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Review Article

Advancement and applications of nanotechnology in breast surgery: a comprehensive literature review

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ABSTRACT

Breast cancer is the most common malignancy affecting women worldwide and remains a major cause of cancer-related mortality. Although conventional treatments such as surgery, chemotherapy, and radiotherapy are effective in early stages, their efficacy decreases in advanced and metastatic cases. Nanotechnology has emerged as a transformative approach in oncology, offering precise diagnosis, targeted therapy, and innovative surgical applications. This review synthesizes recent literature on nanotechnology-based strategies in breast cancer management, emphasizing diagnostic imaging, targeted drug delivery, surgical enhancement, and postoperative wound healing. Databases including PubMed, Scopus, and Google Scholar were searched for relevant studies published between 2015 and 2024, focusing on preclinical and clinical advancements. Nanomaterials such as liposomes, micelles, dendrimers, and metallic nanoparticles have shown significant promise in improving therapeutic efficacy through site-specific delivery and controlled drug release. Intraoperative imaging agents and nanoprobes facilitate accurate tumour margin identification and sentinel lymph node (SLN) mapping. Nanofibers and nanohydrogels enhance wound repair and reduce infection risk. Emerging theranostic and nanorobotic systems integrate diagnostic and therapeutic functions, improving surgical precision while minimizing tissue damage and systemic toxicity. Nanotechnology is reshaping the landscape of breast cancer surgery and treatment. Its integration into diagnostic and therapeutic protocols enhances precision, minimizes invasiveness, and optimizes patient outcomes. Despite promising preclinical evidence, clinical translation remains limited by challenges such as biocompatibility, immune clearance, and regulatory barriers. Continued interdisciplinary research is essential to advance nanotechnology toward safe, effective, and personalized breast cancer care.

Keywords: Breast surgery, Nanotechnology, Targeted drug therapy, Diagnostic imaging, Post-operative wound healing

INTRODUCTION

Breast cancer remains the most prevalent malignancy among women worldwide, with significant morbidity and mortality due to recurrence and metastasis. Traditional treatment approaches-including surgery, chemotherapy, radiotherapy, endocrine, and immunotherapy-have been effective in early stages but show limited efficacy in advanced or metastatic disease.[1] Nanotechnology has emerged as a transformative field offering diagnostic, therapeutic, and surgical advancements, particularly through nanomaterials, nanomedicine, and nanorobotics.

LITERATURE REVIEW

This review synthesizes recent literature on nanotechnology-based strategies in breast cancer management, emphasizing diagnostic imaging, targeted drug delivery, surgical enhancement, and postoperative wound healing. Databases including PubMed, Scopus, and Google Scholar were searched for relevant studies published between 2015 and 2024, focusing on preclinical and clinical advancements.

Nanomaterials such as liposomes, micelles, dendrimers, and metallic nanoparticles have shown significant promise in improving therapeutic efficacy through site-specific delivery and controlled drug release. Intraoperative imaging agents and nanoprobes facilitate accurate tumour margin identification and SLN mapping. Nanofibers and nanohydrogels enhance wound repair and reduce infection risk. Emerging theranostic and nanorobotic systems integrate diagnostic and therapeutic functions, improving surgical precision while minimizing tissue damage and systemic toxicity.

NANOTECHNOLOGY FOR CANCER DETECTION AND IMAGING

Breast cancer is the most common cancer in women with a study as of 2017 in the United States approximating that about 160,000 patients with advanced breast cancer were diagnosed.[1] Breast cancer has higher incidence in high-income countries comparing to low-income countries due to the influence of multiple factors, such as environmental factor, lifestyle and genetic susceptibility entitling the activation of hormone receptors (estrogen receptors and progesterone receptors), BRCA mutations and human epidermal growth factor receptor 2 (HER2, encoded by ERBB2). Intrinsic classification includes four subtypes of breast cancer: Luminal A and luminal B, triple negative breast cancer (TNBC) and HER2-enriched. On the other hand, clinical practice categorises five breast cancer subtypes (luminal A, luminal B, HER2-enriched (HER2+), normal-like and basal like) based on molecular and histological characteristics, including TNBC. TNBC is defined according to the following criteria: high Ki67 index tumors, high grade, and estrogen receptor-negative (ER-), progesterone receptor-negative (PR-), HER2-, either NST (no special type) histology or special type histology (adenoid cystic, metaplastic, secretory, medullary-like). Nanotechnology has advanced the treatment of breast cancer to a greater extent.

