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REVIEW

Prospects of Nano–Material in Breast Cancer Management

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Abstract Breast cancer evaluation and early diagnosis are core complexity worldwide and an ambiguity for scientists till date. Nano-materials are innovative tools for rapid diagnosis and therapy, which may induce an immense result in the field of oncology. Their exceptional size-dependent properties make them special and superior materials and quite indispensable in several fields of the human activities. The major obstacle in finding cure for malignant breast cancer is to increase in development of resistances for tumors to the therapeutic treatments. The widespread mammo-graph particle is being developed by nations to diagnosis disease in primitive stage to decline the mortality rates caused by breast carcinoma. The advancement of nano-particle based diagnostic tools facilitates in evaluation and provides encouraging development in breast cancer therapeutics. In this compact review, efforts have been made to compose the current advancements in the area of functional nano-particles. Furthermore, in vivo and in vitro applications of nano-materials in breast cancer management are also discussed.

Keywords Nano materials · Breast cancer · Biomarkers · Diagnosis

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Introduction

Breast carcinoma is the most common cancer amongst the women worldwide. Although mortality rates from breast cancer have decreased since 1990, it is estimated that ~40,000 women in the United States died due to breast cancer in the year 2011 [1]. From the last 8–9 decades, Africa and Asia have experienced quick increase in the annual occurrence rates of breast carcinoma in comparision to North America, Europe and Asia [2, 3]. Currently, the incidence in the developed and developing world is similar, whereas the incidence rates are tending to plateau or decline in the West, however they are increasing in the developing world, presumably related to the changes in dietary, reproductive behaviors and ageing populations [4]. Rapid improvements in diagnostic protocols in the western countries have improved our ability for an early breast cancer diagnosis, resulting in enhancement of survival rates [5, 6].

Nano-science is the study of molecules along with structures between sizes of one nanometer to hundred nanometers. Nano-materials derived from this technology have unique size-dependent properties. In addition, this technology makes them better and indispensable in various fields of human activities. Biological application of nano-material is

a fast emerging area of nanotechnology that reflects new possibilities in the diagnosis and prevention along with cure of the diverse diseases [7].

Nano-materials are being made for tumour imaging in vivo, profiling of bio-molecular biomarkers related to cancer and targeted medicine delivery. Some biomarkers of breast cancers express protein (eg, progesterone receptor, oestrogen receptor, and ERBB2) and treatment assessment are also made on their basis. Semiconductor fluorescent nanocrystals, such as quantum dots, have been amalgamated to antibodies, by which they allow for simultaneous labeling and accurate quantification of these target proteins [8]. Therefore such conjugation of nano-particles with antibodies permits the chance of simultaneous identification of multiple molecular targets in samples of small tumor [9]. Nanoparticles coupled with cancer specific drug candidates can be used to illustrate the tumours and identify peripheral metastases [10]. Nano-particles have been employed to image the integrins present in endothelial cells, especially those of angiogenic blood vessels's [11].

Early Diagnosis for tumors when they are effortlessly curable and may not need systemic chemotherapy remains a big challenge to the clinicians. To improve an early cancer detection, gas filled hollow boron-doped silica particles have been developed that may be used for ultrasound guided breast conservation therapy. Liberman A et al. 2012 used these particles in-vitro and continuously imaged up to 48 min and their signal lifetime persisted for 5 days. They concluded that these particles could potentially be given by intravenous injection and, in conjunction with contrast enhanced ultrasound may be utilized as a screening tool to detect smaller breast cancers before they are detectible by traditional mammography [12].

A recent study of Qiao G et al. 2011 used a combination of tumor-specific mRNA markers to avoid the inherent limitations associated with the single marker technique. A gold nanoparticle (AuNP) was assembled with a bi-molecular beacon (bi-MB), and termed AuNP/bi-MB, which simultaneously targeted the two types of tumors mRNA in breast cancer cells. This imaging agent could prevent effectively false positive results and provide comprehensive and dependable information for the early detection of cancer [13].

Nano-Materials and Their Categorization

The core of nano-biomaterial is usually made up of nanoparticle. It can be used like a suitable surface for molecular assembly. It may be made up of polymeric or inorganic materials. Nano-materials can also be present as a nanovesicle enclosed through a membrane or layer. They may have spherical, plate-like or other shapes. The approaches used in creating nano-biomaterials are illustrated in Fig. 1 [14].

