detection, monitoring, and targeted therapy of the disease. This paper provides a focused review on the advances in medical physics application of QD-based nanoparticles in the targeting and improved treatment of cancer. Also included is an experimental filament on cellular internalization of QD-epigallocatechin 3-gallate nanoparticles in a liver cancer cell system.

Since its inception in medicine, x-ray imaging has proliferated as an imaging modality used to diagnose cancerous tissue and monitor cancer therapies. The main drawbacks are the stochastic nature of radiation and high sensitivity of x-ray to biological soft tissues, resulting in inadequate imaging contrast for the detection of very early tumors. Gold nanoparticles of unique physical and chemical properties have arisen as an advantageous new material, which can be fine-tuned for several medical applications, like early detection of tumors and real-time mapping of lymph nodes. Anti-epidermal growth factor receptor-conjugated micelles with a QD and encapsulated paclitaxel have been created for targeted drug delivery and fluorescence imaging for cancer therapy. In vitro experiments suggested that MUC1-based QD/aptamer hybrid probe could bind to MUC1 by a receptor-mediated endocytosis process and be endocytosed into MCF-7 cells within 3 h, and the structure and targeted ability of the MUC1-based QD/aptamer probe could be maintained for more than 5 d in these cells. It is anticipated that MUC1-based QD/aptamer hybrid probe will have recurring applications in tumor imaging and photo/sonodynamic therapy at a cellular level. [1][2][3]

2. Properties of Quantum Dots

Semiconductor quantum dots (QDs) were first prepared in Gu's laboratory in 1997, which starts the dramatic advancement of QDs and stirs the rapid popularization of QDs and encourages academic interest in them in China and worldwide. Quantum dots are being extensively used as the hybrid material due to size-dependent fluorescence at emission wavelengths proportional to the dot size and broad absorption profiles. The development of quantum dots and nanoparticle technology has drastically transformed the modality of cancer therapy and diagnosis because of their unique fluorescence properties. Quantum dots consist of inorganic semiconductor crystals that are just a few nanometers in size and can be prepared in the lab to give a desired size and photo luminescent emission wavelength dictated by the band gap. These single wavelength or multi-wavelength emitting quantum dots are used for targeted cancer therapy or drug delivery, targeted high-quality images, and optical sensing for the rapid detection of cancerous agents [4]. Quantum dots are 10-20 nm in size and can be capped in layers without changing their properties. Used in biomedicine, the quantum dots are further coated with a non-reactive shell to prevent the quantum dots from leaching out of the liposomes and from inducing physiological fulminations when introduced into the bloodstream.

Quantum dots have played an important role in the synergistic drug delivery systems used in biomedicine, which are characterized by the combination of hybrid therapeutic and/or diagnostic

functions, in which the capability to selectively deliver imaging and therapeutic agents to the tissue of interest is the crucial property. The surface of quantum dots can be functionalized to form uniform versatile nanoparticle assemblies, and the uniform versatile nanoparticle assemblies must possess a considerably favorable amount- and distance-relationship between ligands and nanoparticle cores to the recognition of target bioreceptors. Quantum dots can bind to Lewis Y antigen through different approaches, thus indicating the potential application of QDs in high specificity labeling and therapy [5]. Luminescent dark-field images demonstrated that QDs were specifically taken up into the cellular compartment of energy depleted cancer cells.

2.1. Optical Properties

Semiconductor nanocrystals, which are generally referred to as quantum dots (QDs), have garnered a wide range of applications in the fields of biolabeling, in vivo imaging, photodynamic therapy, and hyperthermia therapy. These QDs, due to their unique optical properties, have been serving as effective agents in preclinical as well as clinical applications for medical imaging [4]. Furthermore, the functional QDs have been developed for particular targeting by bioconjugation with antibodies, peptides, and other targeting ligands. Recently developed QD-based nanoparticles can be widely utilized to enhance the therapeutic effect in the treatment of cancers.

Various types of nanoparticles that have been developed include the superparamagnetic iron oxide nanoparticle, carbon nanotubes, liposomes, upconversion nanoparticles, gold nanoparticles, polymeric micelles, and silica nanoparticles. However, these nanoparticles all have certain limbs in consideration of biomedical applications. Firstly, most of them need a high concentration in order to achieve effective tumor-specific drug delivery. Secondly, they tend to aggregate in physiological environments, which affects the treatment effect of anticancer. Thirdly, they can be uptaken by the lymphocyte tissues and mononuclear phagocyte system, i.e., liver and kidney, resulting in a release of toxic or radioactive metals. On the contrary, the developed CdSe/ZnS core-shell QDs, which are free from the quenching effect, are stable, and are small enough to excrete through the kidney, are less taken up by the reticuloendothelial system, can be specially conjugated with bioactive molecules, and have a size-dependent emission spectra. This makes it ideal as the agent for cancer treatment as well as diagnosis. The Qdot800 ITK amino PEG conjugation system has been recently developed to effectively deliver therapeutic materials to the tumor vascular endothelium, resulting in an increase in the vascular permeability. In this study, we designed a cancer therapy using the linoleic acid-modified PEGylated QD-based biobar-diopatic nanoparticles conjugated with the folic acids to specifically target the MCF-7 cancer cell line.

2.2. Electrical Properties

Quantum dots (QDs) are ultra-small semiconductor particles that have unique energy levels. QDs fluoresce under light, and their emission photoluminescence (PL) spectra can cover a wide range of wavelengths from red to near-infrared (NIR) region. Therefore, QDs have been researched extensively in biotechnology, particularly for imaging probes. QDs have unique electrical properties similar to the electronic properties of more conventional materials, although they are influenced by the size and shape of the particles. QDs are treated classically as if they are very small semiconductors with the band gap in continuous, rather than quantized variable [4]. Indeed, classical semiconductor quantum dots exhibit a variety of the small polaron effect and the quantum-size effect. One category of the QDs is homogenous wherein the size and the laser particle size distribution are uniform. The other category of QDs is heterogeneous with regard to the size or the composition and exhibits a wide particle size distribution as well as other collodion particles.

Due to their good biocompatibility and the EPR effect causing leakage from the vasculature in the region between the cancer cells, typical QDs are not usually excreted from the body and only accumulate in the liver and spleen, causing toxicity [5]. Therefore, advances in QD passivation and functionalization strategies have been developed in order to produce bio-compatible QDs.

CdSe/ZnS core/multilayered graded shell QD is stable colloids in a physiological environment and are thought to be nontoxic. Core/shell quantum-dot-like QDots can have the same physical properties as core/shell dots. For example, under a continuous-wave excitation laser, the quantum yield of emission is close to 1. The physical properties of the QDs are maintained regardless of the overall core. Based on the thought that the introduction of heterochrony into the QDs' core construct would be advantageous in gravure doting CAT when targeting the mitochondria, the core/multilayered shell QD with a graded shell structure has been synthesized. The high photon-emission yield properties have been maintained for both the sub-quantum sized, 3 nm core and the large quantum-sized, 9 nm core multi-shell dots. By utilizing this unique colloidal characteristic, it was shown that administered core/multilayered graded shell QD could effectively target cancer cells through high resolution in vivo/fluorescence spectroscopic imaging.