Nanotechnology has distinctive physicochemical properties which includes a high surface volume ratio. Recently nanomaterial-based drug delivery systems, including liposomes, nanoemulsions and micelles, micelles are commonly used. Nanomaterials can load and bind bioactive molecules which includes RNA, DNA, proteins and drugs. These bioactive molecules have ability to cross multiple biological barriers easily transporting to the target. Hence, nanomaterials are generally used in the delivery of drugs for the treatment of different cancers improving the effectiveness of chemotherapy combined with photodynamic cancer therapy and radiotherapy. For complete eradication of tumour, therapeutic agents could infuse at very high levels. Furthermore, in nanotechnology-based cancer immunotherapy, nanoparticles carry high concentrations of anti-cancer drugs, natural killer cells and T cells, which eventually achieves a long term anticancer immune response due to decreased level of immune regulators. Improvements in nanotechnology, including virus-like sizes that can be tailored to explicitly target specific cell types which can be extensively used in designing cancer vaccines.[2]

Nanosystems are the new advancement of nanomedicine which crosses biological barriers like blood-brain barrier. Among the nanosystems, nano-lipid carriers have more advanced features strong compatibility, viability to scale up, increased capabilities of drug loading, and regulated release of drugs. In addition, nanoparticles which vary in size from 1-100 nmm also are used to synthesize anticancer, anti-infective and anti-inflammatory medicines. Due its smaller size and lipophilic nature, it is easy to formulate and entrap molecules forming nanodroplets. With the help of nano-emulsion system, nanoparticles are transmitted to surface of cancer cells.[1]

In females, the mortality rate of breast cancer is highest among malignant tumours due to metastasis and recurrence. For application of tumour therapy, nanomaterials can be used for their ability to target tumour sites by the enhanced permeability and retention (EPR) effect.[3]

NANOTECHNOLOGY IN WOUND HEALING AND SURGICAL APPLICATIONS

Nanotechnology plays important role in wound healing with the use of skin regeneration. As it has structural similarity to the extracellular matrix, nanofibers operate as framework for skin regeneration operating as delivery system for growth factors, proteins, medicines and other compounds assisting in tissue healing. In accordance with circumstances of wound healing, the capabilities of nanofibrous materials like biodegradability, shape can be modified which can eventually have several advantages like reduced drugs cytotoxicity, increased skin penetration, administration of poorly water-soluble drugs, properties of controlled release, protecting drugs against light, enzymes, temperature or pH degradation, antimicrobial property, reducing inflammation and stimulating proliferation of fibroblast.

The correct detection of cancerous tissues and complete removal with adequate negative margins are the main concerns for surgeons. The nanoparticles have distinctive features of EPReffect. Gold nanoparticles are characterised by large surface areas and "surface plasmon resonance". These effects have several advantages including treatment of prostate cancer, spectroscopic cancer imaging, functionalized imaging agents to detect cancer with lesser side effects comparing to chemotherapy. The approach combining diagnostic approaches and medicines is called theragnostic which helps in assessing tumour margins, mapping SLNs, identifying micrometastases and recurrent tumour cells. These features enable surgeons adequately removing the tumour cell increasing the survival rates of patients and helps to detect vital structures, eventually decreasing risks of morbidity. When solid tumours collect nanomaterial, the surface area is increased which helps to combine various diagnostic and therapeutic substances for theragnostic.[4]

NANOMEDICINE IN BREAST CANCER TREATMENT

Nanocarriers and drug delivery

Contrast agents and drug delivery carriers based on nanotechnology has contributed to more accurate and targeted disease diagnosis and treatment. Nanocarriers are mostly composed of lipids, metals, polymers, proteins and nucleic acids. These advanced nanoparticles can encapsulate probes or drugs coating with specially modified ligands binding to receptors cell sites and eventually affect cell function for the precise and effective diagnosis and treatment of disease.

