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REVIEW ARTICLE

Nanomedical Devices and Cancer Theranostics

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Abstract:

The current therapies against cancer showed limited success. Nanotechnology is a promising strategy for cancer tracking, diagnosis, and therapy. The hybrid nanotechnology assembled several materials in a multimodal system to develop multifunctional approaches to cancer treatment. The quantum dot and polymer are some of these hybrid nanoparticle platforms. The quantum dot hybrid system possesses photonic and magnetic properties, allowing photothermal therapy and live multimodal imaging of cancer. These quantum dots were used to convey medicines to cancer cells. Hybrid polymer nanoparticles were utilized for the systemic delivery of small interfering RNA to malignant tumors and metastasis. They allowed non-invasive imaging to track in real-time the biodistribution of small interfering RNA in the whole body. They offer an opportunity to treat cancers by specifically silencing target genes. This review highlights the major nanotechnology approaches to effectively treat cancer and metastasis.

Keywords: Nanotechnology, Nanoparticle, Cancer, Diagnosis, Therapy, Theranostic.

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1. INTRODUCTION

Cancer is one of the leading causes of death in the world. It is characterized by an uncontrolled cell proliferation within the body. The cells divide into infinity and lead to the formation of a primary tumor. Some cells of the primary tumor diffuse into the body and lead to the formation of secondary tumors called metastases. The cancer cell is characterized by its independence from the signals of cellular proliferation, to escape apoptosis, to proliferate to infinity, to become invasive and metastatic, and to induce angiogenesis (Fig. **1**). Cancers are linked to environmental and genetic factors. Three types of genes are responsible for cancerization, positive regulatory proto-oncogenes for normal cell proliferation, negative regulatory anti-oncogenes for cell proliferation and DNA repair genes [1 - 3].

The diagnosis of cancer can be made by biopsy, biological analysis, endoscopy, and medical imaging modalities such as Pet, CT, and MRI [4 - 20]. There are other options of therapies, as described in the references, such as immunotherapy and combination therapy [21 - 26]. Surgery and radiotherapy are curative treatments for localized tumors, they have undesirable effects. For metastatic tumors, chemotherapy is privileged, but lacks specificity and is associated with adverse side effects for patients. New targeted therapies or immunotherapies are more effective and less toxic, they are able to specifically recognize and treat cancer cells while preserving healthy cells and having fewer side effects [27 - 33]. Nanomedicine is the set of processes for creating and manipulating devices at the nano-meter scale. These devices could perform cellular detections and repairs in the human body at the molecular level. Conventional imaging detects cancer at about a cm^3 containing about a billion cancer cells, while nanotechnology devices have the ability to detect a single cancer cell. Through nanoparticles (NPs), nanotechnology is a promising strategy for the therapy and diagnosis of various diseases [34 - 45].

2. NANOTECHNOLOGY APPROACHES

Nanomedical devices are designed to perform various biomedical applications in disease sites. They can be introduced into the body and guided to cancer sites to diagnose,

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administer drugs, and perform surgery on an anatomical, cellular and molecular scale. Biochips NPs can take single-cell captures and perform analytical cell separations [46]. Nanotechnologies have theranostic applications, they have the ability to be used simultaneously for the diagnosis and targeted therapy of cancer [47, 48]. For the diagnostic function, nanotechnology has applications in non-invasive imaging, biocompatible NPs are used in tomography as imaging probes to measure and locate tumors [49]. For the therapeutic function, nanotechnologies are applied in chemotherapy, small interfering RNA (siRNA) therapy, photodynamic therapy, and photothermal therapy. Nanoparticles were labeled with specific nucleic acid barcodes, which by their sequencing, allowed to measure the systemic and *in vivo* biodistribution of NPs siRNA delivered to tissues [50] (Fig. **2**).

Nanomedicine through NPs offers better treatments than conventional cancer therapies. NPs have the ability to encapsulate, protect, and release targeted drugs by having better pharmacokinetics, circulation half-life, and bioavailability. The characteristics of NPs, such as size, shape, and surface, offer better biological interactions and stability over large pH and temperature ranges [51]. These platforms allow the selective distribution of drugs to tumor cells, reduce side effects, and avoid the body's defense mechanisms [52]. The effectiveness of protein-based drugs is limited by the formation of antibodies, the combination of these drug proteins with NPs allows to increase their tolerance by the body and restore their antitumor activity [53].