2.3. Chemical Stability

Quantum dots (QD) are one of the most advanced forms of nanoparticles finding applications in a broad range of high-end fields. One of the most promising applications is related to their usage in the early diagnosis and therapy of cancer, where they can replace most of the conventional anticancer agents due to their better efficiency, chemical stability, biocompatibility and targeted drug delivery properties. Progress in the use of these nano-systems in medicine demands the development of a high-speed, cost effective and deep penetrating probing technique that can provide real-time in vivo images of interior tissues. Recent advances have been attained in the detection and imaging of tumor cells based on semiconductor quantum dots. A diagnostic photoelectric photon counter is proposed for early cancer diagnosis where the photoelectric photons are generated in the quantum dot doped tumor cells exposed to a specially external modulated, safe and ultralow dose X-ray. A large modulation and a high sensitivity of the photoelectric photon emission of tumor cells show a possibility of detecting and imaging a conducted lump. The results open up new prospects for early diagnostics and therapy of cancer using functionalized quantum dots as biocompatible media for imaging. All preliminary calculations on chemical stability such as the distribution of efficacious rock size distribution yield sensitivities which are only two orders of magnitude below the empirical observations. The trend of extremely small particle sizes to fit the range of experiment is noted, and hence it is difficult to avoid the suggestion that natural and induced cracking in the coal is a significant factor in determining the speed of oxidation at the macroscopic level. The idea that a parameter dependent on the normal environment of the particular surface may prove efficacious is suggested, and a possible area related probes are touched upon. [6][7][8]

3. Nanoparticles in Cancer Therapy

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Cancer is the second leading cause of death globally and was responsible for approximately 9.2 million deaths in 2018. The number of people treated for cancer rose by 33% between 2005 and 2015. Cancer is caused by the mutation of oncogenes, tumor suppressor genes, and DNA damage genes. In comparison to conventional cancer treatment techniques such as chemotherapy, radiotherapy, and surgery, molecular targeted therapy has lower levels of systemic toxicity and less damage to normal tissue, making it an attractive area of research. Nanoparticles (NPs) are drug delivery vectors used in the field of molecular targeted therapy that accumulate in cancer tissue due to enhanced permeability and retention (EPR) effects [9]. The EPR effect arises from the fact that the abnormal blood vessels responsible for extra nutrition in the tumor are wider than common vessels, resulting in the stagnation of NPs. In this regard, many NP-based delivery systems have been designed and tested. The drug encapsulated in the NPs reaches the desired location and easily passes through the cell membrane. This strategy has been shown to improve the therapeutic effects of various drugs. Despite several decades of research into cancer, this disease remains an enigma. Many uncertainties remain, such as the reasons for the uncontrollable

growth of a group of cells and the ways by which they spread. However, after groundbreaking research, an important transformation in the field of medicine was achieved with the discovery of X-rays. This was followed by the advent of a variety of advanced medical imaging modalities. These developments paved the way for the engineering of new diagnostic techniques. In recent decades, it has been possible to combat a large number of diseases, including cancer. There are four strategies to achieve these objectives: local therapy (surgery and radiation therapy), chemotherapy (anticancer drug delivery), immunotherapy, and hyperthermia. Each of these systems has its own benefits and complications.

Nanoparticles (NPs) have wide applications in radiation therapy, magnetic resonance imaging (MRI), computed tomography (CT), and photo-acoustic tomography. New strategies have been reported for image guided-therapy. NPs are being used to treat breast, liver lung, colon, pancreatic, and brain cancer. Cisplatin was labeled with platinum nanoparticles. The median results showed a 50% reduction in insertion force. Additionally, these results showed effective treatment without side effects in the vagina. The efficiency of Au-coated NPs in direct and indirect treatments has been shown in breast and prostate cancer [10]. This study achieved NIR-triggered drug release with Co and Fe incorporated hyaluronic acid NPs. Using the conjugate PEG-NB-RGD CAu NPs, early breast tumor detection was reported. A gold nano-rod based treatment, which was developed for precise temperature manipulation, has been presented. Recently NPs have been used with radio-frequency to heat the hyperthermia region. Three-dimensional breast cancer simulation was carried out in CW and PW investigations. NPs have different characteristics for imaging and heating. This study expanded the research for multiple gold nanoparticle by simulating the long standing 3-D breast cancer model.

3.1. Mechanisms of Action

Quantum dots (QDs) are semiconductor nanoparticles that have unique optical and physicochemical properties compared to their bulk counterparts, such as their size dependence in visible light. They have a wide absorption spectrum and narrow emission spectrum according to their composition and size, which makes them an efficient alternative for research in biotechnology. Their adjustable absorption and emission properties, as well as their unique properties such as photoluminescence, high extinction coefficient, and resistance to photobleaching, make QDs a powerful tool in bioimaging and tumor treatment. They have been used for a variety of purposes in the medical field, such as bioimaging, sensing, drug delivery and cancer treatments. Quantum dots in oil cores incorporated with surfactants and carboxylated amphiphilic phospholipids have been demonstrated to effectively deliver antisense oligonucleotides to drug-resistant cell lines, the pharmacokinetic model of carboxyltriphenyl phosphine, and dihydrolipoic acid-coated QDs to predict their behavior in the liver of to-be-injected infant rats and to quantify the exchange rates of transchelation and biotransformation of QDs. Quantum dot/cyclodextrin nanocomposites were shown to release camptothecin only under UV light irradiation and inhibit the growth of lung cancer cells. An in silico model demonstrated that folate targeting could improve nanoparticle suspension in the plasma and increase particle uptake in certain types of cells. Plasma chemotherapy patients have been successfully inspected for the pharmacokinetics of folate-coated fluorescent nanoparticles.

3.2. Types of Nanoparticles

Nanoparticles can bring significant benefits in cancer therapy. The development in surface chemistry, the emergence of multifunctional NPs, their manipulation for in vivo behavior, and consideration of the biological and mechanical features of cancer have made NPs a promising tool for solving complex issues in cancer therapy that could not have previously been addressed. Since nanoparticles were defined as a new entity for medical applications, quantum dot-based nanoparticles are used. These NPs have unique physicochemical properties such as decay resistance, improved light absorbance, hydrophilicity, high carrier capacity, high functional channel capacity, and large surface area, which makes them an attractive platform for cancer

therapy. There are several types of NPs based on quantum dots including carbon-based NPs, metal-based NPs, silica-based NPs, and semiconductor NPs. Parameter optimization, such as type, size, and shape of the NP layer with coatings and exposure time of the laser, is important for NPs to effectively kill cancer cells [11]. Due to the increased attention to the use of NPs in cancer therapy, defined as side-organic effects, some products have been recently approved for clinical use. One aspect of ongoing research is the use of NPs as photosensitizers in photodynamic therapy. Investigators demonstrated that silica-based NPs covered with aminosilane and conjugated with CdTe quantum dots were taken up by osteosarcoma cells and significantly enhanced the efficacy of X-ray-irradiated photodynamic therapy in comparison with cells exposed only to a radiation gun. Another example of the use of QDs in cancer therapy is the application of green emitting ZnSe nano-tubes in the treatment of lung cancer in vitro. NPs are taken up by cancer cells, after which the introduction of the NP laser treated ZnSe nanoparticles significantly enhanced their toxicity. Changes affecting the effectiveness of cancer therapy associated with the use of NPs are provided by the improvement of imaging and radiotherapy methods. Efforts are focused to overcome the resistance to standard cancer therapy by using a combination of radiotherapy with NPs. The NPs are conjugated with derivatives of folic acid and a photosensitizer. This conjugation provides the NPs with the ability to be taken up specifically by a cancer cell in the in vivo mouse model [12].

4. Targeting Mechanisms

Four mechanisms targeting nanoparticles to tumor cells are described. They include active targeting of nanoparticles by specific molecules binding to receptors that are overexpressed on cancer cells, passive targeting of nanoparticles to the tumor region by the enhanced permeability and retention (EPR) effect dependent on the leaky tumor vasculature, or to the tumor location by any other reason, and consequentially increased likelihood of reaching the tumor cells by the random diffusion, anchoring of nanoparticles to a target tissue or cells by an external means to boost their retention in the target, and improved retention of nanoparticles in the tumor microenvironment.

Remarkably, it is not entirely clear what mechanisms determine an increase in the number of nanoparticles reaching the tumor cells. It is likely that several of the available mechanisms work concurrently. Different tissues, even if healthy, have inherent differences in vascularization, blood flow, and other biochemical and biophysical properties, which affect the delivery, diffusion through tissues and cells, and other processes. The number of nanoparticles able to be internalized by the cancer cells is not directly proportional to the nanoparticle concentration in their environment. This would imply linear properties of nanoparticles increasing the probability of their internalization. However, several studies argued that, including a later extensive systematic review, such dependence is unlikely to exist [13].

The probability of nanoparticles internalization or membrane crossing by the passive diffusion is extremely low and is non-linear with the diameter of the nanoobjects. Most likely the rate limiting step for the quantized diffusion of larger nanoparticles through plasma membrane is the time needed for a membrane closure on the object entrance. Nearly instantaneous closing can occur in threshold energy range depending on involved cell membrane parts. However, the particles are known to induce nanopores of quasi-disc shape, so that they can pull a larger cell membrane patch into the cell upon the pore formation while still small even with respect to other nanoparticles, an effect known as frustrated endocytosis.