Some nanoparticles have been advanced into biomolecular vectors that has potential to detect the biomarkers of cancer playing an important role in cancer detection and monitoring cancer biomarkers, including DNA and RNA fragments, proteins and antibody fragments. Nanobiosensors are very sensitive and within seconds can identify multiple protein biomarkers. In addition, nanotechnology assisted molecular diagnostic technology has been progressively implemented in imaging applications encouraging the identification of cancer at earlier stages.

Nanodrug delivery systems mostly depend on increased diffusion and retention effects for drug delivery. Generally, nanoparticles that can be useful to cancer treatment having the following physiochemical properties: appropriate encapsulation ability, tailored conformation and size, discerning localization, increased internalization of cancer through endocytosis, improved adhesion to the cancer environment, continued and controlled drug release, reduced systemic toxicity, safe biological elimination, and a long half-life.[1]

Biogenic nanoparticles

Biogenic nanoparticles are also used which are bio-inspired, conjugated nanoparticles synthesized with biological systems like plants, fungi, algae, microbes and phytochemicals. Biogenic nanoparticles have several advantages over chemical and physical nanomaterials including sustainable, environment friendly and hence does not require harmful chemicals; can be synthesized from microbial and plant extracts which reduces cost, having biocompatibility can be used for several biological applications like drug delivery, tissue engineering and imaging. These nano-biocomposite's anti-cancer potential has been investigated on MCF-7 cell line by MTT assay which showed that when treated with the L-asparaginase conjugated zinc oxide nano-biocomposite, the cell viability to 35.02% in MCF-7 cells.[5]

NANOTECHNOLOGY IN EARLY BREAST CANCER

Nanoparticles usage in early breast cancer is rapidly developing to reduce the need for aggressive form of treatments such as mastectomies. New treatment strategies were required which promotes precise lumpectomy by eliminating residual cancer cells with limited side effects to reduce local recurrence. It has been mentioned in studies; residual cells are found in 20-55% of the time at the first operation which is associated with increased incidence of local recurrence.[6]

Promising benefits of nanotechnology include aids in early breast cancer detection and precise imaging of cancer cells. Nanoparticles are gaining popularity for its potential in targeted drug delivery, which concentrates treatments at the tumour site while minimizing side effects on healthy cells and, enabling earlier and more effective treatment interventions.

Benefit of nanotechnology in early breast cancer is early detection of tumours is where they can be used as contrast agents for imaging techniques like MRI and CT scans, increasing the visibility of tumours and microcalcifications for more accurate and earlier detection of cancer cells and metastases, improving diagnostic capabilities. Moreover, nanoparticles can be conjugated with antibodies to detect and quantify specific cancer biomarkers in histopathology tumour samples, aiding in early and accurate diagnosis.[7]

Other application of nanoparticles along with targeted drug delivery to cancer cell is also improved drug efficacy where encapsulated drugs in nanoparticles increase their solubility, stability and circulation time with higher concentration delivery to cancer cells.[8] Nanoparticles have been recognized for their collaborative work where the particles have ability to integrate with existing treatments, such as immunotherapy, to enhance their effectiveness and achieve synergistic effects. Some nanoparticles are known for their promising strategy to reduce tumour growth and suppress cancer-promoting genes at a genetic level, thereby lowering recurrence risk. These smart nanoparticles are designed to exploit the acidic environment of a tumour to trigger the release of their genetic payloads, leading to effective gene silencing.[9]

Nanotechnology is an increasingly promising field with significant potential for improving the accuracy with complete removal of the early breast cancer which will potentially reduce the need for more extensive surgical procedures.

