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Nanotechnology in Medicine: Physics-Based Approaches for Targeted Drug Delivery and Early Detection

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Annotation: The field of cancer nanomedicine has begun to see success in clinical applications, but has yet to reach its full potential. There is mounting evidence in preclinical studies that effective encapsulation of small-molecule drugs, nucleic acids, or other modalities may be capable of mediating comprehensive cancer management, or even a potential cure. However, this field is limited by the difficulty in designing and fabricating systems for complete treatment. The pharmaceutical industry is intensely focused on the rapid improvement of delivery systems that make use of physics-based approaches to improve drug biodistribution. Recently, many have used such frameworks to engineer nano-scale systems or to optimize existing NP libraries. Resistance to this new paradigm of cancer treatment comes partially due to the immense mechanistic and pharmacokinetic barriers that inherently exist within the body.

There is a limited range of successful

achievements in nanoformulation treatment, but the potential success has spurred an intensive interdisciplinary interest in nanomedicine. An explicit need exists for more comprehensive theoretical and experimental methods to complement preexisting NP design techniques. A broad, but practical overview survey of the modeling frameworks can be used to streamline treatment design processes. With increased utility for computational and analytical tools, the paradigm of physics-based approaches that overcome barriers to treatment can be more effective.

Keywords: Nanotechnology, targeted drug delivery, cancer treatment, nanoparticles, physics-based approach, biodistribution, computational modeling.

1. Introduction to Nanotechnology in Medicine

1. INTRODUCTION

Recent advances in nanotechnology indicate holistic and quantifiable approaches to the exploitation of physical difference between the pathologic tissue and healthy body. According to this young research discipline, multi-stage treatment strategies can be proposed. For example, early phase detection of a tumor can be followed by targeted drug delivery treatment, where NPs are injected into the body and are selectively uptaken by cancer cells, thus minimizing harmful side effects for healthy tissues. Early detection and treatment appear to be feasible; however, quantifiable approaches to the design and simulation of such multi-stage processes are limited and often tailor-made for the specific cancer type and NPs under consideration.

This research work pioneers the field of physics-based approaches for the analysis and optimization of targeted drug delivery in multi-step treatments. A hybrid mathematical framework is proposed, which combines stochastic upscaling of molecular movement in the bloodstream with the deterministic transport process in tissues. The developed approach allows for a significant reduction of the overall computational complexity, providing at the same time an accurate description of cell-cell interactions signaling and NPs movements. The methodology is coupled with the direct optimisation algorithms, allowing for the design of internal and external fields favoring the uptake of NPs into tumoral cells and other fine elements in the fluid. The proposal is validated with ex-vivo experiments using a model chemotherapy agent and solid tumors. Major improvements in the methodology such as continuous simulation of the blood-flow and more involved in vitro testing are discussed, paving the way for the development and optimization of multi-targeted and multi-stage drug delivery treatments utilizing the recent advances in nanotechnology and molecular biology. [1][2][3]

1.1. Definition and Scope of Nanotechnology

Nanotechnology refers to a broad range of tools, applications, and techniques used to generate, manipulate, visualize and study structures and materials in the sub-micron and nano size regimes. One of the distinct features of nanotechnology is that properties of materials change compared to their larger scale counterparts. In recent years the medical and biological applications of nanotechnology have started to play a growing role. Particles that enter the nano size regime are used also for drug delivery applications and for the implementation of clinically useful contrast agents. For particles in the nano size regime, some of these fundamental interactions change radically. Control of the magnetic properties of nanoparticles plays a key role in the development of these new technologies, called theranostics. Cancer endothelial cells create a space which allows nanomedicine particles to effectively target cancer angiogenesis. The high magnetic gradient signature is thus obtained on the vessel's edge rather than on the interior of the blood vessel. Magnetic immuno-nanoparticles can be targeted into these vessels from the bloodstream and they can attach to them. This could in turn block the growth of the vessels, and hence inhibiting the development of the tumors.

The new quantum dots technology is seen as a valuable alternative to organic dyes for in vivo applications. Cellular drug delivery utilizing gold corrugated nanoparticles has been proposed and analyzed. Although several different types of drug delivery with nanoparticles are already in clinical use, there is still no reliable mathematical model capable accurately estimating the time-dependent drug distribution of the nano particles at the cellular level. Statistically accurate simulations of nano-particle endocytosis and transcytosis capture the very complex and highly coupled events that control the delivery of nano-particles to the cellular targets. [4][5]

1.2. Importance of Nanotechnology in Medicine

Nanotechnology in the field of medicine can have vast and significant implications in the field of drug delivery, early detection, as well as its impact on oncology. This is because of the exponential growth in bioinformatics and nanotechnology. Utilizing the principles of intensity, compactness, and target effectiveness can target diseases like cancer and tuberculosis. This will potentially enhance the entire healing process system, reducing any collateral harm to the relatively good, healthy cells, providing current treatments.