The effectiveness of tumor administration of nanomedicines depends on biological barriers in the spleen, lymph nodes, and liver [54]. The NPs cross these natural barriers and selectively target biomarkers overexpressed by cancer cells such as αvβ3 integrin and folate receptors [55]. Physiological barriers may hinder the administration of nanomedicines. The NPs at 5 nm are eliminated by the kidneys. The gap between normal endothelial cells is 10 to 50 nm. In cancer sites, the gap between endothelial cells varies from 200 to 1200 nm. NPs greater than 200 nm accumulate in the liver, spleen and bone marrow, where they are taken up by the reticuloendothelial system (RES) and degraded by monocytes and macrophages. NPs at 100 nm leave the systemic circulation through the effect of permeability and increased retention (EPR) and accumulate in cancerous areas [56 - 58]. The NPs are able to distinguish target cancer cells based on their receptors profile allowing selective therapy with fewer side effects [59]. Nanomaterials such as graphene and nanoclays are able to interact with the cell membrane and activate protein kinase. These nanosilicates can provide information on cell signaling involved in tumor growth useful for the development of medical treatments [60].

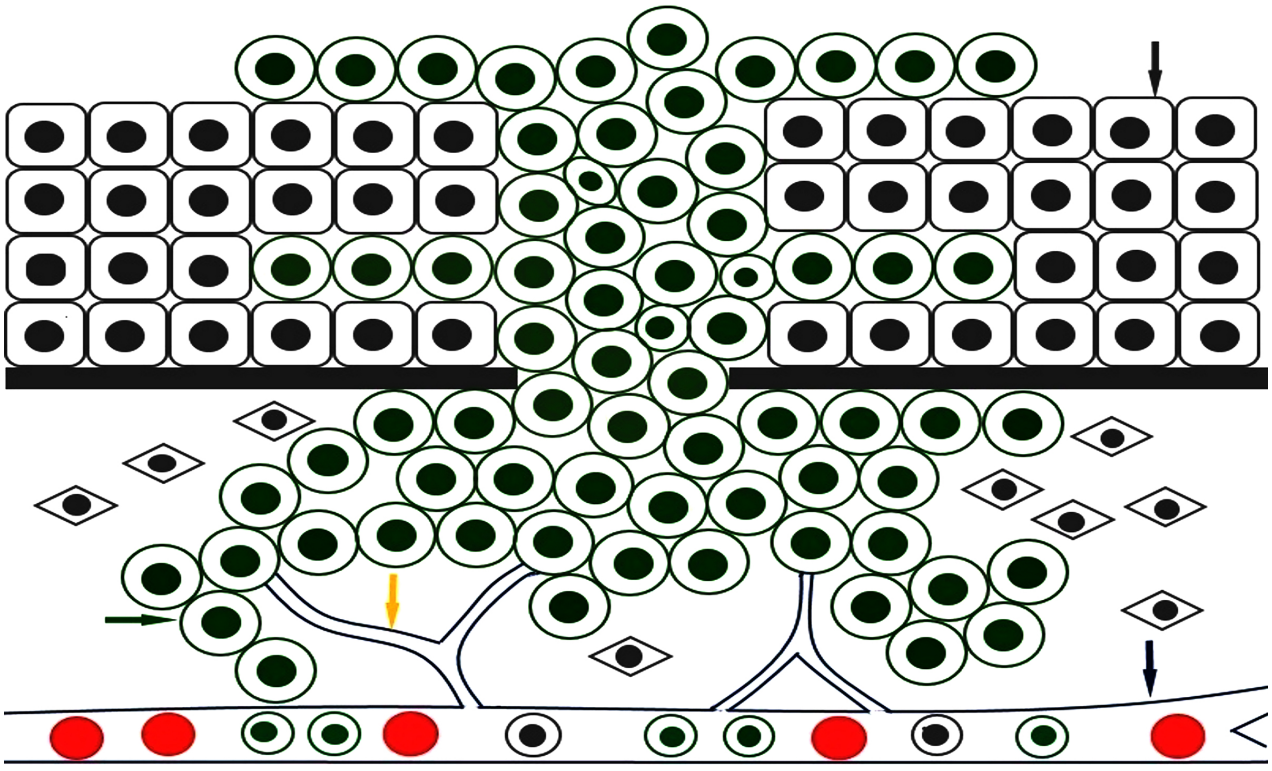

Fig. (1). Representation of cancer. The grey arrow indicates normal cells, the green arrow shows cancer cells, the yellow arrow shows angiogenesis, and the blue arrow indicates blood vessels.