NANOTECHNOLOGY IN METASTATIC BREAST CANCER

Usually breast cancer metastasises in lungs, bone, brain and liver and lung is the second most common metastatic site contributing to 60%. When the tumour has distant metastasis, breast cancer remains untreatable due to less options of treatment. The breast cancer metastasis to lung is a complex process influenced by several factors. Recent data suggest that the incidence of lung metastases in TNBC is very aggressive, contributing to (21-32%). Currently clinical treatment of breast cancer includes surgery, radiotherapy, chemotherapy, endocrine therapy, immunotherapy, targeted therapy. Although these traditional treatments have good clinical effect on early breast cancer, it has less effect on breast cancer with lung/distant metastasis. The implications of nanotechnology have been very effective modality in treating metastatic breast cancer as it has efficiency for improved delivery of drugs, biocompatibility, controlled release and therefore advancing drug efficacy reducing side effects by targeting multiple sites of metastasis at the same time which eventually improve therapeutic effects. The addition of nanoparticles in the drug increases the drugs' solubility, the time of drug circulation can be improved by modifying carrier platform which controls the drug release and reduced drug resistance. The drug delivery system includes three processes including avoiding drug elimination in blood circulation while they are outside the cell membrane, increasing drugs' uptake while they are inside the cell membrane, improving response to cellular environment and eventually release drugs. Currently most used nano-drug delivery system includes polymers, liposomes, carbon, metals, biological etc. The process of drug delivery system targeting metastasis includes two stages, firstly targeting specific organ having metastasis and secondly targeting subcellular organs or cancer cells. Currently there are two approaches for targeted tumour delivery- active and passive targeting. Active targeting discusses about ligand binding to receptor which are expressed on the nanomaterials, so that nanomaterials can bind to the cancer receptor cell and hence act as a role for targeting and responding to stimulation can have controlled release effects. There are several approaches which can increase the ability of the drugs to target tumour cells reducing the interference of the drugs with normal cells and therefore improves the drugs' effect reducing side effects.[10]

In patients with metastatic breast cancer, increasing the dose of radiation can be essential specially for patient having re-irradiation for local recurrence after breast conserving surgery (BCS) and adjuvant therapy for stereotactic radiosurgery. Gold particles could be used in these patients. Gold nanoparticles are used for breast cancer detection where two-photon-induced photoluminescence (TPIP) can be used for visualization of tumour cells inserted with gold, with treatment of trastuzumab-PEG-AuNS, HER-2 positive SK-BR-3 cell line was detected utilizing 10% of laser power of TPIP imaging where normal breast cells were not visualized.[11]

INTRADUCTAL AND LOCALIZED NANO-MEDICINE

Ductal carcinoma *in situ* (DCIS) is type of invasive carcinoma where there is abnormal proliferation of epithelial cells in breast duct exhibiting slow pattern of growth. Radiation has been the treatment modality but does not affect survival rate. The intraductal administration of targeted therapy with nanotechnology can improve the drugs' therapeutic effects. These effects can prolong the retention of drugs which may reduce the administration frequency and increase the outcome of treatment. One of the principles of intraductal treatment is "sick lobe theory'' which explains entire lobe is compromised instead of just the revealed area in images. As surgical removal is not considered for excision of the whole lobe, theoretically direct treatment in specific ducts can reach the whole lobe.[12]

For locally advanced breast cancer (LABC), neoadjuvant therapy is widely used which allows patients to appropriate for radical surgery and subsequent adjuvant therapy. For LABC, assessment with imaging and pathological diagnosis are essential to determine tumour invasion extent, subtypes and features. According to response evaluation criteria in solid tumors (RECIST), neoadjuvant therapy assesses the efficacy and tumour burden as SD (stable disease), PR (partial response), CR (complete response) and PD (progressive disease). Patients who have positive response to treatment with significant reduction in tumour size or complete response (CR/PR), would qualify for mastectomy or BCS. The nanomaterial contrast agents have significantly improved resolution of MRI, CT and PET-CT enhancing accuracy of tumours and assessment of imaging.[13]