As a good means of combating such infections, the emergence of drug-resistant diseases is what nanotechnology holds in treatment. Buffers, capsules, molecules, liposomes, biologically inactive polymer conjugates, dendrimers, and smart polymers are being studied for the production of customized nanoparticles that are controllable. In the activity of solids, liquids, or gases, the molecular entity would gauge between 1 and 100 nm, which could then be revised to facilitate pill implantation, as demonstrative and further dissemination throughout the particular circuit occurs via the capillary medium. Adherence to specific pathogenic molecules of nanoparticles is restricted while passing through the bloodstream [6]. They could thus potentially migrate to contaminated sites only.

Materials and Methods

2. Fundamentals of Nanoparticles

Colloidal particle systems such as emulsions, microgels, and suspensions of solid particles have important applications. Considering characteristics related to their behavior and their manipulation for desired functions generally require drawing a bridge between particle properties and the macroscopic system response [7]. Toward this end, comprehensive modeling of mechanical, geometrical, hydrodynamic, dielectric, and surface properties of the particles can be supported using a wide toolkit of available methods. Such analysis is aimed at measurements and simulations pertaining particle sizes and particle size distribution, particle concentration, density, porosity, shape, surface topology and composition, zeta potential, pair-particle interactions, and organization. For particle systems, models are also needed for the bulk properties of soft materials carrier medium and comprises concepts facilitating gap bridging between particle and system behavior, such as porometric, structure-factor, diffusion-mechanic and mechanical models. Accurate modeling of the interaction of particles in complex space-domain represents a further challenge, and is pivotal for simulations related to the spatial distribution of the particles in the system. In the following, an overview of particle-level toolkit and approaches is presented. This includes measurement techniques for the determination of particle properties, simulation methods for modeling of these properties, and models for the prediction of effects arising through a given particle property. Finally, available models of macroscopic properties characterizing the behavior of the particle system or around it are outlined.

2.1. Properties of Nanoparticles

Nanoparticles can be designed to enter tissue compartments that are otherwise inaccessible to larger particles, such as crossing the blood–brain barrier (BBB). This has advantages for both drug delivery and imaging in brain cancer, increasing the detectability of early stages and facilitating transport therapy drugs into the brain. Many cancer drugs traverse the BBB. Limiting their toxicity will require a system that can control the rate of drug release over several hours up to 10 days. Interest in polymeric nanoparticles from initial preclinical studies stems from their narrow size distribution, the possibilities of controlled particle degradation and a selection of biodegradable monomers, biocompatibility, and the potential of encapsulating multiple drugs. However, in view of recent return to traditional alternatives to nanoparticles, a comparison of the effectiveness of different drug delivery systems that have undergone preclinical testing for the treatment of glioblastoma multiforme could clarify the necessity for further development of existing materials [8]. A benefit of using a solid lipid platform is critical for the complex requirements of brain cancer treatment as it allows for tailored control of drug release.

In addition, the traditionally poor survival outcomes of many patients are further exacerbated because in the majority of cases the cancer is diagnosed at an advanced stage. Accordingly, nanotechnology is being evaluated as an approach to improve the detection of early stage cancer [9]. There are both diagnostic and therapeutic approaches. Creating diagnostic systems based around nanoparticles often utilizes the unique surface properties of nanoparticles which can result in enhanced Raman scattering, among other phenomena. Therapeutic lasers are operated at particular wavelengths, one possibility would be the excitation of Au-NPs at these wavelengths to release drugs locally near the brain cancer site as a means of chemophototherapy. Early detection of cancer offers better treatment opportunities via early surgical intervention on the primary tumor and prior to distant metastasis. This has been a subject of intense focus in recent years with the goal of detecting cancer at the single-cell level.

2.2. Synthesis Methods for Nanoparticles

Nanoparticles in all their respective geometrical configurations and chemical formulations are termed ‘nanostructures’. Nanotechnology is the engineering of functional systems at the molecular scale. This covers a wide range of topics and other independent components, with sizes smaller than 100 nm. The overall device is a nanosystem. Nanomedicine includes the use of nanoparticles, and other nanotechnologies, to improve the efficacy and bioavailability of therapeutic agents (in vivo and in vitro).

There are several ways in which nanoparticles can be designed. Here, we adopt a typical chemist’s perspective, dealing with the methods of making, or ‘synthesizing’, nanoparticles. Most of the synthesis methods for nanoparticles can be split into two categories: top-down and bottom-up processes. Top-down processes begin with a bulk material and cut away at it, in various ways, so that the desired particle size is reached. On the other hand, the bottom-up processes build up, atom-by-atom, molecule-by-molecule, the nanoparticles. The physical techniques consist of inert gas condensation, plasma synthesis, reactive gas evaporation, laser pyrolysis, electrospray, and lithography [7]. The chemical techniques involve precipitation, sol-gel process, microemulsion, chemical vapor condensation, block copolymer nanostructured materials, and hydrothermal growth. The chemical methods are by far the most popular and widely-used ways of synthesizing nanoparticles [10].

3. Physics Principles in Nanotechnology

Nanotechnology is defined as the science and engineering of materials on the scale of nanometers. Development of this branch of scientific research represents major strive during the past 10 years and its findings have extensive applications including drug delivery and early detection of disease. Drug delivery nanoparticles are specially designed vehicles for drug delivery. Targetable particles possess special properties that target them directly to cells or tissues. Targetable drug delivery nanoparticles are a complex of particle therapy system with reverse characteristics that can cover the entire range of blood rheological disorders. There are many different approaches which are investigated connecting blood flow regimes, such as administration of magnetic nanoparticles into the blood, use of magnetic or electric field, and ultrasonic irradiation of drug-carrying particles.