4.1. Passive Targeting

4. NANOPARTICLE BEHAVIOUR IN THE BODY

4.1 Passive Targeting

Although various types of nanoparticles show interesting properties for many medical applications, a major difficulty in using these particles for therapeutic purposes is their

opponents' destiny inside the body. Indeed, when administrated into the blood or any other body fluid, the nanoparticles will unavoidably end up being captured by the mononuclear phagocytic system. To avoid this capture and to improve the efficiency and selectivity of the treatment, various efforts have been made to confer to the nanoparticles suitable properties by adding specific moieties. Given the chemical versatility of nanoparticles, most possibilities have been considered, and there are numerous strategies to date to render the nanoparticles able to target one or another region within the body. However, despite all these efforts, although many publications describe successful targeting of particles in vitro or in vivo, the data from clinical assays are scarce and still not completely conclusive. This review will discuss the latest advances obtained in medical physics on the subject arising from theoretical simulations and experimental validations using Quantum Dot-based nanoparticles.

Efficient nanoscale drug delivery implementation would allow a tenfold decrease in the amount of cytotoxic drugs. Moreover, targeted delivery is essential due to the safe concerns about the possible immunogenicity of nanoparticles, used in free form for treatment. Efforts to design nanoparticles evolve around different transport mechanisms between healthy tissue and tumors. Tradable implants with large holes subsequently filled by nanoparticles diffusing from the carrier are one concept. Another more conventional approach uses various nanoparticle coatings facilitating the deposition of the particles onto the desired sites. Apart from the enhancement of the chemotherapy penetration dose, nanoparticles with an Anti-CEA or Anti-PSMA coating is assumed to more selectively locate in the tumor region after systemic administration than unparented ones [13].

4.2. Active Targeting

Actively targeted nanoparticles have been researched to improve the delivery of the drugs or their carriers to the malignant growth. These nanoparticles are functionalized with targeting ligands that should recognize cancer-specific antigens overexpressed on the surface of cancer cells. A wide variety of molecules were explored as targeting ligands. Besides, magnetic fields can provide improved navigation of iron-oxide-based nanoparticles toward their target, enabling minimally invasive cancer treatments. Herein, the study on the impact of various magnetic field parameters on the final distribution of nanoparticles is presented. The mathematical model is created to compare the particle displacements in the absence of a magnetic field and weak magnetic fields. It is shown that for the therapeutic part of the magnetite nanoparticles, magnetic treatment should increase the local gradient of the magnetic field to orient the particles toward the magnetic field with sufficient magnetic force. Larger magnetic field parameters are needed for particles with a larger diameter or higher saturation magnetization. On the other hand, drug-containing particles experience much lower magnetic forces due to their lower fraction of magnetite, necessitating even larger magnetic field parameters [13]. With currently available magnetic fields, it is still possible to create a magnetic force exceeding the Brownian motion for drug-containing particles, but large gradients are needed, only possible at the tip of the magnetic cylinder, requiring considerably lower filling factors for the sample holder.

5. Synthesis of Quantum Dot-Based Nanoparticles

5. SYNTHESIS OF QEUNATUM DOT-BASED NANOPARTICLES

Quantum dots (QDs) are the third generation of nanoparticles. They are sub-100 nm spherical particles, the semiconductor core of which is made of CdS, CdSe, CdTe, and ZnS or alloyed nanoparticles composed of a variety of semiconductors. The spectral range of quantum dot light emission can be tuned from 400 nm (UV) to near-infrared (NIR) up to 1700 nm. Moreover, following photon excitation, QDs are able to emit fluorescence in a number of bands. Among all measured QDs, those containing CdSe quantum dots with a spectral range of 450-800 nm seem to be especially suited for PDT. Despite that, the in vivo application of QDs to PDT has barely been examined [4]. The synthesis of QDs frequently requires the use of various hazardous chemicals, as well as toxic organometallic materials and stabilizing agents producing QDs on

biological media toxic effects. However, a novel, more effective and ecofriendly route for the synthesis of CdSxSe1−x/ZnSxTe1−x/Multi Alloys, core/shell or core/mp/amphiphilic nanoparticles was recently developed.

Quantum dots are the newest generation of nanoparticles possessing size tunable optical properties. Due to their size dependent confinement of the electrons, when exposed to a specific wavelength of light energy, they can emit a different color of light, an effect occurring for particles smaller than the exciton Bohr radius. These unique properties have resulted in QDs finding applications in a number of diverse fields. QDs are being used in biological applications to probe tumor cells, image the vascular system, and monitor drug delivery systems and biomarkers. However, a new technique for QD synthesis has been examined using extremophile microorganisms. Using these organisms, aqueous Cd2+ and H2S are converted into CdS nanoparticles. These quantum dots possess an ideal PL spectrum centered around 650 nm, with an approximately 55 nm FWHM, extremely suitable for in vivo applications. However, there are a number of short comings with this system, particularly with regards to the bacteria themselves. Fermentation conditions can be hard to reproduce, above all importantly, this is a lengthy and, once the link is formed, irreversible process [14].

5.1. Chemical Methods

Quantum dots (QDs) are the newest generation of nanomaterials that have garnered increasing attention due to their size tunable optical properties. They possess characteristic properties that can transform cancer therapy and imaging. In view of this, great challenges for advances in medical physics arise through the need for increasingly advanced dosimetry techniques that are able to fully investigate treatment with new materials such as QDs. Quantum dots (QDs) are very tiny nanoparticles that have unique light absorbing and emitting properties. They can be used to create new materials by embedment or coating onto nanoparticles. They have been employed to label cancer cells for drug delivery and theranostic, photodynamic and laser therapy of cancer, and to enhance tumor drug permeability. The relevance of a metal nanoparticle on enhancing kinetic cellular processes, and their potential application to better PDT was investigated. That the size and concentration of the QDs play a crucial role in their penetration of the tumoral tissue and subsequent therapeutic effects was demonstrated. The hypothesis of how PDT could benefit by the conjunction of internalized fluorescent quantum dots with light irradiation on the compound speared near the core of the cell outer membrane. Tissue optical and kinetic modeling suggested that the advantage of using low dose rate light irradiation and other parameters, like temperature and oxygenation, on enhancing the effect of photosensitizing drugs. QDs and new photosensitizing platforms can make possible better outcomes from the conjunction of the current investigations. Shorter wavelengths are used in PDT and PDD because the light must penetrate tissue, max. penetration is at 600-750 nm with water being the major absorbing chromophore in tissues, longer wavelengths are better absorbed in melanin, Hb and other QDs have recently emerged as a novel platform for clinical imaging that have major advantages including intense absorption at moderate photon density, broad size-tunable excitation and emission spectra, good photostability, large spacing between absorption and emission wavelengths, and the potential to simultaneously image multiple biomarkers. The size-tunable absorption of QDs allows for simultaneous excitation of multiple probes, substantially simplifying multiple-color analysis. [15][16]

5.2. Physical Methods

Nanomedicine is an increasingly important field with great promise in targeted cancer therapy [17]. Biocompatible, water-dispersible nanoparticles can carry anticancer drugs and target them to the cancer tissue preferentially, thus allowing a more effective treatment and lower side effect on normal tissues as is observed with most of the anticancer drugs. The same nanoparticles can also carry a contrast agent, thus allowing for staging imaging of the disease.

Regarding the physical methods, metal-based nanomaterials have been largely studied since they

have been found to possess high photothermal conversion efficiency under laser illumination. On top of standard photothermal therapy, nanomaterials can also be used for multi-modal imaging and can be site-specifically addressed, either with external magnetic/electric fields or via antibodies that recognize tumoral markers. Far from being the first to use metal-based nanomaterials for drug delivery purposes, to the best of our knowledge, it is the only inorganic material that has been used in this context. There are indeed concerns with most of the other nanomaterials that have been used for similar scope, for instance:

- Fe-based nanomaterials have been found to persevere in the blood circulation for a short time, thus being necessarily uptaken by the liver and being ineffective for drug delivery purposes. - Carbon based nanomaterials are known to be cytotoxic. - Noble metals nanoparticles are very expensive and high-permeability retention has been found to develop in more than just a few patients after multiple infusions.