NANOTECHNOLOGY IN TNBC

TNBC is the most aggressive type of breast cancer which is well known for poor prognosis. Usually required neoadjuvant chemotherapy and surgery; however, chemotherapeutic resistance and relapse of tumours limit the progression free survival and patient life span. Recent advances in nanotherapy in the last few decades has offers significant promise for treating TNBC by overcoming the limitations of conventional chemotherapy, reduction in side effects of the systemic drug administration and by enhancing targeted drug delivery and boosting immune responses. The important aspect of nanoparticles has been spotlighted in cancer research due to their target specific multifunctional characteristics including site specific targeted drug delivery, enhanced drug solubility and overcoming multi-drug resistance. Moreover, nanoparticles can be engineered to carry both chemotherapy and

Immunotherapy drugs, to create powerful chemoimmunotherapy approaches that remodel the tumour's immunosuppressive microenvironment which deliver more precisely to cancer cells, reducing toxicity to healthy tissues and increasing drug effectiveness. Different types of nanoparticles are used in that in clinical trials including liposomes, dendrimers, polymeric nanoparticles, cell derived nanoparticles and metal and inorganic nanoparticles. Polymeric (L-lactide-co-glycolide) (PLGA) is the most studied polymeric carrier for drug delivery and has advantages over lipid-based systems in the aspect of extended circulation time and higher accumulation inside tumour cells. Lipid-based nanocarriers like liposomes are spherical vesicles that can encapsulate drugs and provide better drug distribution throughout the body with high biocompatibility. Metallic and inorganic Nanomaterials like gold nanoparticles can be used for photothermal therapy, generating heat to destroy cancer cells when exposed to light. Cell derives nanoparticles coated with cell membranes, such as those from red blood cells, to increase their circulation time in the body and enhance targeting. Carbon-based nanoparticles are most versatile. In addition to having the advantages of both lipids and polymers, they possess conductive properties that can contribute to the detection and diagnosis of cancers. The rapid evolution of nanoparticle formulation in clinical practice is helpful for suppressing angiogenesis and tumour progression pathways responsible for TNBC. Also, it's worth to mention, CRISPR targeted nanoparticles are emerging to precisely target to modify genes within the cancer cells to remove faulty genes responsible specific protooncogene mutation in TNBC.[14]

NANOTECHNOLOGY IN SLN BIOPSY

Sentinel node biopsy (SNB) is used for axillary staging in patients with breast cancer which is the first draining lymph node of primary tumour. This biopsy requires blue dye and radiolabled tracer with meta-analysis showing 96.4% of sentinel node identification rates and 7.3% of false negative rate. This technique has drawback of depending on radioisotopes and requires transport, handling, access to nuclear medicine and disposal. Blue dye can adversely effect of prolonged skin discoloration and in 0.9% cases it might cause anaphylaxis. With the use of magnetic technique for SNB, superparamagnetic iron oxide (SPIO) nanoparticles are injected interstitially which are identified by a handheld magnetometer intra-operatively and by visualization of node's brown-black staining which has sentinel node identification rates of 97.1%. Selected axillary surgery involves removal of only metastasis involved nodes where multimodal MRI are used. Magnetic nanoparticles (MNPs) are used non-invasively in conjunction with radiolabeled bisphosphonates for better anatomical visualization. In triple modal imaging, magnetic nanocapsules which are encapsulated with hydrophobic SPIO can target solid tumours following intravenous administration which are demonstrated to achieve two-fold rise in tumour uptake in murine model when applied in static magnetic field. The probes utilize MRI, fluorescence and nuclear imaging providing substantial information and discrete distribution of nanocarriers. This also includes fluorescent-ferrite beads of fluorescent europium complexes and magnetic iron oxide labelled with antibodies. The multimodal probes help with pre-operative imaging to characterize and quantify lymph node burden. Open surgery can be performed with the help of handheld magnetometer identifying hot spots of accumulation of magnetic tracers and therefore identifies metastasis involved lymph nodes. Under MRI guided vision, minimally invasive percutaneous technique can also be utilized.[15]