The nano-particles, which are usually used as a diagnostic material, are classified into two major types (Fig. 2) [15].

Organic Molecule

The chief constituent of such nano-material is organic molecule such as dendrimers, liposomes, carbon nanotubes and emulsions. Liposomes are being employed as vehicle for drug delivery in various human tumors along with breast carcinoma [16]. While dendrimers are employed in MRI as contrast agents and have aided visualization of different pathological processes. Carbon nanotubes (CNT) have been evolved as a novel alternative and very efficient device for transporting and translocating therapeutic drugs. They produce low toxicity in comparison to other nano-materials hence may have great prospective in the diagnosis and treatment of the disease [17, 18]. For selective imaging as well as drug delivery of different human cancers, organic nano-vectors amalgamated with pharmacological agents and targeting biomolecules, are potent vehicles [18–22].

The structure, function along with applications of these organic nano-materials have been reviewed in the text.

Inorganic Molecule

Most of the inorganic nano-materials reflect the same basic construction, a central core that characterize the electronic, fluorescence, magnetic and optical properties of the material, in conjunction with an organic coating on the surface. Outer organic layer protects the core from damage by physiologically destructive environment and can form covalent or electrostatic bonds, or both, with positively charged

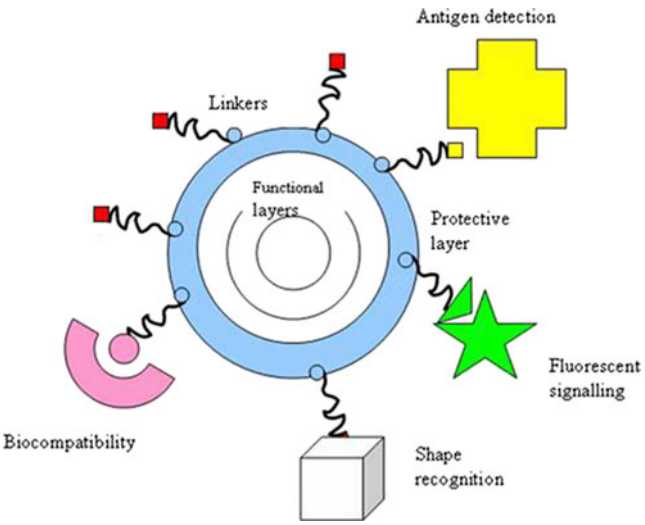

Fig. 1 Basic composition employ in nano-biomaterials applied to multiple diagnostic approaches [Salata OV, 2004]

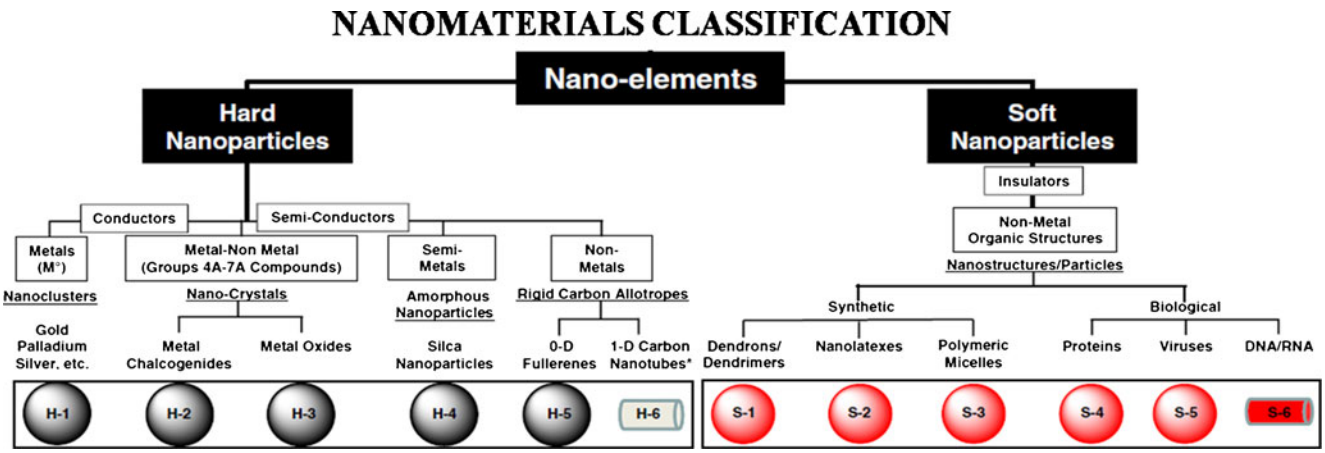

Fig. 2 Nanomaterials classification road map (Tomalia DA, 2009)

particle and bio-molecules having basic functional groups such as amines and thiols. Numerous research groups have successfully connected fluorescent nano-particles to oligo-nucleotides, peptides and proteins [10, 23, 24]