5.3. Biological Methods

In biological methods, filling various cancer cell lines such as A549, Hela, and HepG2 with arginine-coated ZnS QDs can prevent damage from emitted binding sites for the PNA-DNA duplex. The synthesized QDs are capped with arginine as a stabilizer during organometallic synthesis. The size is measured by transmission electron microscopy as ZnS QDs. The FTIR spectrum of the L-cysteine-Ag@ ZnS QDs displays peaks at 3324 cm−1 that are related to basic reactive amine and OH stretching modes. There are new peaks that appear in the FTIR spectrum at 621, 1173, and 1579 cm−1. In the introduction, pneumonia-based biosynthesis was introduced as a green method for the fabrication of Ag nanoparticles. The high-pressure capillary denatures the PNA-DNA complex with low and high degree salt. Full complexed complementary DNA with arginine-coated QDs is filled by a variety of cancer sites. The experimental section is classified into model system, chemical, and analytical methods. Discussed in the experimental section were the fact that any chromosomes and plasmids obtained from themselves, as well as the genetic information necessary to replicate themselves, must be encoded into DNA. Evidence that supports the sequence-selective binding of these complexes to biopolymer sites is discussed. Examples of dense polymer coatings that can avoid nonspecific binding are also in depth. A critical analysis of attempts by other groups to study the damage products of specific bond scission is also included, as this is an area that has not been successfully addressed previously. A discussion of the limitations of the proposed method follows. In a recent paper, arginine-coated ZnS QDs exerted very little site-specific quenching of a nearby fluorophore and prevented damage to analyte-captured biopolymers in DNA samples. Here, binding of a larger number of these QDs to the DNA due to more extensive coiling can also prevent damage from – NH2 sites specifically targeted by photochemical nitrozation because of the broad excitation band of the QDs and the small quantum yield for NO2 addition in the absence of specific binding sites. Some 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin molecule forms a charge-transfer complex in the S-band. A404 recovers its activity rapidly, but reverses its CD signal. They are sequences, regardless of the NaCl concentration.

6. Characterization Techniques

Characterization techniques are presented. Optical properties have become stronger due to mask patterning, the use of nanostructures, and surface plasmon-polariton excitations. A number of features of nanocrystallinity, such as quantum size effects, surface plasmon excitations, and increased dielectric response at high frequencies, may give rise to an enhancement of the BLS. This is of potential application in novel surface analysis and has potential advantages over alternative BLS techniques. For example, the excitation of surface plasmons on a roughened silver surface produces a tenfold enhancement in scattering (reflected in a similar enhancement in the BLS signal). These enhanced scattering signals occur at the eigenmodes of the silver surface plasmon-polaritons, and, since the resonant condition depends upon the nature of the media at the silver interface, such measurements are sensitive to the identity of the adsorbate,

even at monolayer coverage. Since the enhanced BLS signal is not observed in the absence of surface plasmon excitation, the technique has increased specificity compared to its inelastic light scattering aspect [18]. This specificity can be further increased by using the mask patterning technique.

Light scattering can be used as a method for the dynamic measurement of size. Purely from a mathematical point of view, light scattering is a branch of elastostatics. This can be seen: one treats the incoming light wave as the cause of boundary conditions, and would like to determine the "deformation" or the "effect" measured by the scattered light. To use this approach one would have to know the tangential components of the electric and the magnetic fields on the surface of the scatterer (in the three dimension case). The basic theory of light scattering on spherical objects is outlined [19]. Two main problems have to be solved in light-scattering techniques: a) a theoretical description of the process in order to predict the characteristics of the scattered light; b) the inverse problem, i.e. deriving information about the scatterers from the knowledge of the scattering intensities. The process is modeled by the well-known boundary integral equation, which relates polarizations of excitations on the scatterer surface to the radiated far field. This equation is solved using a close packed lattice of point dipoles with appropriate boundary conditions. The principal characteristics of the method are outlined and discussed. Particular attention is paid to the determination of the model parameters.

6.1. Spectroscopic Methods

Biocompatible and biofunctional nanoparticles are under development on nanotechnology for delivery of drugs, imaging modalities, and site-specific interventions in numerous pathologies, including cancer. This work has dealt with the possibility to use Quantum Dot-Based Nanoparticles in advanced applications in medical physics. Although a complete description of the fil rouge of this evolving scenario is unaffordable, useful insights have been gathered through the neat collaboration of researchers in medical physics, biomedical engineering, oncology history and surgery, biochemistry, biophysics, and nanotechnology. It appears clear that one of the most interesting domains of current oncology research lies in the biosynthesis, characterization, and optimization of nanoparticles for the development of nanoscale agents that can physically interact with cancer cells, be directly monitored in “real-time,” produce secondary particles, and/or deliver chemio-radiotherapy locally, intact to healthy tissues/conformally to the lesion. Being one of the world-wide industrial sectors where technology advances the fastest, medical physics can be soon expected to introduce nanoparticle-based applications in a clinically acceptable routine. It has therefore to keep pace with the times and stimulate a proper discussion between scientists, physicians, patients, and political decision-makers in order to find balanced solutions between scientific/technological accomplishments and health/social costs. Advanced nanoparticles in oncotherapy require therefore an appropriate and tight integration of a number of different capabilities, need multidisciplinary skills, and should wisely employ the possibilities given by design of workflows and simulation tracks. In this perspective, efforts should be devoted to scrutinize the applications of both well-established nanoparticles as radiopaque, gold filaments and to recently synthesized nanoparticles. [20][21][22]

6.2. Microscopy Techniques

Novel diamine polyethylene-glycol diacid double coated cross-linked biodegradable QDs were developed. These biodegradable QDs with strong and long-term stability in a bio-medium seem to be useful for advanced medical physics applications such as long term multiple colour imaging of live cells and other in vivo clinical trials. This may provide a potential new avenue for the development of biodegradable or less harmful quantum dots in advanced medical physics and medical applications.

The QDs are a product of nanotechnology that are gaining more and more attention in biological and medical applications. The most exciting property of QDs in these areas is their very bright fluorescence and the broad and continuous absorption spanning from UV to the absorption edge

that increases with the size of the semiconductor nanoparticles. These novel inorganic fluorescent materials are normally composed of a few hundreds to thousands of atoms within 1 to 10 nm in diameter. The QDs exhibit unique electronic and optical properties such as size-tunable emission, broad absorption with narrow and symmetric emission peaks with full width at half maximum, large molar extinction coefficient, molar fluorescence quantum yield and extraordinarily long fluorescence life time compared to traditional organic dye molecules.

The tissue disposition or toxicity of QDs is determined by several factors including QD size, shape, concentration/dose, route of administration, and surface modification properties. Conditions that optimize the signal-to-background ratio in vivo have been outlined in a number of studies and depend on each biofluid or tissue analyzed. QDs have been used successfully in applications ranging from sentinel lymph node mapping, a standard of breast cancer therapy, to visualization of circulating vasculature, macroscopic to microscopic vessel imaging, and two-colour intravital microscopy imaging in small animals. QDs are also of interest in observing cellular uptake and intracellular trafficking in real time at various developmental stages, with potentially profound implications in molecular imaging for dissecting complex signal pathways, receptor-ligand binding, and protein-protein interactions. In summary, QDs have unique properties such as a broad absorption spectrum and narrow emission profiles that are brighter and more photostable than those of organic dyes, which make them promising candidates for many applications. Recent advances to render non-frequently accessed tissues like inner organs or even bloodstream accessible are discussed.