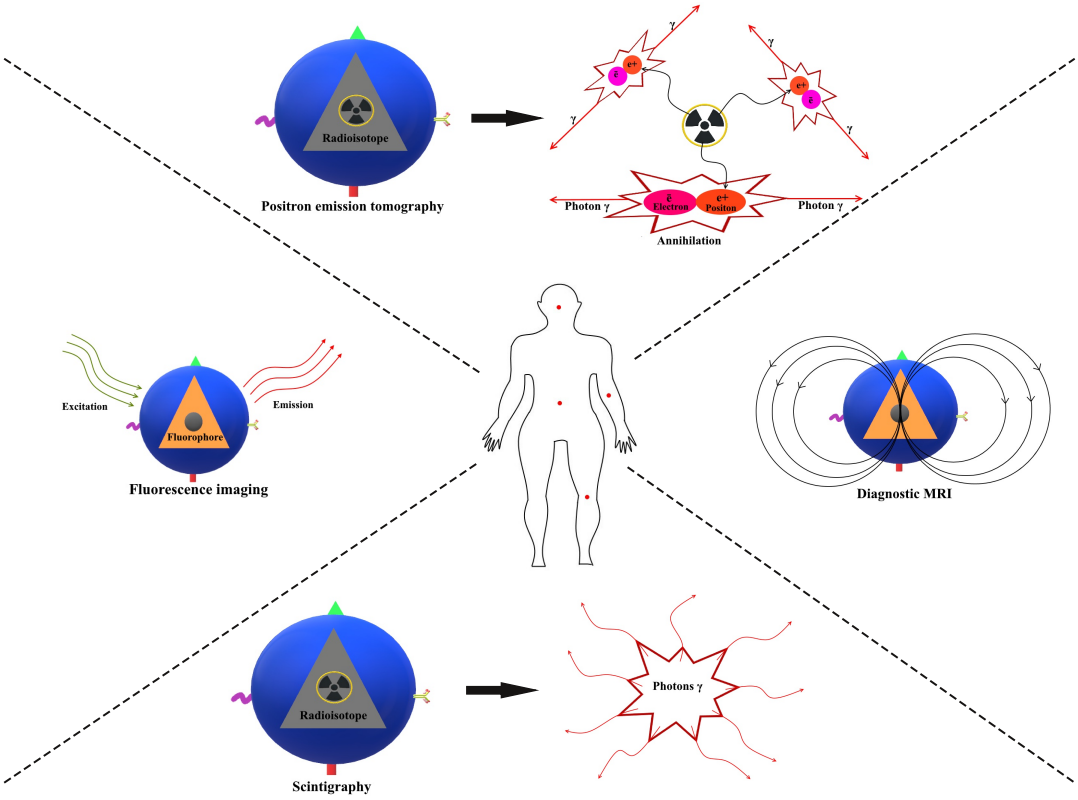

Fig. (2). NPs enabling multimodal *in vivo* imaging of a cancer bearing body. Nanoparticles were injected into the body and guided to cancer sites in order to perform diagnosis and therapy. NP system possesses optical, photonic, radioactive, contrast, chromogenic and magnetic properties allowing live multimodal theranostic of cancer. In the homunculus, imagery shows red signal intensity where NPs were located, different techniques are used. In fluorescence imaging, molecules excited by light emit a higher intensity light detected by a CCD (Charge Coupled Device) camera, the emitted light is in the near infrared (NIR) (700-900 nm) and is characterized by high sensitivity and penetration of deep tissues. Radioactive products are used in scintigraphy and positron emission tomography, allowing functional and metabolic imaging, radioactive radiation is used to destroy cancer cells. Magnetic resonance imaging (MRI) is a method of obtaining imaging inside the body, by applying magnetic fields, MRI uses the quantum properties of atomic nuclei to locate NPs in the emitting space of the nuclear magnetic resonance (NMR) signal.

Nanomedical devices can be nanoliposomes, nanowires, carbon nanotubes, nanopores, gold nanoparticles (AuNPs), magnetic NPs, nanodiamonds, quantum dots, dendrimers, and nanosponges. There are NPs carrying drugs like liposome, mesoporous silica, polymer, and virus. There are NPs of photothermal therapy like gold NPs, and carbon tube. The devices of nanotechnology bring new hope in the targeted treatment of cancer (Table **1**).

2.1. Liposomes

Liposomes are systems consisting of a lipid bilayer enveloping an aqueous central cavity. The cavity can carry hydrophilic drugs, whereas the envelope can carry hydrophobic drugs. Drug delivery into the cell cytoplasm is accomplished by the fusion of liposomes with cell membranes. The hydrophilic polar heads are directed outwards and the hydrophobic aliphatic tails are directed inwards. The size of the liposomes is of the order of 10 to 1000 nm. They are used to convey drugs and siRNAs to cancer cells because of their biodegradability. Liposomal doxorubicin (Doxil) is a chemotherapy drug used to treat various cancer. The fluorescent or radioactive labeling of liposomes is used in diagnostic techniques in medical imaging. Hybrid NPs in which liposomes are incorporated either within or at the surface have theranostic applications in cancer [61]. Liposomal NPs are used as an optical nanoprobe for *in vivo* chromogenic detection of H2O2 produced by cancer cells, and in photothermal therapy of target tumor sites [62]. The encapsulation of drugs by liposomes gives them steric stability, protects them against enzymes and the immune system and avoids their toxicity against the patient. To release the medications, the liposomes fuse with biological membranes and are endocytosed by cells. Molecules such as antibodies are added in liposomes systems to specifically recognize target cancer cells. The half-life of liposomes is short in biological media and their use requires frequent administration. They are chemically and physically unstable because they are sensitive to pH and temperature variations. They are opsonized and quickly eliminated by the reticuloendothelial system (RES). The modification of the surfaces of the liposomes with polyethylene glycol (PEG) chains reduces their immuno-genicity since the opsonins no longer cling to their surface, the organism does not recognize them as foreign and they are not destroyed by the RES [63, 64].