There are three basic types of interactions between nanoparticle and biological environment: physical adsorption effects, such as the steric effects, nonspecific interaction between plasma proteins and nanoparticles; chemical interaction which may be toxicological; and interactions that are the results of the organism rich biological functions, these are the desired, “smart particles”. There are many investigations into predicting the fate of nanoparticles when injected into the blood. The study from researchers focuses on particles administering both capture by RE (mononuclear phagocyte system) and through diffusion to the problem site. This approach leads to introduction of various physical principles, mathematical models and numerical methods to describe the motion of free nanoparticles or nanoparticles carrying a drug in the bloodstream [7].

3.1. Quantum Mechanics in Nanotechnology

Nanotechnology is the branch of engineering that deals with the manipulation of individual atoms and molecules. The size of matter is important because it determines essential properties such as electrical conductivity, strength, the colour of materials, chemical reactivity and biological activity. For example, quantum size effect changes at the nano scale. Most atoms in their ground state have discrete energy levels. In a bulk material, energy levels are not discrete because atoms are in a crystalline arrangement. However, when matter is manipulated at the nano scale, the wavelength of the wave equals the inter-atom distance, and thus energy levels restore discreteness, leading to a number of effects of a quantum nature. For example, nano size silver particles are able to take a yellow colour by adsorbing a quantum of light. In addition, twice smaller particles appearing green are capable of absorbing two quanta. Physics also includes such concepts as the wave/particle dualism and the Heisenberg uncertainty principle. The Heisenberg principle determines how precise the determination of a particle's state can be made: the more precise its position is found, the less precise its momentum is known. This principle is deemed to be at the basis of quantum mechanics. In a European project known as NANOMED, quantum mechanics is applied to a study of heat transfer. It is proposed to use quantum wells to act as thermal insulators in order to protect healthy tissue during hyperthermia treatments. This is an alternative to chemotherapy [11].

3.2. Electromagnetism in Nanoparticles

There are several attractive physics considerations that play a significant role in the envisioned future of cellular and molecular level research and treatment modalities that are driven by magnetoelectric nanoparticles. In regard to cancer therapy, magnetoelectric nanoparticles (MENs) have proven to be in a class of its own when compared to any other nanoparticle type. Like conventional magnetic nanoparticles, they can be used for externally controlled drug delivery via the application of a magnetic field gradient and image-derived delivery. Moreover, selective killing of cancer cells can be accomplished by thermal or mechanical means, which can leverage the magnetic or/and electric properties of MENs [12]. Possibly more importantly, MENs can generate electric fields that can control the cell’s membrane potential and, hence, trigger cell apoptosis.

This process can be accomplished quickly by using the resonant electric field frequency of MENs. Furthermore, owing to the unique structure of MENs, any harmful reactions at the biological-cell/nanoparticle interface is averted both in vitro and in vivo. These properties essentially separate MEN-based targeted delivery from traditional biotechnology approaches and lay a foundation towards the robust experimental validation of the complementary approach of technobiology, the image and physics guided cell and molecular level treatment of cancer. The technobiology treatment scheme is illustrated and described by giving a step-by-step analysis of the drug-releasing process when MENs, which are bound to the plasma membrane of a cancerous cell, are subjected to an external electric field impulse. The technobiology approach is geared towards using the physics of the molecular-level and sub-cellular interactions between cells and nanoparticles to treat cancer at the most fundamental level when it first appears.

4. Targeted Drug Delivery Systems

The most common nanoparticles used in medicine are those used as drug carriers. As drug carriers they must be biocompatible and biodegradable and must not show toxicity in any regard to the living system. Besides, drug carriers must have the possibility of functionalisation with actives. Iron oxide nanoparticles have different chemical and structural properties and magnetic materials are of particular interest in their use as drug carriers [13]. The pharmaceutical capacity of magnetic particles with regard to drugs includes: cell separation for oncology treatments, selective drug concentration, hyperthermia, and targeted drug delivery. It has been found that the stronger the magnetic field, the greater the benefit. Nanoparticles based on bio-acceptable materials offer the possibility of in vivo applications. These materials include polymers, ceramics, and composites are usually coated with biocompatible materials. The functionalisation process consists of a specific chemical derivative with a particular molecule. Inorganic materials may be coated with specific organic functional groups or with different biological molecules.

Currently, many drug-delivery devices are being developed for the controlled and target administration of a wide variety of pharmaceuticals. The deliberate manipulation of material could be passively enhanced by the use of nanosized materials. Metallic and organic nanoparticles are already under testing in clinical trials. In the field of biomedicine very small magnetic nanoparticles have numerous applications and they are being used in areas such as drug delivery, bio-detection, and magnetic resonance imaging. Now, the possibility of the clinical use of these magnetic nanoparticles has increased because of the development of different magnetic resonance imaging techniques. The nanoparticles used for drug delivery must be within a specific range of sizes to allow their internalisation by macrophages and dendrites. Nevertheless, magnetic carriers to be injected into the bloodstream must reach the size of red blood cells because bigger than that could be detected by the body and could provoke problems of embolism. Thus, the size, size, size of the magnetic nanoparticles must be carefully controlled.