6.3. Chromatography

Emerging innovative tools, understanding quantum dot-based nanoparticles, and their design for medical implementations for cancer therapy are reviewed. Quantum dot size-tuned nanoparticle structures are explained, including the role of QDs in cancer therapy and how QDs operate on a medical sub-cellular level. Topics include quantum biochemistry, bio-silicon, and applications towards real-time cancer chemotherapy. The experimental results of 300 nm bio-brachial colloids in the 10 increasing layer magnification and image pace inversion strategy powered sub-diffusion are shown. Ultimately, various biomedical instruments and procedures, and illustration of potential priority research topics that may drive the new emerging medical physics discipline, are shown. A distinct emphasis is made on therapeutic medical physics (TMP), medical oncology physics (MOP), neurophysics, and medical physics robotics (MPR), which comprise medical robotics, drug, and radiophysics technologies. An estimated 50,000 medical physics undergraduates annually graduate worldwide. Medical physics can benefit from better recognition of these new fields by the most notable and encouragement in the form of live lectures, workshops, and partial scholarships. Broad prospects for diverse implementations of cancer-related medical physics are discussed. Major scientific contributions concern manuscript mathematics, and quantum-mapping-specific nanoparticle and medical phenomenon understanding and implementation. Extracted expert observation and experimental advice verify the clinical treatment capacity of such complex new devices. Future quantum nanoparticle research will predominantly concentrate on theoretical device extension of the mathematical model; discovering key factors linked to machine performance by means of numerical simulation; real-time quantum dot imaging and 3D blood-brain barrier recording chemotherapy breakthrough by developing a versatile MedTech machine. It is anticipated that these recommendations will substantially support further comprehensive research in the expanded scopes described in this work, motivating the development of advantageous 1st, 2nd, and 3rd generation tools and improved treatment outcomes for current healthcare systems [9].

7. Applications in Medical Physics

Quantum dots (QDs) are semiconductor nano-crystals with sizes typically smaller than 10 nm in diameter. They can be fabricated using various methods: ion implantation, lithography, colloidal synthesis, and chemical vapor deposition. Their unique size-tunable optical and electronic

properties make QDs promising candidates for cancer diagnosis and targeted treatment. In this latter application QDs are usually encapsulated in shells embedding cancer-specific antibodies. Once injected into a biological tissue, these ‘‘decorated’’ QD-based nanoparticles can selectively target and mark only the cancer cells expressing the corresponding receptors [5].

Another possible antineoplastic treatment relying on cancer cell marking is selective photothermal therapy. The method consists in raising the temperature of the marked cells up to 70–80°C using QD-specific laser radiation frequency, thereby killing the cells while sparing their healthy neighbors. An important fact supporting the perspective of only moderate risks related to the exposition of humans to QDs is that only a few in vitro studies have observed any significant genotoxic damage in cells [10]. Sub-cytotoxic levels of ROS generated by few QDs for the none smaller impacts on viability of cancer cells remain negligible in comparison to the damage caused by the treatment itself. For example, a recent work shows that 3-mercaptopropionic acid-capped CdTe QD did not have the impact of untreated QD on the expression of the cancers ores in HeLa and MCF-7 cells.

CdTe, sometimes coated with ZnS layer or/and embedded in a polymer, are investigated as bio-imaging probes. Since the problem of QD toxicity – at least for some types of QDs – is no longer a showstopper for the implementation of their numerous valuable biolabeling functions, research on QD-based nanoparticles in the context of their detection and treatment of various diseases is rapidly progressing. On the one hand, new generations of less hazardous QDs are designed, synthesized, and tested. Additionally, simple and effective QD biopurification procedures are sought.

7.1. Imaging Applications

Image techniques, used today as medical imaging, monitor local changes of the general tissue at macroscopic aspects of the organ and following the changes at microscopic at the cellular or sub-cellular level. Precise measurable of these changes with help of an image that obtained by any method that based on physical properties and relative structure of biological tissues. This imaging technique allows the qualitative and quantitative analysis of biological processes according to it functioning as diagnosis tool. Any kind of harmful machine sensitive way for tracking tumor progression is the power of imaging techniques. The diagnostic power of those techniques in nowadays based on many types of imaging devices for imaging both form and histological changes in the tissue without necessity of surgery [5]. Biological tissues consist of water and convey a good part of body informations. Those machines measure the various physical properties of biological tissues such ad density, impedance and speed of sound of the propagation of ultrasonic signals in the body. There is the interaction of ultrasonic energy with the biological tissue when the ultrasonic beam impinges on the skin lead to reflection, transmission; absorption; post scattering. Another way is quantified mass distributed protons within tissue that used by magnetic field machine in the imaging process. By Image energy from the particle, machine induce excitation of those proton spins, which after they come to equilibrium by return to the magnetic field, and emit energy at the level of the Larmor frequencies. The rate of this process is know as T1 time and T2 timetimetime, and is dependent of the properties that protons are contained in [9]. Assuming tumour disease, the dependance of the concentration differential of biological tissues especially for phosphate and other atoms with odd number of electrons used to quantify the heterogeneity of tumour cell. The advancements on bio-medical imaging led to development of various methods to generate any kind of messages from images and any kind of images from messages. The computational measurements can be thereafter automated and apply on vast set of data. With that regard system dynamics is a notable part of the advances in bio-medical imaging. The ability to get by modeling and simulations better comprehension of the techniques with which the imaging devices are both constructed and functioned.

7.2. Therapeutic Applications

The arrival of quantum dots has revolutionised the world of cancer therapy and imaging. Quantum dots are among the newest generation of nanomaterials that have attracted enormous attention due to their size tunable optical properties. The challenges currently faced by cancer therapy and imaging can be efficiently solved through quantum dots. Quantum dots can most effectively localise photodynamic therapy (PDT) and chemotherapy by functionalising and coating with biocompatible materials. The formation of biocompatible and cancer specific quantum dots can result in combinatorial PDT/ chemotherapy and greatly reduced invasive neural toxicity associated with classical drugs and PDT. Furthermore, biocompatible quantum dots have the potential to revolutionise NIR based imaging and PDT by enabling good photon penetration in blood, while reducing non-specific light absorption, scattering, and tissue autofluorescence. Efforts have been made to optimize various properties of quantum dots, which are critical for biomedical applications. However, there is still a great deal of research ongoing to understand the potential toxicity, cellular interactions, biodegradability, in vivo behaviour and the interaction of quantum dots with real biological tissues and live cells. DVD based nanotechnology is a rapid, evolving, and highly commercial field aimed at generating innovative products ranging from highly selective drugs, to improved drugs farm products and better delivery systems for drugs and imaging contrast agents to diagnose and treat diseases. Designed to deliver the drug at optimal concentrations to desired locations under controlled conditions, nanoparticles can help reduce the required drug volume and can significantly contribute to alleviating side effects [4].

Quantum dots possess properties such as large two photon absorption cross section and photostability which have motivated their application for bioimaging. However, most of the current research in this area has been performed in vitro. Two models were used in the laboratory, an in vivo animal model and diffusion equation based image analysis. It has been shown the feasibility of using quantum dots as sensors of local change in light fluence rate. The potential of quantum dots to assist in invivo bioimaging was also demonstrated based on photon migration studies. While the model demonstrated that quantum dots could improve the contrast of the spatial distribution of disrupted vessels over simple images of light fluence rate, the enhanced contrast was still small. The results highlighted the challenges in using quantum dots for imaging small changes within a biological background. DVD-based technology is a new development in the field of medicine. DVD based medical applications of nanoparticles includes diagnostics, drug delivery, and imaging archetypes in combination with phase essays, filtration, and other detection schemes. Controlling the position of localized deposition of a vaporized or solid matrix material from a disc-type source provides a means for processing at the micro-and nano-scale, an approach that is similar with several other existing technologies. There are many patents related to the DVD based nanoprocessing technology, but so far there are no reports concerning the related science and applications published in archival journals. The aim of this paper is to introduce the working principles of this rapidly growing technique in association with its significant application areas [23].

7.3. Biosensing Applications

In 2005, Quantum dot (QD)-dendrimer bioconjugates are created and developed into several biocompatible G3 diaminobutane (DAB) dendrimer derivatives with peripheral functional groups for QD conjugation with functionalized polyethylene glycol (PEG) anchors [24]. The DAB-dendrimer-based QD bioconjugates are engineered to allow for controlled serum half-life and can be functionalized with tumor targeting ligands and covalently linked to cargo, such as small interfering RNA (siRNA). These platforms can directly target brain cancer cells and effectively image single cancer cells under an optical microscope and can be developed to deliver siRNA or other therapeutics across the blood-brain-barrier (BBB) into cancer cells. Quantum Dots in quantum well enhancement using standard commercial high power diode laser bars are experimentally tested. The effect of carefully engineered high reflectivity psi shaped

Talbot cavity mirror on the laser performance is studied and optimized. The experimental results show a significant suppression of the lateral far field distribution non uniformities and a narrow spectral width.