SLN biopsy is useful in axillary lymph nodes biopsy. Radiocolloids and organic dyes are used for mapping of SLN, but this causes exposure to radiation resulting in tissue damage. Quantum dots (QD) can be used for SLN mapping without the requirement of biopsy. Though surgical resection for the primary tumour is the treatment of early breast cancer, as it is difficult to assess tumour margins, often cancer cells lead to recurrence. For image guided resection tumours, functionalised QD can be used for visualization of cancer cells. Near infrared QD has better penetration of deep tissue and photostable. Cadmium-free QD are also in stage of trial for potential cancer diagnostics. QD are nanocrystals which are 2-10 nm in size where the surface could be coated with different molecules reducing toxicity, increasing solubility and allowing targeting to tumour markers. Usually, QDs are colloids where core is made of semi-conductor of group II/IV metals, like cadmium sulphide, cadmium/technetium and cadmium/selenium.

SLN mapping (lymphoscintigraphy) is necessary for surgeries of various cancers including breast carcinoma. Currently SLN mapping procedure includes injecting a blue dye and/or acidic sulfur-radiocolloid which is monitored by gamma probes sometimes with the help of X-rays to detect SLN. During primary tumour resection, for achieving complete elimination of malignant cells, all remnant cancer cells have to be removed. If cancer cells remain following surgery, they can result in relapse in 20-40% of patients. In a clinical trial, intra-operative real-time fluorescence imaging was utilised for visualization of breast cancer cells. Overexpression of Human epidermal growth factor receptor 2 (HER2) occurs in 25-30% of invasive breast cancers. HER2 is a predictive and prognostic biomarker associated with decreased survival rates with increased tumour growth. HER2 positive breast carcinomas are usually aggressive and have poor prognosis. NIR-QD (near infra-red QD) could be considered as alternative to intra-operative imaging and SLN mapping.[16]

MNPs are emerging new technologies where multifunctional and dual nanoparticles are used. Currently MNPs can be used in SLN biopsy (SLNB), magnetic hyperthermia, drug delivery system and imaging of metastatic and primary disease. MNPs helps to provide focused therapy which could decrease adverse effects of cancer therapies.[17]

Dual localization is well known and considered reliable and practical approach to determine impalpable axillary lymph node mapping with reasonable accuracy. However dual localization which involved using blue dyes and radioactive colloids for mapping can be associated with adverse effects such as allergic reaction to the blue dye, short retention time, trainset skin staining in urine or skin colour, and radiation exposure from radioisotope. In recent years, it's has been reported that integration of nanotech with SLN biopsy offers higher accuracy, improved patient safety by eliminating radiation, and potential theranostic capabilities for more effective cancer management. Nanoprobes probes can be used with adjustable optical and magnetic properties for better visualization of SLNs, even with deep tissue penetration with precise localization which can improve better visualization with elimination of the risk associated with radioactive material. Moreover, nanoparticles can be engineered to carry both diagnostic and therapeutic agents, enabling targeted drug delivery and combined imaging and therapy. Inorganic nanoparticles based on iron oxide, QD and organic nanoparticles based on nanogels, liposomes have been used for SLN mapping. SPIO nanoparticles used for magnetic detection and imaging of SLNs, offering comparable or superior detection rates to traditional methods without radioactivity. Also, QD which are fluorescence-based nanoprobes with potential for deep-tissue penetration and photostability, allowing for non-invasive imaging providing entirely radioactive-free localization. Properties of nanoparticles are related to its shape, size and biocompatibility. Small size below 50nm is considered ideal size for SLN retention to help to improving the visualization and identification of SLNs during the biopsy procedure.[18]