2.2. Nanowires

Nanowires are wires of nanometric size, their diameter is of the order of 1 to 900 nanometers. They are made of plastic or metal conductive materials. The molecules of the nanowires are organic or inorganic. Nanowires applications are mainly *in vitro* and have many medical interests. They can be coated with antibodies that bind to target molecules for the diagnosis of cancer. Nanowires are highly more sensitive and specific than conventional biochemical tests and represent a powerful method of prognostic evaluation of cancer [65].

Table 1. Nanoparticles for cancer théranostics.

Nanoparticles	Therapy	Diagnostic	References
Liposomes	**Pharmacotherapy**: medicine **Gene therapy**: siRNA **Phototherapy**: photothermal, photodynamic	**Medical imaging**: optical, fluorescent, radioactive, contrast, chromogenic, magnetic resonance	[61, 62]
Polymers			[106 – 108] and [112]
Quantum Dot			[97, 98] and [100 - 102]
Gold			[70], [72], [76] and [80, 81]
Magnetic			[83], [85], [89, 90]
Nanodiamonds			[91, 92] and [94]
Carbon Nanotubes			[66]

2.3. Carbon Nanotubes

Carbon nanotubes (CNTs) are fibrous nanomaterials composed of layers of carbon atoms forming a tube. They have mechanical properties of rigidity, deformability, and lightness. Carbon nanotubes called “armchair” have a metallic character and they are conductors. Carbon nanotubes called “zig-zag” and carbon nanotubes called “chiral” are semiconductors, they have electrical conductivity between that of a conductor and an insulator. Owing to their physicochemical properties, they have many biomedical applications. They are used in drug delivery, chemotherapy, photodynamic therapy, and gene therapy. They have optical properties of luminescence with NIR absorbance, because of their fluorescent capacity they are employed in the detection of cancerous cells. They have properties of thermal conductivity; under laser irradiation, they produce heat allowing the thermotherapy of cancer cells [66].

2.4. Nanopores

A nanopore is a hole of the order of 1 to 100 nm in a synthetic material such as graphene or biological material such as protein. Nanopore technology is used to characterize DNA molecules. The passage of individual nucleotides through the nanopore under tension triggers a signal which varies according to the bases of the DNA strand, making it possible to distinguish the four standard DNA bases and to read the genetic code. The sequencing of DNA by nanopores is less expensive and offers the possibility of detecting genetic mutations responsible for cancer. It has been utilized in patients with chronic lymphocytic leukemia and has been shown to be more sensitive than traditional sequencing methods. Nanopore-based DNA sequencing presents various advantages compared to traditional methods such as i) label-free ii) ultralong reads iii) high throughput reads iv) requires low material v) use unamplified genomic DNA [67 - 69].

2.5. Gold Nanoparticles

AuNPs have optical properties of plasmons, they are contrast agents in biological imaging. In the treatment of cancer, they are used in imaging, photothermal therapy, photodynamic therapy and for targeted drug delivery. AuNPs are biocompatible and may have sites for attaching molecules to their shells that specifically recognize cancer cells. Nanoshells are AuNPs consisting of a dielectric core composed of silica and a metal shell made of gold (SiO2 core, Au shell). Nanorods are AuNPs of 1 to 100 nm containing semiconductor materials. Nanoshells and nanorods are used in photothermal therapy because of their NIR absorption. Under magnetic resonance guidance, the exposure to NIR light of tumors treated with AuNPs induces irreversible cancer cell lethality [70 - 76]. Multifunctional nanoshells have a greatly increased relaxivity of T1 enhancing MRI T1 properties used for quantitative monitoring *in vivo* therapeutics. These nano-particles of Au core-silica layer-Au shell contain internal gadolinium ions for T1 imaging contrast, encapsulated within the silica layer between an inner core and outer Au layer, in a multilayered geometry [77]. The absorbing NIR is used to trigger the release, localized in space and time, of drugs conjugated to nanoshells in order to treat cancer cells while minimizing the toxicity of normal cells [78]. Nanorods have been activated with NIR to generate photothermal therapy to treat metastases, they have the ability to inhibit the migration of cancer cells by targeting the cytoskeletons and integrins [79]. Gold nanocages are porous AuNPs of 10 to 150 nm, they are biocompatible and absorb in the NIR, they are contrast agents in medical imaging. Gold nanocages conjugated with antibodies are employed in cancer thermotherapy [80, 81].