The principal components of the inorganic nano-materials used in the cancer diagnosis are super magnetic nano-materials and Quantum dots (QDs).

These Quantum dots are fluorescent nano-particles (size: 2–10 nm) that hold a core of hundreds of atoms belonging to group II and VI elements (eg: cadmium, zinc, technetium, and selenide) or group III (eg, tantalum) and V elements (eg, indium). The mostly used biological application holds a zinc sulphide shell and a cadmium selenide core, enclosed by a coating of an amphi-philic polymer and a coordinating ligand [25, 26]. This structure allows the quantum dots to emit powerful fluorescence that differs in nature from organic dyes. These QDs can be changed to emit fluorescence in between 450 nm to 850 nm (ie, from ultraviolet to near infrared) by altering the size or chemical composition of the nano-materials. This quantum confinement effect generates many quantum-dot colours. These colours can be visualized simultaneously with single light source. However, application of QDs in imaging and therapeutic in vivo has potential limitation of toxic effects because of the heavy-metal core [8].

Supermagnetic nano-particles contain a core which is composed of metals (eg, iron, cobalt, or nickel). This core is magnetically active, and is used as a contrast enhancement representative to make MRI, more sensitive. Magnetic particles, layered with an organic outer coat, can also be amalgamated to bio-molecules and employed as site specific drug-delivery candidates for the cancer therapeutics.

Iron-oxide based magnetic materials hold a broad range of application as magnetic resonance in clinical practices, gene expression, cellular trafficking and in studies of angiogenesis imaging. For combined magnetic and optical imaging, metal nano-materials in amalgamation with active fluorescent molecules can be used [27, 28].

Diagnostic & Therapeutic Use of Nano-Materials in Carcinoma of Breast

Gold (Au) Nanoparticle Used to Treat Breast Cancer

Proteins play an essential part in the cell's machinery, language and structure. It is of great importance especially understanding the protein functionalities for further improvement in human well being. Immuno-histochemistry is the renowned scientific approach for determining the expression of breast cancer by specific biomarkers such as ER, PR, HER-2 etc that are required for managing patients. Gold nano-particles are comprehensively used in immuno-histochemistry to spot protein-protein interaction. Recently James Xing explored gold based nano-particle bond with breast cancer receptor such as EGFR [29].

Some metal particles hold strong surface plasmon fields that can effectively adjust fluorescence. By using this fluorescence adjustment, a NIR fluorophore based, nanometer sized contrast agent for breast carcinoma diagnosis has been formulated. The fluorophore is capable of conjugating the gold nanoparticles (GNP) with a small spacer. The spacer's length is specially adjusted to have the strong plasmon field to quench the fluorescence. Moreover, the spacer has a special molecular sequence. Enzyme secreted by targeted cancer cells can cleave this sequence. Normally, the unit does not fluorescence. When it reaches to the cancer site, the small spacer would be broken through the enzyme secreted via the cancer cell. Thus the material can be used to comprise a cancer targeting molecule for the precise type of cancer. The material specifically aims cancer cells and fluoresces only when the spacer is broken through a biomolecule secreted by specific cancer cells, providing twofold specificity for cancer identification [30–32].

The photothermal effects of different Au nanostructures are recently established, and all are qualitatively capable to demolish the targeted cancer cells leading to irradiation by

means of a near-infrared laser [33]. Leslie Au et al. conjugated gold nanocages, comprising a normal edge length of 65±7 nm as well as a powerful absorption peak at 800 nm, with monoclonal antibodies (anti-HER2). This conjugation was targeted on the breast cancer cells (SK-BR-3) via epidermal growth factor receptor predominantly in the case of HER2 that is over expressed on the cell surfaces. It was observed that the cells aimed with immune Au nanocages responded instantly to laser irradiation and the cellular destruction was not reversible at power densities larger than 1.6 W/cm2. Cells with increasing exposure time of laser irradiation up to 5 min, the percentage of dead cells were greater than before and then became steady [34].