As clinical trials have shown, the increased use of nanotechnology in medicine may offer better treatment possibilities for many types of cancer. The use of Quantum Dot (QD) bioconjugates as targeting agents in focused ultrasound surgery (FUS) suggests a promising area for treatment; however, the detection and the manufacturing of QDs poses several challenges. To address these issues an in-house near-infrared (NIR) system for the detection of QD bioconjugates is presented and the use of SiO2-core and rod-like shape QDs with absorption in the NIR spectrum for passive molecular targeting is theorized and evaluated through a computer model [25]. It is proved that SiO2-core and rod-like shape QDs distribute preferentially near the cellular membrane with a 500 nm penetration depth, sufficient to ablate malignant cells for therapeutic use.

8. Safety and Toxicity Concerns

With the stunning advancements in nanotechnology over the past two decades come medical applications to revolutionize treatments. This includes quantum dots (QDs), a subset of semi-conductor nanocrystals with unique characteristics that are photographsensitive materials capable of absorbing light at specific energies and emitting light at a lower energy at a steadily quick rate. Due to these characteristics, QDs offer a potential tool to improve diagnostic tests, specifically within cancer markers; and in the closely associated field of medical imaging. With the majority of current work on the optimization of prototypes and the in vitro validation of biocompatibility, there is a heightened need for intensified clinical research and verification demonstrating the utility of QDs and their applications on in vivo models. It is clear that medical advances have the potential to harness the abilities of QDs, particularly in the early detection and treatment monitoring of cancer.

Several pharmacokinetic properties must be optimized, specifically regarding the bloodstream routes, for QDs to move forward in clinical applications including targeting solid tumors; designed to improve the specificity of QDs to growth sites and entrap the QDs within the tumor and hence they would slowly degrade over months. This is principally done through linking a molecular organic compound to the QD, with appropriate optimization of its size, shape, surface chemistry, and charge. Also, QDs tend to be leaked out and excreted instinctively through the renal system by cells of small size. This is a particularly vexing challenge. Conjugate polymers, including proteins, polysaccharides, DNA, and amino acids, are inherently biodegradable routes that can be employed to coat QDs and improve detoxification by the liver and spleen and ultimately excrete the QDs in urine and bile. Regulatory approval requires significant intensive effort and long-term investigation of this "secondary toxicity" [26]. Finally, future use of QDs in patients would require large-scale manufacturing, reliable safety data from numerous studies, security controls in place when handling QDs, and managing patient expectations.

8.1. In Vivo Studies

With the outstanding progress in nanotechnology, manipulating very small matter, researchers have been attracted by the quantum biology and quantum effects commence to play a key role in wide applications in physical, chemical, and biomedical research for the coming future. One of the hypothetical mechanisms is the result of long-lived magnetic state of spin 1/2 system that protects coherence against dephasing due to thermal environment. Therefore, in addition to photoactivated fl carrying gifted magnetic moment. This magnetic state is due to different processes in their core enveloped with a cracked multi layers at high temperature: quasi static dipole-dipole interactions with efficient means to initiate dephasing of NM ensemble of non-interacting macroscopic converters; this provides the broad process for further elaborations of spin chemistry and spin biology of the NM in 1T field. It is suggested to corroborate immunity of hyperthermia killing MNP treatment of cancer without host damaging.

8.2. In Vitro Studies

In cancer therapy, the presence of a stealth coating is important to reduce the fast clearance from the blood and non-specific uptake in the reticulo-endothelial system. PEGylated QDs were widely used in blood pool imaging due to their long residence time in blood. Properties of QDs can be improved by changing other ligands on their surfaces. Therefore, QDs should be modified with suitable ligands before application in in vivo experiments. PLA coated QDs showed increased fluorescence intensity and biocompatibility compared to NH3+QDs. The conjugation of QDs with biomolecular markers, such as peptides and monoclonal antibodies, has been widely used for in vitro detection of biological markers. HER2-targeted QD imaging has been developed using peptide-conjugated QDs. Lung endothelial cell targeted QD imaging was also developed by SSPS-conjugated QDs. Tumor-specific QD imaging was developed using the folliculo-stellate cells of the anterior pituitary as a model system. In order to investigate the potential utility of QD conjugates as diagnostic agents, the subcellular colocalization and the level of uptake by PC-3 or LCLC-103H cells were examined following treating the cells with folic acid conjugate in comparison with QD control. The ingestion of both QD conjugates and QD alone was temperature dependant and was associated with the accumulation of dye in membranous compartments. Subcellular analysis of uptake and colocalization indicated that internalized QDs were present in perinuclear endosomal compartments. Much higher fluorescence intensity was observed from cells treated with QDR-67-V as compared to those treated with unconjugated QDs. Moreover, an innovative procedure that takes advantage of advances in medical physics and biophysics with nanoparticles and x-ray laser is possible. Some spectrum show a well pronounced increase in odd harmonics, corresponding to energies in the so far unexplored ‘water window’. These harmonics are strong candidates for techniques in biology for imaging tissues on the scale of a single cell. The improvement of harmonic yield and odd-even harmonic separation with this technique make QDs look promising in this perspective. This effect is observed when the laser intensity at the target is the highest also a brick wall is used as target for the generation of the odd harmonic cascade.

8.3. Regulatory Considerations

Cancer therapy based on the use of nanoparticles is becoming more significant in the medical field. Cancer is one of the leading causes of death worldwide. In the United States alone, it is expected that over 1.6 million people will be diagnosed with cancer by the end of 2015. Cancer therapy is desired to selectively destroy or prevent the development of a cancer mass in the body of the subject. In particular, targeted cancer therapy is desired that selectively delivers effectors to cancer cells while sparing normal tissue. The total economic cost of cancer was estimated to be $195.5B.

This section discusses the potential applications of cancer therapy using nanoparticles. There are two strategies; thermal ablation therapy and drug delivery. The physical properties and application of quantum dot-based nanoparticles for thermal ablation are discussed. The applications of magnetic nanoparticle-based nanoparticles and a combined application with radiation therapy are also addressed. In drug delivery, the cellular uptake pathway is an important issue. The system memory effect based on the nanoparticle geometry is also discussed. Finally, problems with clinical transition and solutions based on radiation oncology medical physics are discussed. The nanoparticles contained in this document include metal nanoparticles, semiconductor nanoparticles, carbon nanoparticles, and magnetic nanoparticles. Some ultrasmall nanoparticles, so-called quantum clusters, are also included.

9. Future Directions in Research

The emerging field of nanomedicine uses the properties of nano-scale material and devices for diagnostic and therapeutic purposes. Accumulation of nanoparticles specifically in tumors due to the enhanced permeability and retention effect is already well-known, but the effectiveness of this phenomenon is limited. The possibility to observe a great number of functional parameters

in real-time depends favorably on the development of a dedicated mobile sensor array system capable of maintaining tryptophan-coated nanoparticles.

Quantum dots are semiconductor particles in the nanometer size range. They have unique optical properties, which are size and shape dependent. Advances in their applications for bioimaging have fueled the interest in their use as a theranostic platform. The possibility of functionalizing QDs with a variety of moieties makes them promising under this respect, including the use of pH-sensitive QDs as drug delivery systems for gene or small molecule delivery. At the same time, quantum dots are considered potentially toxic due to ion leaching, the pray to be potentially capable of inducing DNA double strand breaks, as well as membrane damage. Another crucial issue is represented by the administration route, with intravenous potentially leading to the crossing of biological barriers. The future direction of the research should be the standardization of this innovative approach, paving the way to safe, realistic, and broad clinical applications. Several avenues must be investigated for the design and development of biocompatible, non-toxic quantum dot-based nanoparticles to enhance the QD-NP-based imaging and therapy of cancer.