2.6. Magnetic Nanoparticles

Magnetic NPs are nanomaterials of about 10 to 100 nm, they are composed of magnetic materials of iron, nickel or cobalt. The magnetic NPs most adapted for biomedical applications are nanomaterials composed of iron oxides, magnetite or maghemite. There are contrast agents in magnetic resonance imaging, using a magnetic field gradient, they can be directed to cancer sites. Magnetic nanoparticles are used in various applications for cancer therapy: i) hyperthermia-based therapy ii) selective photodynamic therapy of cancerous cells iii) targeting and extraction of cancer cells iv) targeted and controlled drug delivery to cancer cells [82 - 90].

2.7. Nanodiamonds

Nanodiamonds are NPs of about 10 to 100 nm and can be produced by meteorite impacts. Due to their hardness and wear resistance, they are used in industrial and scientific applications. Due to their biocompatibility, photostability, electrostatic properties, and surface functionality, they are employed in biomedical applications to treat a wide range of diseases. These are platforms for localized drug delivery and monitoring of imaging-guided treatments. The nanodiamond technology system facilitates the targeted and sustainable

delivery of drugs. The nanodiamond platform maximizes the effects of drugs by ensuring their prolonged administration. Nanodiamonds have a capacity in drugs sustained-release. The adsorption/desorption on nanodiamonds is the basic mechanism for targeted drug delivery. These are applications of cancer nanomedicine and cancer cell biomarkers [91 - 96].

2.8. Quantum Dot

The Quantum Dots (QDs) are fluorescent semiconductor nanocrystals of about 10 nm, composed of a core coated with an envelope. QD-containing NPs represent an approach in cancer medical imaging, cancer cell tracking, cancer photodynamic therapy, and cancer diagnosis. They are contrast agents and have tumor imaging properties. When injected into the body, they infiltrate cancerous sites and produce images of these sites. The toxicity of QDs limits their use for *in vivo* applications. Thus appropriately coated, QDs can be rendered non-toxic in biological media. Polymer-coated QDs have properties of biocompatibility, solubility, targeting cancerous cells and drug delivery. QDs based on a core with lead sulfide (PbS) and shell with cadmium sulfide (CdS) and covered with PEG, emitting at about 1600 nm allow 3D tumor fluorescence imaging *in vivo* [97, 98]. QDs can target specific receptors. Folate is vital for cell growth; the folate receptor is overexpressed in the cancer cell. QDs conjugated to folate are used to diagnose cancer. QDs have higher optical properties than organic dyes. They are photostable and possess quantum properties with excitation and emission of light in the NIR. The signal emitted is 100 times more intense than fluorescent dyes allowing deep tissue analysis [99, 100]. When placed in the body and illuminated by light, QDs heat the surrounding tissue allowing hyperthermic cancer therapy. Considering that hyperthermia between 42°C and 45°C induces cell apoptosis while a temperature above 45°C causes cell necrosis. In photodynamic cancer therapy, QDs react with molecular oxygen producing peroxides and hydroxyl radicals, which lead to the death of cancer cells [101, 102].

2.9. Polymer-based Nanoparticles

Dendrimers and nanosponges are polymers of size from about 10 nm to 1000 nm. They have better solubility, stability, absorption, and *in vivo* bioavailability. They are the most promising drug carriers in targeted cancer therapy [103]. Dendrimers are polymers of macromolecules, their size and shape are variable. Dendrimers are tree branch molecules composed of a nucleus of branching units and functional end groups. Drugs can be incorporated into the central nucleus or conjugated to the functional extremity, to be transported to the cancer cells. These are contrast agents used in MRI for the diagnosis of cancer [104, 105]. Nanosponges are a scaffold of polymers filled with nanocavities in which molecules can be stored. These are NPs that take the form of red blood cells and move throughout the living body. They can trap bacteria and toxins in their scaffolds and filter them into the liver. Nanosponges injected into the living body are used to deliver drugs to cancer cells [106 - 108]. Human ferritin heavy-chain nanocages coupled to polyethylene glycol constitute a drug delivery system able to overcome multiple biological barriers, to penetrate preferentially into tumor tissues, to distribute selectively and dependently on transferrin receptor in cancer cells [109]. Polymer-based NPs can be wrapped in macrophage-derived cell membranes which neutralize endotoxins, sequester pro-inflammatory cytokines, and inhibit the onset of immune activation against these NPs [110]. To develop interfering RNA (RNAi) - based cancer treatments, albumin is conjugated to siRNA to increase their half-life in the circulation, their bioavailability, their accumulation in tumors and their uptake by tumor cells [111]. Nano-encapsulation of multiplexed RNAi in lipopolymeric NPs is a therapeutic targeting strategy to meet the challenges of therapeutic resistance and tumor heterogeneity [112]. Spherical nucleic acids (SNAs) nanoconjugate-based RNAi constitute an *in vivo* nanotherapeutic strategy, they are capable of performing non-invasive imaging and inactivating *in vivo* intratumoral proteins [113].