Gold-gold sulfide nano particles (GGS-NPs) were first formulated by Zhou et al. and explained to have a core/shell structure [35]. GGS-NPs have been employed as drugs carriers with minimal toxicity and have recently been illustrated as a photothermal cancer therapeutic material [36]. According to Day ES et al, when GGS-NPs are conjugated with anti-HER2 antibodies, the resulting nano-particles interact more specifically to SK-BR-3 breast carcinoma cells. SK-BR-2 breast carcinoma cells overexpress HER2 receptor directed to the enabling of cells to be imaged through multiphoton microscopy with an intense laser power of 1 mW [37]. Supplementary excitation power up to 50 mW could be employed to induce thermal destruction to the cancerous cells, producing wide-ranging membrane blabbing within few seconds giving rise to cell death [38]. Nanoparticle heating and successive cell destructions were restricted to the field where the laser was raster-scanned across the sample.

Lu W et al. reported for the first time a very sensitive and simple colorimetric two-photon scattering assay for selective identification of breast carcinoma SK-BR-3 cell lines in 100-cells/ml level using multifunctional (monoclonal anti-HER2/c-erb-2 antibody and S6 RNA aptamers conjugated) oval shape nano-particle of gold based nano-conjugate. On mixing assay along with breast cancer SK-BR-3 cell line, a distinctive color change took place and two-photon scattering intensity raises about 13 fold. This experimental result indicates a new opportunity of fast, easy and trustworthy diagnosis of carcinoma cell lines by monitoring the colorimetric change and measuring TPS intensity from nanosystems of multifunctional gold [38].

Tamoxifen-Poly(ethylene glycol)-Thiol Gold Nanoparticle conjugates can be applied for selectively target identification as well as to deliver plasmonic GNP to estrogen receptor positive carcinoma of breast cells with about three fold increased potency of the drug in vitro. The optical microscopy/spectroscopy, time dependent response of dose dataset, and estrogen competition studies point to that improved activity is due to raised rates of intracellular tamoxifen brought by endocytosis of nanoparticle, more willingly than by passive diffusion of the free drug. Receptor as well as ligand dependent intracellular delivery of nanoparticles of gold suggests that plasma membrane confined estrogen receptor alpha may lead to selective uptake or retention of this along with other therapeutic nanoparticle conjugates [39].

Carbon Nanotubes (CNT), Imaging and Therapeutics

Single Walled Carbon Nano Tubes (SWCNT)-based contrast agents have shown promise for molecular imaging by MR, PET, photoacoustic imaging modalities and nuclear [40–42]. Functionality of these particles with tumor targeting biomarkers may strengthen their accumulation properties in tumors [43–45]. The presence of CNT in or near a malignant lesion will lead to adjustment to the dielectric properties of cancer tissues. If these modifications are significant enough, then they can be adopted to increase the sensitivity of low power microwave imaging of breast carcinoma via differential imaging [46, 47] and selectivity of greater-power microwave thermal therapy.

Recent study by Mashal A et al. characterized the dielectric properties of tissue-mimicking materials (TM materials) using various different concentrations of SWCNTs. They pointed out that the lower concentrations of SWCNTs considerably influence the heating response and dielectric properties of TM materials. They showed that at 3 GHz, SWCNTs concentrations of 0.22 % by weight enhanced the relative permittivity of the TM material by 37 % and the effective conductivity by 81 %. In this experiment of heating, concentration of SWCNTs led to an average steady-state temperature increase of 6 °C more than that monitored in TM material in absence of SWCNTs. These results indicate that SWCNTs might increase contrast for microwave imaging and assisted selective microwave heating for breast cancer therapeutics [48].