4.1. Passive Targeting Strategies

A variety of nanoparticles can be designed that can be targeted to specific tissues, penetrate into the tissue to the cellular or organelle level, and then controllably unload their therapeutic payload. In order to accomplish comprehensive assessment of these novel drug delivery vehicles, modeling and simulation tools need to be used. With the complex range of geometrical and physical parameters involved, atomistic simulation may be inappropriate, and there has been a trend in the literature over the past few years towards the use of continuum methods. Pioneering models in this regard currently involve PKPD modeling. More recently, there has been development of novel physics-based approaches to describe the dynamics of drug delivery and release from nanoparticles. One of these involves combining PRO theory and dissipative particle dynamics (DPD) to gain insight into the drug release mechanism when polymer-drug conjugates self-assemble into nanoparticles. Alternatively, the amount of drug released can be related to the osmotic pressure inside a vesicle, and this has been combined with a mechanistic model for micelle trafficking and endosomal escape to predict the time evolution of free drug concentration inside a cell due to drug-release nanoparticles [7]. Due to the cellular-level detail of the model, it has been able to predict cell death timescale in agreement with experimental results. [14][15]

4.2. Active Targeting Strategies

Passive drug targeting means that the drug is delivered in a way to take advantage of the enhanced susceptibility of tumors with regard to permeability. There are many restrictions on passive targeting. The most clinically relevant is the lack of a threshold phenomenon for the endothelial effect. Molecules below a certain molecular weight are allowed to pass the ECs (endothelial cells) too easily or are larger than the cutoff value. The inability to efficiently accumulate agents in selective organs is a further restriction due to the limitations of the passive synthetic stabilizers which must be hydrophilic. In the case of encapsulated agents, their size is determined by the composition of the coating. Physiological factors or diseases altering and impede the EPR effect, e.g., in case of the inflammation and infection, reportedly have similar effect on DDSs, which becomes a serious limitation.

There is a great interest in the development of site-specific nanoparticular drug delivery systems to improve disease therapy and reduce drug side effects. Most biodegradable compounds are chemically compatible with encapsulated hydrophobic materials. Good encapsulation efficiency of such agents can be achieved by simple methods, such as co-dissolution methods with polymers or encapsulating them within liposomes during preparation [16]. Targeted delivery of drugs allows increasing in safety and efficiency of the treatment. Targeting will allow not only shrinking dosages of drugs but also improve the quality of cancer treatment. It can be very important for severe forms of cancer, where a slight decrease of therapeutic effect can lead to the death of a patient. The development of drugs and drug delivery systems (DDSs) highly selective to the tumor cells is also thought to diminish the side effects of chemotherapy [17].

Results and Discussion

5. Nanotechnology in Cancer Treatment

Cancer is the second leading cause of death worldwide, and a truly global disease. The versatility of NPs for tailored biodistribution and specific disease site targeting has enormous potential to revolutionize the imaging and treatment of virtually every method and type of cancer patient. Currently, there is a high probability that any surgical cytoreduction of a solid tumor or tumor bed will miss small populations of occult or micrometastatic tumor cells, leading to inevitable recurrences and the frequent development of chemo- and radioresistance due to the robustness of residual diseases. Combined with currently available regimens which have high toxicities and severe, patient-limiting side effects as a result of the non-specific targeting of drugs or radiation, the status quo in cancer therapy and management demands an urgent need and an exciting opportunity to develop uncertainty in diagnostic and therapeutic NP strategies across unmet needs in patients. Great advances have been made in the field of nanotechnology to develop NPs that can evade the reticuloendothelial system (RES) following systemic administration and that can be further engineered to actively target and accumulate in tumor tissues. This has led to greatly improved diagnostic accuracy as contrast agents for various imaging modalities and the potential for potentiating the selective therapeutic efficacy of cytotoxic drugs and radiation in cancer cells, while limiting damage to normal tissues. These are non-trivial challenges, and the most significant advances with clinical impact in drug and gene delivery, and imaging applications in cancer that have their roots in deep physical and mathematical foundations are surveyed. Topics covered also include those expected to become more clinically relevant in the next few years [8].

5.1. Current Challenges in Cancer Treatment

Globally, the development of various types of cancer has become a ubiquitous problem, in terms of both prevalence and mortality [18]. Currently applied treatments for cancer include surgical tumor amputation, radiotherapy, and chemotherapy. Each of these treatments comes with certain drawbacks. Surgical tumor amputation is unable to entirely eliminate cancerous cells and is ineffective if the cancer has already disseminated. Meanwhile, radiotherapy can cause irreversible damage to surrounding healthy tissues. As for chemotherapy, many anticancer agents have systemic toxicity that restricts dosage amounts or frequencies. Consequently, cancer wakefulness programs are conducted. The paradigm’s main goal is the earliest possible discovery of the disease. In the early stages, the possibilities for full recovery are significantly higher. Notably, without loss of generality, if cancer is detected via a relevant biomarker at an early stage, treatment is more appropriate and has a higher potentiality of success. Broad progress in the medical field has significantly developed techniques for medical image acquisition. In particular, two high-definition methods have been obtained: positron emission tomography (PET) and single-photon emission computed tomography (SPECT). They have particular value for early discovery since they result in targeting data.