NANOTECHNOLOGY IN BREAST CANCER SURGERY

Wire localization has been standard for pre-operative breast tumour localization which helps with intra-operative localization. Currently recent advancements include non-wire devices such as radar reflectors, magnetic and radioactive seeds and radiofrequency identification tags. The gold standard for intraoperative localization of SLN is the dual tracers combining radionuclide and methylene blue dye which achieves a lower false-negative rate (FNR) (<5-10%) and higher SLN identification rate (>90%). Nevertheless, it has disadvantages like radiation exposure, allergic reaction and inadequate targeting. To avoid all these disadvantages and to achieve more precise assessment of tumour margins, fluorescence imaging and nano-radiopharmaceuticals have developed real-time surgical navigation. With help of evolving nano-radiopharmaceuticals, Derya et al developed an innovative technetium-^{99m}-labeled trastuzumab-decorated methotrexate loaded human serum albumin nanoparticles, abbreviated as [^{99m}Tc]-TRZ-MTX-HAS which has higher cellular binding percentage with MCF-7 cells.

Nanomedicine is helpful with intra-operative lymph nodes and tumours localization where nano-radiotracer can be used for breast cancer imaging with help of ^{99m}Tc-Anionic dendrimer targeted vascular endothelial growth factor. Also, with help of near-infrared turn-on fluorescent nanoprobes, image guided surgery can be performed for precise detection of tumour margins. In addition, a fiber optoacoustic guide can be used to detect implanted biopsy clips. Although pathological examination is gold standard to assess tumour margins, it could be time consuming. For evaluating tumour margins, nanoparticles like NIR-II fluorescence imaging guided surgery can be beneficial where synthesized Gd-coated and tetrasulfide bonds doped mesoporous virus-like SiO_2 nanoprobe are used with surface modification of folic acid and encapsulated with indocyanine green, named as VGd@ICG-FA. These nanoparticles have virus-like morphology facilitating strong adhesion to tumour cells.

Intra-operative fluorescence has more advantages like strong sensitivity and differentiation, safety, simplicity, and affordability. 'Smart probes' were designed to be active at tumour locations which is triggered by enzymatic degradation of cathepsin that expressed at tumour sites resulting in fluorescence signal production. The three Turn-ON probes were PGA-Cy5-Quencher (PCQ), PGA-Cy5 (PC), and HPMA copolymer-GFLG-Cy5 (P-GFLG-Cy5). In these probes, polymeric backbone composed of poly-glutamic acid are broken down by the enzymes which releases free dyes emitting fluorescence. The P-GFLG-Cy5 probe shows increased accumulation after 4 hours of intravenous administration in a model of breast cancer where position of tumour can be identified without invasive procedures.

To increase the sensitivity of probes to capture signals, a fiber optic acoustic guiding system (FOG) included with augmented reality (AR) to locate tumours accurately and deliver instinctive surgical navigation which can be surgically implanted prior to operative procedure. The FOG emits acoustic waves on exposure pulsed external light. An AR setup using ultrasound sensors' converts and coordinates FOG tip position into visual guidance. This helps surgeons to directly observe location of tumour and accurate resection of tumours which would eventually reduce reoperation rates and decrease duration of surgeries.

As mastectomy and breast reconstruction involves trauma to skin, subcutaneous gland and fat which might cause delayed wound healing by infection. Nanomedicine including dressings like nanofibers, hydrogels, and films can be of great help in wound recovery by the properties of drug incorporation, haemostasis, increased ability for absorption and antimicrobial functions. Following breast cancer surgery, due to deficiency of skin and changes in microenvironment in surrounding residual tumours, produces environment for colonization of bacteria. When bacteria are exposed to ZnO nanoparticle, cell membrane, genome and proteins disrupt leading to demise of cell. The Van-ICG@PLT nano-sensor mimics like platelets and therefore on exposure to the laser light the membrane permeability increases which helps in eradication of bacteria. In BCS patients usually have radiotherapy which reduces recurrence and improves survival. Due to lower levels of circulating tumour cells (CTCs), it is essential to develop a technology with higher specificity and sensitivity detection. The hydrogel systems implantation after resection has demonstrated improved efficacy. In addition, photothermal tumor ablation is an advanced treatment approach where heat produced by specific nanoparticles on exposure to light, eliminates cancer cells without radiation-related damage.[19]