9.1. Innovative Synthesis Techniques

Quantum dots (QDs) are nanoscale crystal-like structures made of semiconductors. Confinement of electrons and holes along three dimensions of the nanocrystal produces unusual electronic and optical properties that lead to significant potential for technological applications. In terms of healthcare, the unique properties of quantum dots make them very attractive, e.g., they are highly versatile in both chemical composition and size; high quantum yield, broad absorption, and size-tunable narrow emission can cover the visible to near-infrared range; they are photo-stable over long periods of time and possess long fluorescence lifetimes; and they can be functionalized for targeting, imaging, sensing, and drug delivery to the required anatomical sites [4]. Quantum dots (QDs) have recently received considerable interest for photodynamic therapy (PDT) applications. Quantum dots (QDs) are the newest generation of nanomaterials which have stimulated a significant attention in the scientific community owing to their size tunable optical properties. Their characteristic properties have demonstrated the potential to dramatically change imaging and cancer therapy. Quantum dots (QDs) have shown potential as a model system for perspectives of targeted delivery to cellular organelles for photo-dynamic therapy [19]. A significant number of nanoparticles, particularly iron oxides, gold, carbon-based and silica, has recently been proposed with designs that can be used for medical applications.

9.2. Combination Therapies

Section 9.2. is devoted to Combination Therapies. Sub-sections are: 9.2.1. Combining Optical and Radiotherapies, 9.2.2. Dual-Drug Delivery, and 9.2.3. Photo-Immunotherapy Combined with Radiotherapy.

9.3. Personalized Medicine Approaches

The multifaceted role of Quantum dots (QDs) in breast cancer research has shifted the paradigm of scientific inquiry. Continuous advancements underscore the marked importance of QDs in diagnostics, targeted therapy, and drug delivery systems. A synthesis of evidence is provided, highlighting significant headway in QD research that is poised to change the current understanding and management of breast cancer. A comprehensive overview is given of the collective efforts across the disciplines of physics, chemistry, biology, and medicine that have pushed the boundaries of current knowledge. Significant achievements in cautiously establishing novel imaging techniques that show the potential for early cancer detection are reviewed. Furthermore, an insight into the current understanding of QD interactions with cancer cells is provided in the hopes of elucidating their ability to induce cytotoxicity and potentially facilitate gene therapy [9]. Finally, a critical analysis of collective outcomes is provided in the hope of addressing and overcoming the challenges currently faced by this exciting new field of breast

cancer research. The multifaceted role of QDs in cancer research is presented with possible future research directions opportunities and potential pitfalls also discussed. Scientific and clinical advances inherently depend on a synergistic, transdisciplinary approach to research characterized by collective efforts in physical, biological, pharmaceutical, and medical sciences. Such an unprecedented breadth and depth of research has motivated this critical review, which examines recent advances and existing challenges inhibiting the translation of QDs from laboratories to clinics.

10. Case Studies

1. Description

In this section, a physiologically based pharmacokinetic model is developed and applied to predict the behavior of these nanoparticles in vivo, thereby aiding in the optimization of quantum dot-based medical physics treatment for inflammatory breast cancer as a case. To test the validity and utility of the model, Cd-based carbon dots with anti-PDL1 antibodies are used for targeted theranostic applications in triple-negative breast cancer. In both in vitro and in vivo applications, these carbon dots have been reported to significantly enhance the effect of the anti-PDL1 antibody by localizing in TDL and delivering anti-PDL1 with higher efficacy; hence, they were able to promote apoptosis and reduce the viability of the CD8+ population and hence the whole tumor significantly more than that of anti-PDL1 treatment alone [9]. 10-15 invisible ns-laser pulses are delivered to a 2.5 mm watery volume, resulting in microbubble formation. The subsequent expansion and collapse of the micrometer size bubbles excite shock waves which promotes the fragmentations of solid materials in solution or in living beings.

2. Pulsed Transient Electromagnetic Field

The computer simulation is performed to analyze the electromagnetic field which consists of the coaxial transmission line type electrode side grounded and the plate electrode. The field has various field dynamics as functions of the radius and angle at the distance from the electrode surfaces. For the transient field, the induced electric field from the external applied magnetic field which is the reflection of the field-dependent current flow is calculated in depends on the time. Effects of the nano-second pulse EMF are investigated with the L and L/P block of the rat at the right back leg with the concentration of the QDs. Both lead to the maximum local temperature. Micrometer size indentation is formed at the edge of the gap between the CdTe concave shaped part and the skull.

10.1. Case Study 1: Breast Cancer

Breast cancer is the most common cancer in women worldwide and remains the second most common cause of cancer death in the United States. Every day, approximately 1900 women are diagnosed with breast cancer and 500 of them will die from this disease. Therefore, breast cancer research has attracted significant interest, with developing novel and advanced technologies aiming to improve early detection, imaging, diagnosis, delivery, and treatment of breast cancer. As breast cancer is one of the primary health concerns, it allows targeted theranostic applications and diagnosis through imaging technologies, specially in the early stages. In recent years, Quantum Dot nanoparticles have become a new frontier in scientific research, especially in materials science and medical physics; QDs have potential uses, such as amplified detection in biological systems, targeted drug delivery, and targeted cancer therapy. Based on their size-tolerant light emission properties, super sensitivity, and wide excitation, QD-based nanoparticles have been used as theranostic agents and have become potential candidates for targeted cancer diagnosis and treatment.

Prior to the experimental design of the quantum dot-based nanoparticles in targeted breast cancer therapy, the physiologically based pharmacokinetic modeling of the nanoparticles mechanism was developed and validated. QD sensors for the early detection of breast cancer are compared with other conventional breast cancer detection methods, including annual mammography, self-

examination, and ultrasound imaging. Furthermore, the QD distribution and clearance kinetics in different organs of mice are studied and the feasibility of spatial frequency-domain imaging to quantitatively detect fluorescent QD agents in different tissue layers is presented. Simulations based on both 2D and 3D geometries are conducted to understand the distribution of QD agents in in-vivo tissues. An optimal frequency range for SFDI detection depth in biological tissues is obtained by Monte Carlo photon migration simulations using absorption and reduced scattering coefficients. The developed PBPK model can be potentially used to design QD-based nanoparticles for tumor delivery and minimized exposure to other healthy tissues in physiologically based optimization.

10.2. Case Study 2: Lung Cancer

Lung cancer, NSCLC, is one of the most prevalent diseases and causes of death worldwide, and it is considered very aggressive, with high mortality and short survival. Tumorigenesis is a multi-step process that includes mutations and alterations in gene expression profile. A common alteration is protein expression change, inducing sequential upregulation and downregulation in a set of proteins. Thus to control the cell's quantity and quality, two major protein degradation pathways evolved in eukaryotic cells, the ATP-dependent ubiquitin-proteasome pathway (UPP) and the lysosomal pathway. The complement system, as a part of the innate immune system, could protect the apoptosis-resistant cancer cells from the complement-mediated cytotoxicity. CD59 is a potent inhibitor of the terminal pathway by inhibiting the polymerization of the complement molecules C9, forming the membrane attack complex [27]. Since this particle can control the cell's quality and quantity by inhibiting the reverse degradation pathways, it will be safer to be selected for cancer treatment.

10.3. Case Study 3: Leukemia

Quantum dots are highly fluorescent semiconductor nanoparticles that have been developed for many biotechnology applications. Their routine application in vitro includes cellular image, sensing and drug delivery, but their utility in vivo is still in its infancy because the exact behavior and resultant toxicological burden is not fully understood. A physiologically based pharmacokinetic model was developed in order to predict the behavior of these QDs in vivo during and after a short-term intravenous administration. Such predictions are useful for the design of QDs with toxicological and biological concerns minimized and for clinical applications where the safe administration of predetermined doses is important. Moreover, this model serves as a platform from which other similar studies can be conducted with different QDs using a minimal number of in vivo experiments. The model was applied to two experimental conditions – the direct intravital laser scanning microscopic observation in the mouse ear chamber and time-resolved in vivo fluorescence detection. Improved signal processing of non-invasively observed fluorescence allowed us to quantify the fluorescence kinetics in terms of the model-extracted parameters. Taking into account the same structure and window view geometry, both methods provided a similar temporal distribution of QD concentration in the vasculature.

This work confirms the practical predictive ability of the model against experimental findings. This model can be expanded to consider other modes and conditions of QD administration such as oral consumptions, inhalation or other means of instillation. Possible alteration of the QD applications can be investigated such as surface structure modification, changing the QD composition material or using them in different nanocomposite systems. For all these applications, the designed model can be used to investigate the redistribution of QDs in the organism using a minimal number of in vivo experiments.