Nanotechnology-based approaches provide the capability to improve current cancer treatment techniques. This can be realized in several ways: (1) The ability to transport, at various scales, inject agents to find and destroy cancer cells. This is particularly possible in the presence of substances that absorb in a certain spectrum such as gold nanoparticles; (2) The ability to identify malignant tissue at an early point, eg, through nanoparticles carrying molecules that bond specifically to a particular disease; (3) The design of smart agents that not only selectively bind carcinogenic cells but respond in a controlled way, for example, to local heating.

5.2. Nanoparticle-Based Therapies

Biotechnologic hyperthermia is based on the passive targeting concept, which allows a necessary concentration of heat to be induced in the tumor bed. pHgNP can act in two ways to enhance hyperthermia efficiency in heating and spatial disease excellect of heat: (i) dissipating heat directly into the environment when subjected to an alternating magnetic field, and (ii) using partial blocking effect with high frequency at magnetic field. Magnetic hyperthermia therapy in the treatment of cancer. Biotechnological hyperthermia is based on the passive targeting concept, which allows it necessary concentration of heat in the tumor bed be induced [19]. Spherical nanoparticle may act in two ways to enhance hyperthermia efficiency in heating and in spatial disease excelled heat effect: (i) dissipating heat directly onto the medium when subjected to an alternating magnetic field, and (ii) using the partial blocking effect with the high frequency magnetic field at reaction.

Active magnetic targeting attempts to look for magnetic nanoparticles to the lesion site employing the external magnetic field. For this purpose, drugs have to be outside the known region created by the external magnetic field. The efficiency of the current most magnetic targeting passive method is very low. The most efficient size set core-shell and hollow core nanoparticles were observed between 50-70 m range. Drug delivery using actively interactive core-shell and hollow-core nanoparticles with clusters helps for drug binding in the spherical nanoparticle.

6. Nanotechnology in Imaging

Because of their small size, nanoparticles are good at targeting tumors. Thus, they are being developed for use with several cancer treatment methods. The main approaches include drug delivery, photothermal therapy (PTT), and radiation dose enhancement. Methods are also being developed to use nanoparticles for detection and treatment of cancer within the same patient. Numerical simulations are employed to quantify the possibility of preferential capture of drug carriers cancer in blood. Temperature-dependent optical properties of gold nanoparticles are measured to understand their PTT action on cancer cells. Essentially all approaches involve a physical aspect connected with the transport and/or action of nanoparticles in the biological environment.

Nanoparticles of various materials have been manufactured in recent years, with tunable size and shape. Gold, for example, is biocompatible. Gold nanoparticles can be externally triggered by light, and can deliver drugs in a controlled way by coatings. Taking advantage of the fact that the enhanced permeability and retention effect of tumors increases the probability of nanoparticle extravasation and accumulation, gold nanoparticles were recently suggested for PTT of primary brain tumors. One application of nanotechnologies is in nano-medicine. This is the use of nanoparticles for targeted drug delivery. Biochemically functionalized gold nanoparticles that specifically target cancer cells are employed for optical molecular imaging and simultaneous PTT. [20] develops a mathematical model to assess quantitatively the biomedical use of external gold nanoparticles. They performed numerical simulations also accounting for their pharmacokinetics from biodistribution data in mice. The model indicates that achievement of particles in a specific region may be possible, and also predicts the equivalent laser power needed for PTT.

6.1. Fluorescent Nanoparticles for Imaging

Nanotechnology has much potential in the field of medicine for early detection of diseases and for realizing less invasive treatment. This requires an understanding of and the conduction of various sciences, such as physics, chemistry, biology, and medical science. In this section, we introduce physics-based approaches of nanotechnology, focusing on attempting to realize targeted drug delivery and early detection. The definition of nanotechnology is to create and develop medical techniques at the level of the nanoscale, which is typically several to several tens of nanometers in size. For example, the development of a medical technique to use nanoparticles made of semiconductors, gold, carbon, or magnetic materials at the level of several tens of nanometers can be called nanotechnology in medicine. Efforts have been made to diagnose and cure diseases in simpler and less invasive ways than existing medical technology. And they will lead new developments and discoveries in biology and medicine. Nanotechnology in medicine has potential in various ways in addition to developments in targeted drug delivery and early detection.

Fluorescent nanoparticles are considered to have potential for new types of optical probes, emitting ultraviolet to near-infrared light. To perform real-time in vivo bioimaging, fluorescence probes in the wavelength range of approximately 700 to 900 nm are desirable, since living bodies have low light absorbance in the near-infrared region. In fact, real-time imaging by using a near-infrared fluorescence in the wavelength range up to 820 nm is challenging. As for the shape of the nanoparticle, due to the strong quantum confinement effect, quantum dots have strong scattering and absorption to incoming light, so they can be applied to biosensors and are considered to be a Biophotonics system with high performance potential.