Magnetic Nano-Particle Used in Imaging and Therapy

The magnetic particles have exclusive characteristic of their own reaction to a magnetic force. Such aspects have been used in diverse applications like bio-separation and drug targeting, including cell categorization. Nanoplatforms such as magnetite-dextran nanoparticles, aminosilane iron oxide and magnetic cationic liposomes have been fruitfully studied in vitro, in vivo, as well as in human trials [49]. Recently, magnetic nano-particles have drawn concentration because of their potentialities as contrast entities for MRI and heating mediators for cancer therapy (hyperthermia). The magnetic cationic liposomes (MCLs) that are cationic magnetic particles can be applied as transporter to bring in magnetic nano-particles within target cells since their positively charged surface interacts with negatively charged cell

surface. In addition they have also been used in hyperthermic treatments. Conjugated magnetic nano-particles with antibodies are well applied to hyperthermia and comprise facilitated tumor-specific contrast increase in MRI via systemic administration. Magnetic nano-particles are concerned to a high magnetic flux density. In view of this property, it is possible to influence cells labeled with magnetic nano-particles by means of magnets. Such attributes have been used in tissue engineering. The magnetic force and MCLs were employed to build multilayered cell structures and heterotypic layered 3D co-culture system. Therefore, the uses of these magnetic nano-particles with their exclusive characteristics will further advance the medical techniques [50].

Ferumoxtran-10 with diagnostic accuracy of MRI, which is an especially very small super-paramagnetic iron-oxide nanoparticle, that is specific, sensitive and applied as a contrast agent for identification of lymph-node metastases for different carcinomas. It offers greater diagnostic accuracy than does decreased MRI for identification of lymph-node metastases. Moreover, it permits anatomical and functional definition when applied as an imaging modality [51].

Recently Tran LA et al. reveals that under a distantly applied radiofrequency magnetic field, precisely nanocapsules display on-off switchable discharge of the inside loaded drug payload. In vitro as well as in vivo investigations using MT2 mouse breast tumor cell models reveal that the magnetic targeting of present nano-capsules permits for deep tumor access, furthermore subsequent on-demand release of the medicine cargo, considerably decreasing carcinoma cell viability [52].

Dendrimers and In-Vivo Imaging

In-vivo imaging with dendrimers is potentially useful tool in biomedicine, as it is non-invasive and presents large quantity of information relating to the native states of a diverse range of tissue types. Initially in vivo uses of dendrimers were as carriers MRI contrast reagents. An additional non-invasive imaging application of dendrimers includes photonic oxygen sensing, because the concentration of oxygen (O2) in certain tumors can point out whether the carcinoma will give response to therapy, methods to establish precisely this parameter are desirable [20].

Dendrimers have functional and structural advantages deriving from their specific architecture and decrease polydispersity with respect to conventional polymers that are synthesized as a layer-by-layer manner (called generation) surrounding a central unit. This outcome in an immense level of control over size, surface functionality, and branching points [53]. The capacity to modify dendrimer properties to the therapeutic requirements make them perfect carrier agents for small molecules such as biomolecules and therapeutic drugs. Dendrimers have nanosize containers along with nano-scaffolding properties. In addition they are bio-compatible [54]. Amalgamation of methotrexate (MTX) and folic acid (FA) to hydrazide-terminated dendrimers revealed that these MTX and FA could be joined to dendrimer with respective amalgamation ratios of 4.7 and 12.6 [55, 56]. Furthermore another diverse group of researchers reported dendrimer-based drug conjugates that target cancer cells via the folate receptors [57], PSMA (prostate-specific membrane antigen) [58], $\alpha\upsilon\beta3$ integrins [59] and Her2/neu [60]. The compounds have to deliver consistently specific destruction of the targeted cells only then they can be valuable as ‘targeted’ drug delivery candidate for clinical application [61–64]

Recent study of Myc A et al, applied a coculture assay and an artificial hetero-geneous xenograft tumor model into NOD C.B-17 SCID mice to assess new generation of applicable nanotherapeutics both in-vivo and in vitro. Dataset generated from both studies show preferential destruction of targeted cells using the nanotherapeutics. These data reveal the specificity and efficacy of the G5-FA-MTX nanotherapeutic and envisage its clinical application for targeted anticancer therapy [65].

Early Breast Carcinoma Diagnosis Using Quantum Dots (QDs)

QDs are prepared from inorganic semiconductors and comprise novel optical properties, which can be employed to optimize the signal, background ratio. It has a high molar extinction coefficient [66] that builds them brighter probes in photon-limited in vivo environments (where light intensities are rigorously attenuated by absorption and scattering). Theoretically, the lifetime-limited emission rates for individual QDs are five to ten times lesser than those of single organic dyes, because of their longer (20–50 ns) excited state lifetimes.