2.10. Hybrid Nanoparticles

Hybrid NPs are multifunctional systems in which nanostructures such as liposomes, polymers, noble metals, and nanotubes are incorporated inside or on the surface of a nano-assembly. They combine both diagnostic and therapeutic functions. These nanodevices are able to perform multiple tasks, they are utilized in drug therapy and medical imaging for *in vivo* targeting of cancer sites (Figs. **3** and **4**). Polymer hybrid NPs aim to offer biocompatible and biodegradable materials suitable for therapeutics and diagnosis applications. They can incorporate QD and magnetic NPs. They combine medical imaging and drug delivery in cancer therapy. Conjugated with folate, they selectively target cancer sites.

Table 2. Hybrid Nanoparticles for cancer theranostics.

Hybrid Nanoparticles	Therapeutic Functions	Diagnostic Functions	References
Mesoporous silica-based	**Pharmacotherapy**: radionuclides, toxin...	**Medical imaging**: gold, magnetic nanocrystals, quantum dots...	[70] and [114]
Polymer-based	**Phototherapy**: gold, quantum dots, upconversion...		[70], [117, 118] and [120]

Mesoporous silica-based hybrid NPs are the best drug carriers because of their large surface area, size, porosity, chemical stability, and biocompatibility. They can incorporate theranostic molecules and magnetic nanocrystals [70] (Table **2**). AuNPs have photonic and magnetic properties, but their toxicity to cells and their lack of solvent stability limit their use. The creation of mesoporous silica-based hybrid systems stabilizes AuNPs by allowing them to retain their properties in biological media while being biocompatible. In these hybrid systems, the AuNPs absorb light in the NIR, convert it into photons through the tissues and deliver treatment. QDs are promising in tumor multimodal imaging, hyperthermic therapy, and photodynamic therapy. Mesoporous silica is employed in these systems to host the drug load and control its release [114].

Drug delivery is focused on lipid NPs which have pharmacokinetic, stability, biodistribution and toxicity limitations. Polymeric NPs are drug delivery systems that can escape endosomal activities and offer greater anticancer

efficiency [115]. NPs composed of a combination of mixed lipids are vectors for delivering oligonucleotides across the cell membrane. The mechanism for releasing oligonucleotides is endocytotic. These various lipid block hybrid NPs have a high efficiency of transfection of cells with the ribonucleic acid messenger (mRNA), allowing protein expression. These lipid hybrid NPs have minimal toxicity and promising medical strategies [116, 117]. Mechanisms that involve tumor growth and metastasis depend on the genetic mutations of oncogenes. RNAi represents a promising strategy for the treatment of human diseases, including cancer. Hybrid polymer NPs used for *in vivo* and systemic delivery of siRNA to tumors specifically deactivate the expression of mutated oncogenes. These siRNA-conjugated polymeric NPs have no toxicity risk to patients and are photostable. They provide theranostic follow-up by non-invasive imaging of tumors ; also long-term circulation, prolonged-release, and significant accumulation of drugs in tumors. They are capable of efficient gene silencing and have negligible side effects [118].

Fluidic microchips were used to probe the translocation of hybrid polymeric NPs through endothelial cells and *in vivo* imaging monitoring of their transvascular permeability [119]. The hybrid anti-cancer systems integrate Yttrium 90 (^{90}Y) beta-emitting radionuclides inside of nanocrystalline matrix coated with NIR light upconversion polymer and coupled to recombinant proteins composed of two modules: i) the DARP in module targeting cells overexpressing the HER2 receptor oncomarker ii) the Exotoxin A cytotoxic module inhibiting the synthesis of HER2-positive cell proteins. These nanocomplexes have diagnostic functions and selective drug therapy of cancer cells [120].