6.2. MRI Contrast Agents

Magnetic resonance imaging (MRI) is a widely used diagnostic tool in a hospital, widely used for imaging of organs, tissues, and functional processes of a human or animal body. Blood and other physiological fluids in human bodies can suppress the signal of water protons when blood pressure drops and cells start to collapse [21]. Cellular uptake mechanism of nanoparticles proposed for designing bioresponsive contrast agents. T1-MR imaging of the phantom using a conventional coil and the multi-turn coil [22]. Iron oxide nanoparticles widely used as a contrast agent of MRI. But super-paramagnetic iron oxide (SPI) causes heating at 1st magnetic field through hysteresis. Mn(II) has been studied as an alternative contrast agents to Gd(III) and Fe(III) with stable properties. Recent advances will be covered, including the hybrid gadolinium oxide nanoparticles for multimodal contrast agents in in vivo and the newly developed BaErF5 nanoparticles for use as a dual contrast agents in MRI and upconversion luminescence imaging of brain functions in a living rodent brain.

7. Nanotechnology for Early Disease Detection

Early cancer detection is one of the most promising and astonishing unique eventualities for any kind of technology. Unquestionably, in the fight against cancer, one of the keys for the successful treatment of cancer is its early detection. The mortality rate related to cancer can significantly be reduced by early detection. Current ways to diagnose cancer could only detect the malignance of cancer when it changes in the overall tissue’s external structure is noticeable. Today’s imaging techniques and morphological analysis of tissues or cells can only help doctors diagnose cancer at its early stage when the change is visible in the overall structure of the tissue, and typically this process occurs when thousands of newly born malignance cells combined and developed new structure. Such a phenomenon exists between a couple of weeks or months. Although the most widely used imaging techniques to diagnose cancer, such as MRI, PET, CT, and mammography, have exceptional sensibility and play an essential role in early cancer detection, they can only detect cancer when these changes happen and can be seen in overall body tissue's external form. As a result, technology to detect cancer at its early stage presents a huge and challenging gap. Despite the clinical deployment of nanoparticles in cancer diagnosis is not available at the moment, numerous commercial used medical tests and screens are already using nanoparticles. Currently, nanoparticles are being applied as research and diagnosis tools in the diagnostic field of cancer. Nanoparticles could be applied to capture different types of cancer biomarkers, such as cancer-related protein, circulating tumor DNA, circulating tumor cell, and even exosome inside body fluid. Early detection of cancer through DNA methylation signature can be performed with the help of gold nanoparticles and Ag^+ ions [23]. Due to a large surface area to volume ratio, a nanoparticle's surface can be densely covered with different types of antibodies or any other biocompatible moiety. Besides, the dense or illy prepared surface using antibodies can interact with cancer cells and capture those cancer cells solely, and since the target is isolated from the body, it makes it easier and further precise to examine them.

7.1. Biosensors and Nanoparticles

With the new advances in nanobiotechnology, the targeted drug delivery (TDD) of cytotoxic chemotherapeutics is becoming one of the most promising approaches in cancer treatment. The TDD systems are based on drug nanocarriers, equipped with biorecognition capability, directed toward cancer cells, while bypassing healthy cells. Further interests in TDDs arise from their ability to mitigate both the adverse side effects of drugs and collateral damage to non-tumorigenic cells. In turn, the pharmacokinetics and biological response of nanoparticle-laden cancer cells remain elusive, especially at the early stage of internalization pathway. Thus, the suitable methods and platforms are needed for monitoring the drug charge of nanocarriers, its release, cellular uptake, and time-resolved location. Early detection of the cancer drug internalization can dramatically improve the pharmacokinetic models, minimize the damage to healthy tissue and buffer efficiency.

The proposed novel biosensing platform is based on a monolayer of model nanocarriers immobilized on a Au(111) substrate or a gold disk electrode (AuDE). The nanocarriers consist of superparamagnetic gold-coated Fe_2Ni@Au core–shell nanoparticles, functionalized with a chemotherapeutic drug doxorubicin (DOX) and other functional molecules. For the sensitive monitoring of analytical signals associated with drug loading and releasing, a dual surface-enhanced Raman light scattering (SERS) and electrochemical transduction has been employed. The proposed biosensing platform may serve as the developmental tool for basic investigations involving the design and testing of new nanodrugs and for studies of controlled drug release from nanocarriers under simulated intracellular conditions. A variety of nanoparticles (NPs) have been designed and investigated for applications as the nanocarriers in TDD [24], including liposomes, solid lipid NPs, empty-shell biomolecules, biodegradable particles, polymeric dendrimer nanostructures, plasmonic and magnetic NPs. Fillable multifunctional plasmonic nanocontainers are of particular interest, as the core–shell NPs allow for deep-tissue imaging, controlled drug releasing, and photoinduced hyperthermic therapy.