Wu et al. [67] linked polymer protected QDs to streptavidin and showed detailed cell skeleton structures using confocal microscopy. The improved photostability of QDs permitted acquirement of numerous successive focal-plane images and their reconstruction into a high-resolution three-dimensional projection. The high electron density of QDs also allowed correlated electron and optical microscopy investigations of cellular structures [68]. Various results of researchers indicate that large amounts of QDs can be delivered into live mammalian cells via three different mechanisms: non-specific microinjection, pinocytosis, and peptide-driven movement (e.g. using protein transduction part of HIV-1 Tat peptide and Tat-PTD) [10]. A remarkable finding was that two billion QDs could be subjected into the nucleus of an individual cell, without any compromise with its proliferation, migration or viability [69–71].

Akerman et al. [72] firstly reported the application of QD–peptide conjugates to specifically target tumor vasculatures, while the QD probes were not identified in living animals. However, in-vitro histological outcome revealed that QDs homed precisely to tumor vessels directed by the peptides and were competent to escape clearance by means of reticuloendothelial system. Most recently, Gao et al. [10] accounted a novel category of multifunctional QD probes specifically for tumors in live animals, which can be used simultaneousaly for targeting and imaging. This category of QD conjugates precisely hold an amphiphilic triblock copolymer, which can be for in vivo fortification, multiple PEG molecules for enhanced biocompatibility as well as circulation and targeting ligands for tumor antigen identification. Various researchers also revealed, the application of an amphiphilic triblock copolymer, competently solved the difficulty of particle aggregation as well as fluorescence loss formerly encountered for QDs stored up in physiological buffer or introduced into live animals [72–75]. Thorough studies were accounted on the in-vivo behavior of QD probes, together with their biodistribution, cellulartoxicity, nonspecific uptake and pharmacokinetics.

Specific delivery of QD probes to tumor either by an active targeting or as a result passive targeting mechanism under in vivo condition. In the passive mode, nanometer sized particles and macromolecules are accumulated preferentially and precisely at tumor sites by an enhanced effect of permeability and retention [76]. It is believed that such effects arise from two factors. Primarily, angiogenic tumors generate vascular endothelial growth factor, which hyperpermeabilizes the tumor-associated neovasculature and reason for the leakage of circulating macromolecules along with small particles. Subsequently, tumors are deficient in an efficient lymphatic drainage scheme, which lead to subsequent nano-particle or macromolecule accumulation.

In a study Gao et al. [75] used antibody conjugated QDs toward target a prostate-specific membrane antigen (PSMA) for active tumor targeting. Prior research recognized PSMA like a cell-surface marker for both neovascular endothelial cells and prostate epithelial cells [77].

The property like narrow emission spectra and photostability of inorganic quantum dot fluorophores build their desirable possible alternative for fluorescent in situ hybridization (FISH) to examine and explore the expression of definite mRNA transcripts. PokMan Chan et al. explored a new approach for direct QD labeling of customized oligonucleotide probes through interactions of streptavidin and biotin, in addition to procedure for their employment in multiple-label FISH. They established enhanced sensitivity of FISH with QDs in respect of organic fluorophores. Such techniques furnished excellent histological results both for FISH (multiplex and combined) and immuno-histochemistry. Ultra sensitive concurrent study of multiple mRNA as well as protein markers in tissue culture alongwith histological section can be facilitated by this approach effectively [24].

Xiaohu Gao et al, explored insightful as well as multicolor fluorescence imaging of cancerous cells in in-vivo conditions and furthermore integrated an entire macro-illumination system through wavelength resolved spectral imaging for competent background elimination and specific delineation of pathetic spectral signatures. These results explore new possibilities for more sensitivity in addition with multiplexed imaging of cellular and molecular targets in vivo [75]. Jaiswal JK suggested that improved making of water stable QDs, the advancement of approaches to label cells competently with QDs, and enrichment in conjugating QDs to precise biomolecules have caused the recent ignition in their use in molecular imaging [78].

Recently Amit Agrawal et al. accomplished routine two-color ultra resolution imaging and single-molecule recognition with standard level of fluorescence microscopes and economical digital color cameras. By using green and red nano-particles to concurrently identifying two binding sites on a particular one target hence individual bio-molecule like nucleic acids are noticed and identified without probe/target separation or target amplification. They also reveal that a potent astrophysical technique can be employed for automated and speedy statistical analysis of nano-material co-localization indicators. Capability to quickly localize intense nano-material probes at nanoscale accuracy has inference for both high sensitive medical detection and structural mapping of biological (at molecular level) complexes in which color-coded nano-particles are tagged with individual components [79].