The nanosystem is comprised of 24 monomers of H-Ferritin (HFn) which forms a spherical structure encompassing the indocyanine green, fluorescent tracer. Fluorescence-guided surgery (FGS) is an intraoperative procedure providing real-time fluorescence images during operation. It helps to visualize of tumour margin and identify tumour deposits. indocyanine green (ICG) is the most used probes which uses water soluble, tricarbocyanine fluorescent dye with extensive fluorescence emission in the wavelength region of near infrared (NIR). It is used in various surgical oncological applications, such as SLN mapping, angiography, lymphography, identifying solid tumours and intra-operative anatomical imaging. H-ferritin (HFn) nanoparticles act as a natural homing for cancer cells for its explicit recognition of the transferrin receptor-1 (TfR1), overexpressed in various tumour subtypes representing a molecule for tumour targeting because of its higher expression in tumour cells than normal cells. Its capacity to encapsulate fluorescent probes or drugs makes their platforms applicable in surgical oncology such as diagnostics and drug delivery. FGS helps with accurate tumour resection improving safety by decreasing damage to normal tissues which is beneficial for both cancer patients and surgeons.[20]

NANOROBOTICS IN BREAST CANCER

For precision surgery, the use of nanorobots has advanced cancer treatment. The commonly used miniature devices as microtraps, microgrippers and microdriller are widely used for incision operations, tissue penetration and sample collection. Self-folding thermo-magnetically responsive soft microgrippers are used biopsy or sample collection which combines stiff segmented polymer (polypropylene fumarate, PPF) with swellable, photo-cross-linked pNIPAM-AAc soft-hydrogel which is embedded with iron oxide (Fe_2O_3) nanoparticles helping microgrippers to remotely guided by external magnetic fields. In addition, cobalt-nickel microrobots helps in tissue penetration and nanoshells are used for intra-cellular delivery.

Nanorobots are biological combinations of molecular biological species and nanomechanical devices acting as miniature doctors which becomes molecular robots after injecting into human blood vessels. This is sometimes described as “nanosubmarine”. With the help of drug delivery nanocarriers which are functionally modified, tumour microenvironment could be precisely regulated. It blocks tumour vascular supply and causes vascular modulation in tumours.[21]

Nanomachines/nanomachines/nanomotors/nanorobots are pre-programmed or self-propelled bodies that can travel in the body being able to “sense-and-act” by detecting materials, kill cancer cells, drug delivery and microsurgery. Micro/nanorobots (MNRs) work as “motile-cancer targeting” helping in diagnosis and detection of early cancer executing precision tasks at nanoscale level (1-100 nm). In addition, these are used for gene therapy and precision surgery. MNRs are able to cross biological barriers like extracellular matrixes and blood-brain barrier and becomes nanosubmarines in bloodstream.[22]

CHALLENGES AND FUTURE PERSPECTIVES

Despite promising preclinical data, clinical translation of nanomedicine in breast cancer faces challenges including off-target effects, biodistribution variability, immune clearance, and regulatory barriers. For example, theranostic gold nanoparticles show strong laboratory efficacy but risk accumulation toxicity. Similarly, while QDs provide excellent imaging resolution, their long-term biocompatibility remains under investigation.

Future directions include: Personalized nanomedicine using biomarker-driven targeting, smart nanoprobes integrating diagnostics with therapy, biogenic nanomaterials for sustainable large-scale applications and nanorobotics for precision microsurgery and real-time intravascular monitoring.

CONCLUSION

Nanotechnology has revolutionized breast cancer management across the spectrum of prevention, diagnosis, surgery, and treatment. From nanofibers supporting wound healing to nanocarriers enhancing chemotherapy, from FGS to autonomous nanorobots, the field continues to push the boundaries of precision oncology. While translational hurdles remain, the integration of nanotechnology promises to transform breast cancer outcomes by offering minimally invasive, highly targeted, and multifunctional therapeutic strategies.

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