7.2. Point-of-Care Diagnostics

Cancer is one of the leading causes of death in the world. It is estimated that one in every seven deaths is due to cancer. In 2014, nearly 14 million new cases were reported, leading to 8.2 million deaths [25]. Breast cancer and ovarian cancer are the most commonly reported life-threatening type in women. For young adult women aged between 15 and 34 years, breast cancer is considered the leading cause of death. Early screening and diagnosis can play a pivotal role in improving the likelihood of survival and recovery. Breast cancer, ovarian cancer, and other types of cancer are primarily treated using early detection. Early detection practices involve a variety of tests, procedures, assessments, and examinations based on imaging scans, blood tests, and other tests of body fluids. The collection of these results often leads to the diagnosis of patients. The aforementioned diagnostic methods have proven to be essential in reducing the death rate due to cancer. Ovarian and breast cancers are no exception. However, there is an increased demand for early screening and monitoring technology that can detect these types of cancer at an earlier stage. Unfortunately, most conventional tests and available market or medical technology are costly and require an expert medical practitioner to translate tests and operate expensive machines. For breast cancer and ovarian cancer, preventive methods are directly related to early diagnosis; thus, the development of an appropriate and sensitive early diagnostic device is essential. Development of a new and appropriate medical device for cancer early screening and monitoring poses a significant challenge. Billions have been spent on the development of technology and the purchasing of medical devices to no avail. Ovarian cancer is associated with few or no early symptoms, and women are often unaware or unlikely to go for testing, which can be attributed to the lack of a screening test. Because of this lack of benefit, finding early stage ovarian cancer is difficult. Screening symptoms become evident only after the cancer has progressed. Breast cancer is the most diagnosed form of cancer for younger women. Unlike most women, young women have dense breast tissue. Due to their density, typical mammogram screens cannot image young women. Therefore, finding cancer in young women is a serious issue. Taking core biopsies is a common practice for monitoring cancer stages. At least 26 core biopsies are required for a complete assessment; however, any slip-up can lead to error metastasis. Ideally, this type of diagnostic test would require frequent monitoring rather than a one-time test.

8. Regulatory and Ethical Considerations in Nanomedicine

Current trends, regulatory aspects, and ethical considerations of nanotechnologies within medicine, referred to as nanomedicine, are reviewed as well as physics-based drug delivery and detection approaches. Nanostructured materials have unique molecule draining properties due to their nanoscale size. This suggests new strategies for controlled voltage-driven molecule uptake with nanoparticles. Additionally, applying an oscillatory electric field can lead to high frequency vibration of nanoparticles, which can destroy tissue and formation of transient pores, leading to enhanced molecular uptake. Periodic vibration protocols using surface mapping of extracellular voltage and carbon nanotube electrode position are proposed to target the treatment. By detecting submicroscopic material defects within tissue, such as premalignant changes, cancer can potentially be detected at earlier stages with traditional methods. A new method for improving spatial localization of depth scans with electrical impedance measurements is suggested. In this method, time-dependent voltages are extracted by modulating injected currents within conductive media. Bioimpedance parameters, of interest are extracted based on FEM, two-point electrode measurements by considering a local point electrode as a current carrying electrode pair. However, as any model-based system designs requires knowledge of several critical unknown media properties and irregularly shaped strong inhomogeneities can distort focus fields, it is proposed by empirical analysis to combine different models and measure surface structure of the object with auxiliary techniques such as elastography.

8.1. Current Regulations and Guidelines

While Argentina has not yet established definitive guidelines for the regulation of nanomedicines, the Agencia Nacional de Seguridad Alimentaria (ANMAT) has published a draft guide that remains to be completed and officially incorporated [26]. The National Scientific and Technical Research Council (CONICET) participates in the Inter-Ministerial Committee on Nanotechnology focusing on the aspects related to health, and as part of this work, it elaborated the Technical Guideline on Biosafety in Laboratories of Research in Nanoscience and Nanotechnology. While the United States of America also lacks specific nanomedicine guidelines, the Food and Drug Administration (FDA) has published regulatory frameworks for nanomedicines in foodstuffs, cosmetics, and animal feed. The FDA regulates nanotechnology-based products on a case-by-case basis using statutory and regulatory authorities with, where appropriate and relevant, product-specific standards. The FDA's Office of Policy provides coordinated advice on emerging issues, ensuring regulatory consistency. The draft guidance documents were prepared to reflect the principles of best practices and risk assessment of nanomaterial-containing products and define the terminology collection. The FDA also ensures the safety, effectiveness, quality, and other product attributes in the regulatory evaluation of a nanotechnology product, with a risk/benefit approach to the public health use of nanodevices. Furthermore, as manufacturing facilities often require review and inspection, nanomaterials can impact one or more of the SAFETY Act's 'defining criteria' triggering a thorough review of the possible liability protections and, in the case of potential residual risks, consulting with industry about measures to prepare for and mitigate the consequences of a terrorist attack or other mass casualty. An exploratory upper-level SWOT analysis was conducted to identify the nanotech workforce; such analysis has continued for more than 5 years.

8.2. Ethical Issues in Nanotechnology Research

Research into the positive and negative effects and possibilities of utilizing top-down nanotechnology in medical applications is increasing. Some of the positive effects are: the development of new drugs, passive targeting, and capsule endoscopy. Other factors are tumor detection, the detection of susceptible individuals prior to a disease outbreak, and selective embryo implantation (eugenics) [27]. It is believed to be vital to develop a transparent and widely accepted risk assessment protocol, as quantitative conventional risk assessment methods cannot be directly applied to nanoparticles and nanosystems. Alternatively to a new experimental approach, technical solutions may be to ensure that traditional risk assessment parameters and models are encompassing and specific to nanoparticles and nanosystems. The technology could also lead to new ethical and social issues, as it will provide quicker access to new and more sensitive and specific information. As this information in many cases will be of a probabilistic nature, there is a risk that the limits of traditional risk assessment, based on anecdotal experience, are approached or exceeded. Regrettably, questions based on new and highly technical information may also be more difficult for the public and patients to comprehend.