Therefore, molecular imaging used to direct drug development and on the other hand pre-clinical assessment can be used to early clinical studies and also to give proof of concept, quick evidence of efficacy as well as pharmacodynamic assessment to optimize dosing [80].

Image Enhancement by Paramagnetic Metals

The paramagnetic metal chelates like Gd(III)- N,NV,NW,Nj-tetracarboxymethyl-1,4,7,10-tetraazacyclododecane (Gd(III)-DOTA), Gd(III)- diethylenetriamine pentaacetic acid (Gd(III)-DTPA) as well as their derivatives augment the relaxation speed of nearby water protons and are utilized as contrast candidate for magnetic resonance imaging (MRI) [81, 82]. The (Gd(III)-DTPA) conjugate commercially known as MagnevistR (Schering AG) that is a widely used as MRI contrast candidate. However, limitations of this low molecular weight contrast candidate are small circulation times into the body and incompetent discrimination between normal and diseased tissues. Consequently, macromolecular Gd(III) complexes have been built up by conjugating Gd(III) chelates to biological polymers, comprised poly

(amino acids), proteins and polysaccharides to achieve enhancement in image resolution and contrast. These macromolecular candidates have established finer contrast enhancement in support of imaging blood pool as well as cancer in animal model [83].

Liposome Mediated Drug Delivery System for Breast Cancer Management

Liposomes as a drug carrier, employed for the delivery of anticancer agents in vivo can be distinctively targeted to tumors through their coupling with a range of tumor cell-binding ligands [84]. The monoclonal antibodies (mAbs) are frequently used [85], while their wide use is limited by their instability as well as high production cost. Additionally, whole mAbs illustrate nonspecific uptake through the phagocytic cells arbitrated by their Fc region as well as due to large in size not able to efficiently penetrate solid tumor. Smaller antibody fragments (e.g., Fab', scFv) lacking the Fc region can improve tumor penetration and biodistribution of targeted drug carriers [86]; however, amalgamation of mAbs as well as antibody fragments with drug-loaded nano-carriers need special task. The integration of phage-display expertise with a nanocarrier-based drug delivery policy is promising as a new approach [87].

A recent study of Wang T et al. suggested enhanced efficiency of drug-loaded liposome customized with tumor precise phage fusion coat protein that specifically perform recognition and killing targeted tumors. The amalgamation of nanotechnology with combinatorial phage technique corresponds to a paradigm shift during the development of more efficient, novel and target specific nano-medicines [88].

Miscellaneous Nano-Particles Promising in Diagnosis and Therapeutic in Carcinoma of Breast

Selective Targeting of Carcinoma of Breast with Calcium Phosphate Nanoparticles

Calcium phosphate nanoparticles (CPNPs) have been technologically engineered to be non-toxic vector for the deliverance of various therapeutic as well as imaging agents in in-vivo condition [89, 90]. Preliminary in-vivo imaging trials confirmed that CPNPs, functionalized through polyethylene glycol (PEG), accumulated in solid tumors through the effect of enhanced permeation retention (EPR), whereas EPR works as an efficient passive targeting approach, particular attention lies on the ability to actively target tumors to deliver anti-neoplastic drug, thereby declining effective dosage and restrictive off-target toxicity.

Recent studies validate CPNPs bioconjugation of anti-CD71 antibody, holotransferrin, and short gastrin peptides through a novel PEG-maleimide-coupling or an avidin-biotin- strategy. The conjugation of avidin conjugated CPNPs (Avidin-CPNPs) to biotinylated anti-CD71 antibody (anti-transferrin receptor antibody) and biotinylated human holotransferrin (diferric transferrin) allows transferring receptors targeting, which are highly expressed in carcinoma of breast cells. In the same way, the conjugations of Avidin-CPNPs to biotinylated pentagastrin and PEG-CPNPs to decagastrin (gastrin-10) through PEG-maleimide pairing allows targeting of gastrin receptors (GR) that are over expressed in lesion of pancreatic cancer. The theranostic modality has been performed potentially with these bioconjugated CPNPs and at the same time they are enhancing drug delivery, imaging and targeting of pancreatic and breast cancer tumors [91].