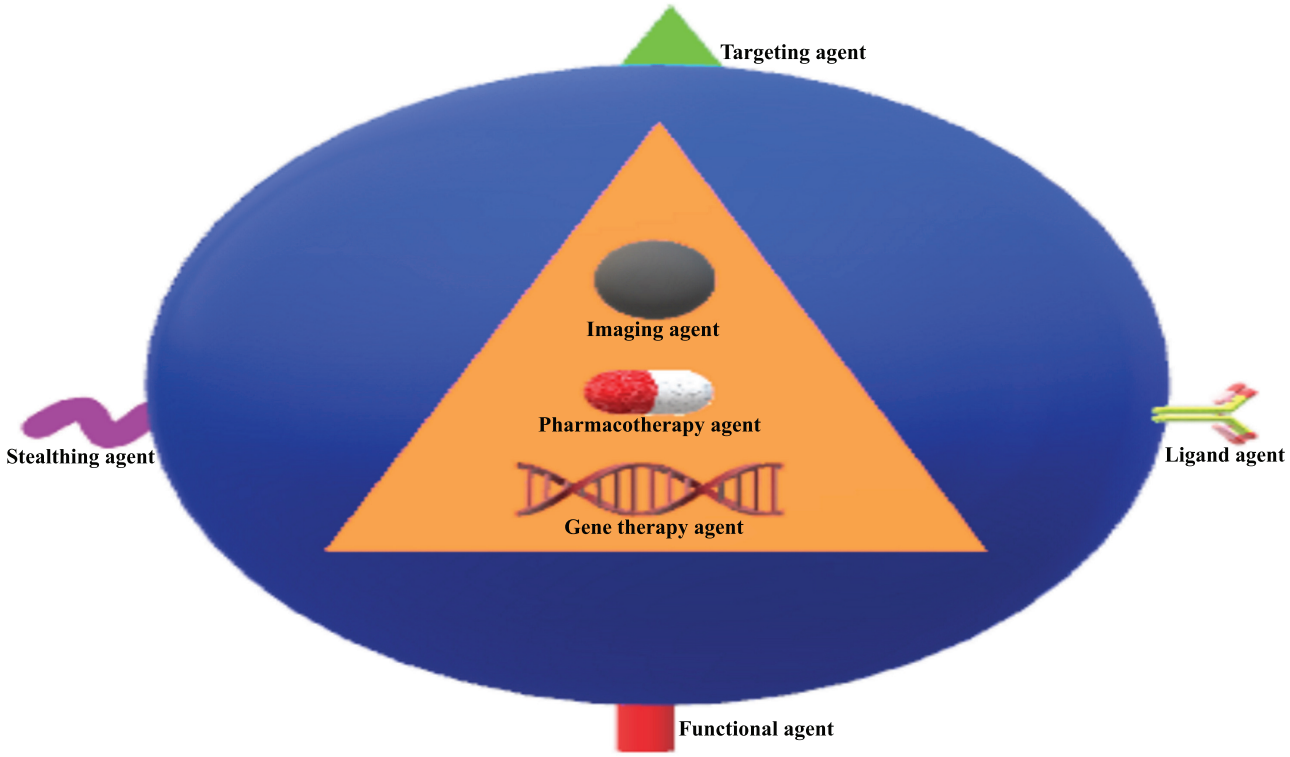

Fig.(3). Schematic design of the hybrid NP platform. Hybrid NPs are composed of an inorganic or polymeric core (orange) and a polymeric shell (blue). The hybrid NPs host NP agents within their shell and or inside their core. Schematic design showing imaging agent (radio-isotope compound, fluorescent compound) allows the visualization or detection of NPs. The pharmacotherapy agent (active pharmaceutical ingredient) allows drug delivery. The genetic therapy agent (siRNA) allows genetic material delivery. The stealthing agent (PEG, dextran, phospholipids) increases the circulation half-life of nanoparticles. The specific-ligand agent (antibody) allows specific binding to antigen. The specific-targeting agent (HER2, ERBB3, BRAF) allows targeting specific receptors of cancer cells. The functional agent (enzyme) allows biochemical reactions.