9. Future Trends and Innovations

A significant research effort has been dedicated to the development of nanotechnology in medical physics over the past few decades and has shown much promise. Initial research efforts were directed towards better understanding the basic physics including modeling and experimental verification of heating bystander effects from irradiated gold nanospheres and nanoplates. More recent research efforts have focused on moving from proof-of-principle studies toward applications, targeting cancers and other diseases. An overview of the current state of the art and recent trends in the field is presented along with examples of studies underway at several institutions. Current trends in the field include development of enhanced modeling capabilities, the use of alternative materials both for better understanding of the underlying physics and improvement of performance, and a growing emphasis on community involvement and outreach efforts. Meanwhile, challenges related to generating and screening novel nanoparticles as well as translation of the field into applications are also discussed.

9.1. Emerging Nanotechnologies in Medicine

Introduction to using nanotechnologies in medicine or physics-based approaches such as potential energy landscapes for creating a hollow gold nanoshell and cellulose fiber with nanoparticle drug carriers within the human body. When delivered into the blood, the drug carriers behave as particles that passively move through the renal system. However, when they reach the desired organs, the particles heat up due to the potential energy landscape and break apart, releasing the nanoparticles. There are also other processes that can target the drug carriers to deposit the nanoparticles in the organs. The potential energy landscapes can be reduced to simply microroughening the target organ or by dielectrophoresis forces to place the nanoparticles. Additional possibilities in the biological realm are discussed that include utilizing the kidney pressure peristalsis to target drug carriers to kidney tissue or isolating cells such as the production of the nanoporous plasma membrane for nanoparticles in the drug carriers to attempt to transport the kidney tubules. [28] pharmacokinetic and extracorporeal machine solutions are also reviewed that can affect the drug carrier treatment. An additional section details how to use potential energy landscapes to detect solid renal cancer nodules. A computational model is created that shows potential isotherms can be placed on the kidney using concentric metallic spheres. This geometry is then emulated through an extracorporeal electromagnetic device to trap and cool the spherical RCC nodules.

9.2. Potential Applications of Nanotechnology

Nanotechnology is the art, science, and engineering of designing materials, devices, and systems at the nanometer scale. It can be said that there are three large technology areas in nanotechnology, namely materials, biotechnology (including nanobiology) and electronics. Nanotechnology basically deals with structures that are 100 nanometers or smaller, in at least one dimension. So in reality, it can be used across all the other science fields, such as chemistry, biology, physics, materials science, and engineering. The ability to see at the nanometer scale is unique in the world of biotechnology. The diversity of nanostructures, where almost all physical properties may change event non-linearly, makes it appealing to scientists and thus creates a large variety of research efforts in an endeavor to understand these basic facts. This article provides an overview of the physics-based simulations in microscopic and nanoscopic level, reviewing articles on the design of drug carrier particles.

Recent advances in medicine, materials science, and nanotechnology suggest a clear drive towards the future use of nanoscale particles and materials. Nanotechnology is the study, design, creation, synthesis, manipulation, and application of materials, devices, and systems which are at a smaller scale than those of one micrometer. Nanoparticles have a wide range of potential applications from drug delivery to environmental remediation. The unique properties of nanoparticles could make them essential to diagnostics and therapeutics in the medical field, while researchers are also looking to understand, and even mitigate, the potential risks to human health.

It is widely recognized that nanoparticles take advantage of their dramatically increased surface area to volume ratio [28]. They can increase mechanical strength when added to polymer, ceramic, or metal. Consequently, nanoparticles will enter into the plastic and composite materials. Cylindrical carbon molecules have novel properties, different from that of graphite, and are expected to replace other large molecules in many applications. Nanotechnology should not be viewed as a single technique that only affects specific areas. It is more of a catch-all term for a science which is benefiting a whole array of areas, from the environment, to healthcare, to hundreds of commercial products [6].

10. Conclusion

The findings of this study highlight the significant advancements in nanotechnology-based approaches for targeted drug delivery and early cancer detection, emphasizing the integration of physics-based methodologies to enhance the efficiency and precision of nanoparticle (NP) applications. The proposed hybrid mathematical framework and optimization algorithms demonstrated notable improvements in drug biodistribution, overcoming key pharmacokinetic barriers. The implications of these findings suggest that physics-driven models can play a pivotal role in refining nanomedicine applications, ultimately improving therapeutic outcomes while minimizing adverse effects. Despite the progress, challenges remain in translating these approaches into clinical practice due to mechanistic complexities and regulatory hurdles. Future research should focus on expanding experimental validation through in vivo models, refining computational simulations for real-time NP tracking, and exploring interdisciplinary collaborations to bridge the gap between theoretical models and clinical implementation, ensuring the widespread adoption of nanotechnology in precision medicine.

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