11. Ethical Considerations

Please consult journal for summary and analysis of related ethical considerations.

11.1. Patient Consent

Consent should be obtained from all applicable patients by draft text or any accompanying image and videos. Patient consent will be staged later in the submission process. Shortly before a manuscript is accepted for publication the author will be provided with standard Consent Form and will be asked to obtain written consent from the patients. All consents must be available upon request by the Editorial Office. The safety of the patients is paramount, and it is important to ensure that no individual can be identified from the draft text or any associated material. It is the responsibility of each author to ensure that the draft text is free from anything that might be construed as a breach of patient confidentiality. This includes, but is not limited to, the clinical history, examination data, details of investigations, and photographs. Scans will be provided later if any of the text is clearly relating to an individual patient.

11.2. Equity in Access

Almost 10 million people die annually as a result of cancer, and the number of new cases is projected to increase by 70% in the next two decades. Many approaches are being used in the treatment and diagnosis of tumors, but many cancers are still discovered too late for effective therapy. However, the most successful method in combating cancer is still early diagnosis, when cancer is localized and the patient is not showing any other symptoms.

Quantum dots made of metals or semiconductors such as cadmium, selenide, and tellurium, with a diameter of only about 10 nanometers, have properties different from larger particles. Small size increases the ratio of the surface to volume, which causes quantum confinement, a material that requires a fundamentally different quantum mechanical treatment. The other unique property of these particles are the quantum dots, which can be adjusted to emit different colors.

These properties gave quantum dot researchers the opportunity to use them as a biosensor in biomedicine for the first time. Quantum dots that act as platforms with their optical and electrical properties are becoming increasingly important in imaging techniques for different cell types, studying molecular structures in biochemistry, and tracking cells labeled with them. Most biotelemetric studies on quantum dots focus on the immunodetection challenges facing the synthesis, the correct spectral selection, the surface coating and the detection sensitivity of the contaminants purified after the synthesis. The results of immunodiscumized quantum dots are generally positive. Immune-marked quantum dots can be manufactured that are more intense and are not made more intense by non-mapped quantum dots. The mapping rate for quantum dots is higher than that of enzymatic markers.

12. Regulatory Framework

Building and apply quality assurance (QA) protocols is a necessary component associated with the development of theranostic agents [9]. The purpose of the literature review presented here is to summarize the current state of QA protocols and outline emerging trends that future protocols might consider. Peer-reviewed journal articles, review papers, and information gathered from experts in the field of QA and nanoparticles were utilized to build a critical discussion on the viability of current and future QA protocols. In doing so, a comprehensive overview of current research practices can be developed. Topics discussed include the assessment of nanoparticle characteristics (size, shape, coating, solubility), the potential toxicity of nanoparticle constituents, biological effects and the influence of surface modifications to nanoparticles, in vivo properties, and autofluorescence.

Given the range of preclinical studies involving nanoparticles, it is important to produce high quality, relevant data. QA measures may be tailored to the specific needs of a particular study and the efficacy of QA protocols in improving data quality may be assessed. Successfully adopted QA protocols may also act as a reference for future studies and build capacity that would benefit integrated research and management of research sites. Conventional QA protocols have been established in radiation oncology, nuclear medicine, and recently in diagnostic

radiology. Conversely, the compilation of guidelines on medical physics applications of quantum dots in terms of QA metrics and methodology is currently less developed. With the ongoing rapid evolution of molecular imaging and targeted therapy, there is a recognized need to expand QA protocols to include emerging technologies. Specific QA challenges and common problems in research endpoints for molecular imaging and targeted therapy have been outlined. Intensified efforts to address these issues have been initiated.

12.1. FDA Guidelines

The US Food and Drug Administration (FDA) has recently issued guidance for industry describing the agency's current thinking on the marketing and regulation of investigational use of new drug (IND) and biologic (IND) products in the form of nanoparticles derived from or containing a solid core of 100 nanometers (nm) or less in diameter and intended for use in the diagnosis, monitoring, and treatment of cancer. The guidance does not apply to products composed of quantum dots and to products intended for non-medical uses, such as sunscreens or ink toners. Instead, this guidance applies to quantum dots and other nanoparticles used to transfer energy or generate radiation within a patient labeled as a drug or to detect cancer biomarkers composed of or coated with inorganic materials. The guidance differs for diagnostic use in managing individual patient treatments on a repeated basis and for nanoparticles intended for use as a single imaging scan for each suspected case of cancer [9].

12.2. International Regulations

Multifunctional quantum dot-based nanoparticles are emerging as promising cancer treatment options due to their excellent chemical and optical properties. They can become a crucial nanotechnology-based agent in the field of medical physics to treat the hardest to fight cancers. The current state of the art in MQDs is comprehensively reviewed, with an emphasis on their application in radio oncology. Bottlenecks surrounding their clinical translation and potential future research opportunities are also discussed [4]. The International Journal of Nanomedicine is granted in Nanomedicine as well as work on prevention and controlled drug release in a broad range of medical physics applications. Articles should contain sufficient information on experimental methodology. It is important in their full range of applications. The latest advances in nanomedicine are closely followed in the journal, with a view to promoting an active role in the exploitation of new, multidisciplinary techniques and approaches. Shall only consider manuscript in the context of invited review as the extremely high volume of submissions on general nanomedicine topics worthy of review.

13. Commercialization of Quantum Dot Technologies

Quantum dots (QDs) are fluorescent nanometer-sized crystals and are commonly defined as QDs with a dimension between 3 and 6 nm representing 20-100 atoms. They can be excited by UV light or a high-energy photon source and emit a larger wavelength of visible light. Many different types of QDs have been used experimentally since their discovery in nanoparticles (NPs) for cancer theranostics and drug delivery applications. These NPs can be loaded with cytotoxic drugs or imaging agents and conjugated with cancer-specific macromolecules such as monoclonal antibodies or specific peptides for efficient targeted drug delivery and therapy. It has been shown that QD-based NPs have unique features for cancer bio-imaging and in vivo studies. In vitro studies have shown the growth inhibition of MDA-MB-231 and MCF-7 human breast cancer cells using folate-conjugated QD-based NPs combined therapy [9]. Among the various imaging modalities, fluorescence-based bioimaging has gained significant attention for its capacity of accurate, high-throughput, and in vivo imaging capability. In tumor anatomy, the structural layout and the dependence of a solid tumor on host capillary networks are crucial physiological features exploited in treatment therapy or therapeutic imagery for achieving more precise tumor targeting by preventing distribution throughout the body of administered CD-based pharmaceuticals. Continuous advance in the field of cancer research has significantly helped in the early detection and therapy at the molecular level. CD-based nanotheranostics

represents the novel cancer therapy area, and only limited studies have been undertaken in pharmaceutical departments worldwide. Furthermore, integration of QD-based NPs with photodynamic therapy (PDT) has been explored in cancer research, but no such attempt integrating PDT with QD for imaging of nanoparticles in tumor vessels has been reported that the author are familiar. The most striking feature of the new nanocomposite is the visualization of CD-based NPs in the tumor vasculature of a live mouse at 48 hours after the administration of composite drugs.

14. Conclusion

A new era in cancer therapy using nanoparticles has opened thanks to advances in medical physics. Quantum dot (QD)-based nanoparticles that can be specifically targeted to bind to cancerous tissues have been developed. These nanoparticles take advantage of a property of the vascular system near tumors known as the Enhanced Permeability and Retention effect (EPR effect), which allows nanoparticles to preferentially accumulate in tumors. By modifying the surface of such nanoparticles with a polymer carrying succession of a cancer-specific ligand and a pH-sensitive, cell penetrating peptide, selective binding to cancerous tissues, followed by internalization should be possible. Combination use with various anticancer drugs and X-ray irradiation has allowed the temperature of cancerous tissues to be locally elevated to a temperature of about 41°C, which is sufficiently to damage the cancerous tissue. Photothermal therapy is a clinical treatment that employs near infra-red (NIR) light. Cancerous tissue containing nanoparticles will locally absorb NIR light and be turned into heat, allowing the tumor to be killed. In a study on mice using QD-based particles, the temperature of a tumor was locally elevated to about 42°C by 808 nm laser irradiation, causing the tumor volume to decrease.

References:

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