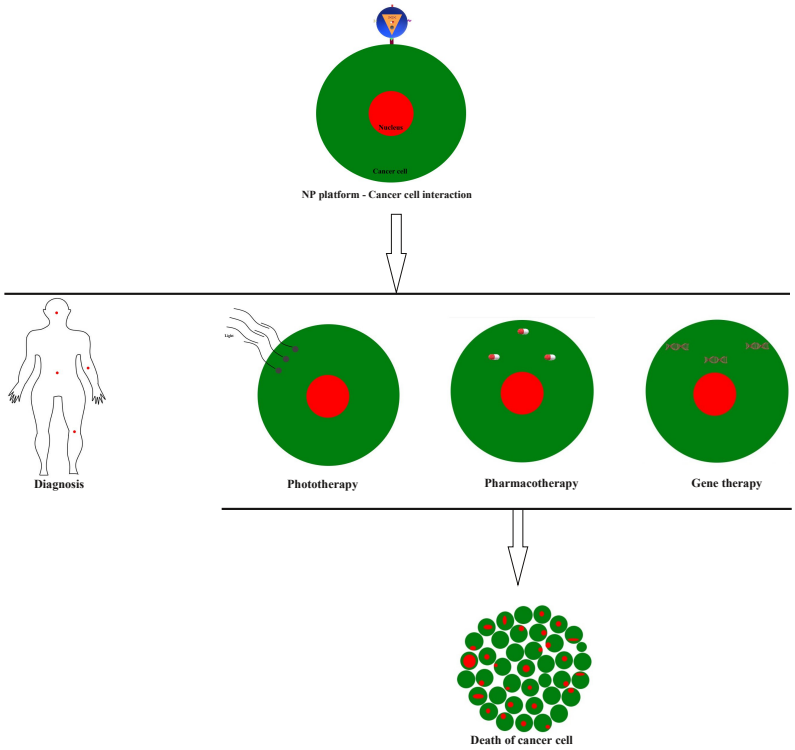

Fig.(4). Schematic illustration of cancer theranostics by the multifunctional NPs hybrid platform. In the interaction between the NPs and the cancer cells, the ligand targeting agent binding to tumor receptor induces internalization and endocytosis of NPs in cancer cells. In diagnosis, the cells are labeled following NPs agent release, which is localized within the cancer cells through various methods. In thermal treatment, the cells are treated with NPs, which are activated by radiation to induce the destruction of cancer cells. In therapy with NPs siRNA delivery, the cells are treated with NPs loaded with siRNA (NPsi oncogenes), which mediate gene silencing and functional effects in mutated cells, to induce effective and cytotoxic destruction of cancer cells. In pharmacotherapy, the therapeutic agent drug release molecule induces the destruction of the cancer cells.

CONCLUSION

The tools of nanotechnology are promising for the treatment of a wide range of diseases. Several nanotechnology platforms have been developed and several clinical trials have demonstrated their anticancer benefits, thereby liposomes are widely used. Dendrimers, cantilevers, and CNTs are emerging nano-applications in cancer medicine. Drug resistance results from the accumulation of lactic acid in poorly vascularized cancer sites, the NPs make it possible to overcome these problems of administration of the drugs to the cancerous tissues. NPs are characterized by their modular size, their high surface-volume ratio, their loadable surface with biological substances of interest, and their stability in wide ranges of temperature and pH. Nevertheless, nanoparticles have many challenges to overcome, notably their accumulation in the liver and the spleen, as well as the different barriers to cross to reach the cancer cells. Antisense oligonucleotides or RNAi offer an opportunity to treat cancers by specifically disabling the expression of target genes that lead to tumor growth. Nevertheless, this approach confronts problems of side effects related to their pairing with non-target mRNA, the induction of the innate immune response, their short half-life and their destruction by serum nucleases. Hybrid NP polymers effectively protect siRNA and allow NIR imaging to track in real-time the systemic and *in vivo* biodistribution of siRNA to tumors. Polymeric hybrid NPs show photostability and significant systemic circulation time. Nanotechnology presents new ways to diagnose, treat and follows patients. The characterization and lack of biodegradation of NPs raise concerns about the safety of their clinical use. The toxic effects of NPs are not sufficiently known. Regulations hinder the widespread application of NPs in cancer medicine because of potential health risks for patients. Successful clinical trials and compliance with quality guidelines would address the challenges facing the NPs on the marketplace.

LIST OF ABBREVIATIONS

AuNPs	=	Gold Nanoparticles
BRAF	=	B-Raf proto-oncogene
CCD	=	Charge Coupled Device
CdS	=	Cadmium Sulfide
CNTs	=	Carbon Nanotubes
CT	=	Computerized Tomography
DARPin	=	Designed Ankyrin Repeat Proteins
DNA	=	Deoxyribonucleic acid
ERBB3	=	Receptor tyrosine-protein kinase erbB-3
EPR	=	Effect of Permeability and increased Retention
HER2 receptor	=	Human Epidermal Growth Factor Receptor-2
MRI	=	Magnetic Resonance Imaging
NIR	=	Near-infrared Region
NP	=	Nanoparticle
(NMR)	=	Nuclear Magnetic Resonance

PbS	=	Lead Sulfide
PEG	=	Polyethylene Glycol
Pet	=	Positron Emission Tomography
pH	=	Potentiel Hydrogen
QD	=	Quantum Dot
RES	=	reticuloendothelial System
RES	=	Reticuloendothelial System
RNAi	=	Interfering RNA
mRNA	=	Ribonucleic Acid Messenger
siRNA	=	Small Interfering RNA
SNAs	=	Spherical Nucleic Acids
T1	=	spin-lattice Relaxation Time in Contrast
Theranostics	=	Diagnosis and Therapy Coupled in the Same System

CONSENT FOR PUBLICATION

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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