Human Serum Albumin (HSA) Nano-Particles

Nanoparticles of the least size can increase drug metabolism efficacy with negligible side effects since they allocate for the prospect of site-specific targeted delivery. HAS nanoparticles can be well tolerated devoid of any severe side effect that supported by clinical trials/studies through registered HAS-based nano-particle formulations as Albunex [92, 93]. Albumin has been made known to be biodegradable, easy to purify, nontoxic and water soluble, allowing effortless delivery by injection and therefore an ideal agent for nano-particle foundation.

A recent study of Sebak S et al. accounted for the first time the assimilation and targeted delivery of noscapine-loaded HSA nano-particles to tumors. The nano-particles were mechanically designed and optimized to attain a material size in the range of 150–300 nm with 85 %–96 % drug-loading efficiency. These nano-particles were assessed in vitro for their antitumor activity as well as efficacy on carcinoma of breast [94].

Current Ongoing Clinical Study with Nano-Particles

The approval of drugs for human use by the US Food and Drug Administration (FDA) through the Center for Drug Evaluation and Research (CDER) is a time-consuming and expensive process, and approval rates are low [95, 96]. In general, the FDA drug approval process can be separated into preclinical, clinical, and postmarketing phases. At each step from the point of discovery through demonstration of safety and efficacy in humans, drug candidates are closely scrutinized. Advances in nanotechnology are being applied in the development of novel therapeutics that may address a number of short comings of conventional small molecule drugs and may facilitate the realization of personalized medicine [97–99].

Recently Charles LU et al. 2012 reported for the first time in-human systemic gene therapy clinical trial of tumor suppressor gene TUSC2. In his study patients with recurrent and/or metastatic lung cancer previously treated with platinum-based chemotherapy were further treated with escalating doses of intravenous N-[1-(2,3-dioleoyloxy)propyl]-N,N,N-trimethylammonium chloride (DOTAP): cholesterol nanoparticles encapsulating a TUSC2 expression plasmid (DOTAP:chol-TUSC2) every 3 weeks. Thirty-one patients were treated at 6 dose levels (range 0.01 to 0.09 milligrams per kilogram). He concluded that DOTAP: chol-TUSC2 can be safely administered intravenously in lung cancer patients and results in uptake of the gene by human primary and metastatic tumors, transgene and gene product expression, specific alterations in TUSC2-regulated pathways, and anti-tumor effects [100].

Discussion and Conclusion

Nanotechnology advancement opens an innovative possibility for imaging and management of carcinoma of breast. Antibody conjugated nano-materials offers the new approach of simultaneous recognition of small tumor at multiple molecular targets on which therapeutic decisions can be made. Gene and protein expression in a particular tumor can be correlated through employing nano-particle tag. Imaging through the use of nano-particles in vivo is speedily growing and it could also allow concurrent recognition of antigens related to cancer.

These Nano-particles offer a novel approach for tumour targeting, already to be had in clinical practice, which may concurrently decrease the toxicity and improve the efficacy of accessibility to new anticancer drugs. QDs have already fulfilled a number of their promises as an incredible class of agents for molecular imaging. Through their versatile polymer coatings, QDs have also provided a 'building block' to assemble multifunctional nano-structures and nano-devices. The distinctive stability and spectral assets of QDs have directed to their rapid implementation for a large range of molecular imaging applications. Photostable properties of QDs allow them for extremely long exposures and afford increased levels of target mRNA sensitivity. Quantum dots have also a wide excitation range, offering flexibility in the wavelength utilized for excitation. Further, the advancement of QDs in the vicinity of infrared range, a frequency that penetrates tissue, supplies fluorophores compatible for the recognition of molecules in thick sections. The use of nanotechnology possibly will revolutionize the breast cancer management in near future.

Persistence of these multidisciplinary studies will be required to authenticate products. For instance, nanoparticle-based contrast agents are being constructed to be selective to molecular receptors, which will necessitate expertise in target recognition, biochemistry, colloidal chemistry, stabilization and analysis.

Prospects of nanoparticles in molecular imaging appear promising. Synthesis approach should persist to build up biocompatible, non-toxic and bio-degradable nanomaterials that overcome nonspecific organ uptake. Scientists working in this prospect should also believe potential costs of executing sophisticated molecular imaging instrumentation and be thoughtful to the challenges of handling as well as interpreting huge data sets obtained employing nanoparticle contrast agents.

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