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Review RRJoOH

Recent Development Technique in Management of Cancer

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Abstract

Cancer develops when a change in one's genetic makeup leads to the development of tumour cells. These clusters of malignant cells eventually develop into tumours. Tumours can shed cancerous cells, which can then travel through the lymphatic system or the circulatory system to other organs. In the medical field, this occurrence is referred to as metastasis. Cancer cells proliferate even when they have no instructions to do so. Despite the notable advancements in medical technology, such as stem cell therapy, targeted therapy, ablation therapy, nanoparticles, natural antioxidants, radionics, chemodynamic therapy, sonodynamic therapy, and ferroptosis-based therapy, traditional treatment methods such as surgery, chemotherapy, and radiation remain prevalent. These traditional procedures continue to be utilised due to their established efficacy, widespread availability, and proven track record in treating various medical conditions across diverse patient populations. Today, oncology practices are centered on developing safe and efficient nanomedicines for the treatment of cancer. Nanoparticles have provided new diagnostic and therapeutic options, and stem cell treatment has shown extraordinary efficacy in regenerating and repairing sick or damaged tissues, including those at the main and metastatic cancer foci.

Keywords: malignancy, ablation therapy, ferroptosis-based therapy, radionics, apoptosis, sonodynamic-based therapy

INTRODUCTION

Cancer originates with mutations to the DNA of cells. Most of the cancer-causing DNA mutations occur in the genetic material. The term "genetic modification" can be used interchangeably with this term to describe these alterations. Cancer is the abnormal transformation of normally functioning cells into tumour cells, which occurs over the course of a multistep process spanning from precancerous lesion to malignant tumour. These alterations occur as a result of interactions between a person's genes and environmental variables (including physical carcinogens such as ultraviolet (UV) and ionising radiation). Apoptosis refers to a natural and helpful process that causes cells to die, despite its negative connotations. Cancerous cells lack the factors that normally signal cells to cease dividing and eventually die. They consequently amass throughout the body and devour oxygen and nutrients that might otherwise nourish other cells [1].

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Etiology

Lifestyle Elements: Smoking, a high-fat diet, and exposure to chemicals at work are all factors that have been linked to an increased chance of getting various types of cancer in adults [2].

Encounter with Certain Viruses: Hodgkin and non-Hodgkin lymphomas are among the paediatric cancers linked to an increased risk of contracting Epstein-Barr virus and HIV—the virus that causes acquired-immunodeficiency syndrome (AIDS). The

virus might cause cellular alterations. After that, the transformed cell divides to produce more of its kind, starting the vicious cycle of cancer [3].

Exposure to the Environment: Pesticides, fertilizers, and power lines have all been investigated for their possible links to cancer in children [4].

High dosage Chemotherapy and Radiation Therapy: Children who are exposed to these treatments have a marginally increased chance of growing cancer again as adults. These very effective anticancer drugs can alter immune system cells and molecules [5].

Tobacco & Smoking: In addition to causing cancer, smoking can prevent the body from launching an effective defense. Cigarette smoke contains toxins that suppress the immune system and make it more difficult to eradicate cancerous cells [6].

CANCER GENES

Our understanding of the disease has advanced significantly with the identification of specific gene types that are linked to cancer [7].

Types of Cancer Genes

Oncogenes: This set of genes controls how quickly or slowly cells divide. An oncogene is a mutated gene with the capacity to cause cancer. Proto-Apoptosis—a predetermined kind of fast cell death—is a process that most normal cells go through when crucial functions are distorted or failing. Oncogenes are healthy genes that stimulate cell growth and are mutated (gain-of-function mutation) to upregulate their expression, predisposing the cell to cancer [8].

Tumor Suppressor Genes: These genes are able to identify faulty proliferation and reproduction in cells that have been damaged or are cancerous, and they can halt cell division until the problem is resolved. In addition to the activation of cellular oncogenes, tumour growth is also facilitated by the inactivation of tumour suppressor genes. Tumor suppressor genes represent the other side of cell growth regulation since they normally work to reduce tumour formation and cell proliferation [9].

Mismatch Repair Genes: These genes play an important role in detecting faults that might occur during DNA replication, which is necessary for the creation of a new cell. If the DNA does not "match" exactly, these genes fix the mistake and make it a perfect match. DNA mutations in cells with impaired mismatch repair (MMR) frequently lead to cancer [10].

DEVELOPMENT & SPREAD OF CANCER

Step 1 - Initiation

Initiation is the first stage of cancer growth, during which a mutation in a cell's genetic make-up prepares it to produce cancer. The mutation, gene change, or external exposure to a substance that causes cancer could all be responsible for the alteration in the cell's genetic makeup (a carcinogen) [10].

Step 2 - Promotion

Promotion is the second and last stage in the growth of cancer. Environmental pollutants and some medications, such as sex hormones (used to increase a man's energy and sex drive) can act as promoters, or agents that generate promotion. Promoters do not by themselves cause cancer, unlike carcinogens. Instead, promoters permit a malignant cell to spread after it has experienced initiation. Promotion has no effect on cells that have not undergone initiation [11, 12].

Step 3 - Spread

Cancer can spread to nearby or distant tissues or organs or grow into (invade) surrounding tissue directly. The lymphatic system can help cancer spread. Carcinomas commonly spread in this manner. For instance, breast cancer typically spreads first to the local armpit lymph nodes before moving on to distant places. Bloodstream circulation can also help in cancer spread. Sarcomas frequently spread in this manner [13–15].

TYPES OF CANCER

Leukemias, lymphomas, and other blood-forming cancers are examples of cancerous tissues (malignancies), as are "solid" tumours (a solid mass of cells). There are two distinct kinds of malignant solid tumours—sarcomas and carcinomas. Squamous cell carcinoma of the skin is one example of a specific cancer that may be further classified based on the organ in which it initially manifests and the type of cell from which it originates [16,17].

Lymphomas & Leukemias: Lymphomas and leukaemias are cancers that begin in the immune system and spread to the blood and blood-forming tissues. Cancers called leukaemias start in the cells that make blood and prevent the bone marrow from producing healthy blood cells on a regular basis. Lymphoma cancer cells can spread to other organs and cause large lumps to form in the armpit, groine, abdomen, or chest [18].

Carcinoma: Carcinomas are cancers of the cells that coat the skin, lungs, digestive tract, and other internal organs. Cancers of the skin, lungs, colon, stomach, breasts, prostate, and thyroid are a few examples of carcinomas. Lung cancer is more common in older adults than in younger adults. Cancers known as sarcomas are derived from mesodermal cells. Muscle, blood vessels, bone, and connective tissue are frequently formed from mesodermal cells.

Leiomyosarcoma is a sarcoma that forms in the lining of the intestines; it is a cancer of the smooth muscle that lines the intestines (bone cancer). Cancer of the sarcoma more commonly strikes younger people than the elderly [19].

STAGES OF CANCER

A person's medical care may involve the staging of a malignancy at various points.

TNM Staging

Tumor (T): The tumour is denoted by the letter T and the number that follows it by providing the following responses, A letter, number, or string of letters are placed following the letter T. This provides more details about the tumour [20].

Node (N): The letter N and the number following it indicate whether or not lymph nodes have been afflicted by malignancy. Small, bean-shaped lymph nodes aid in the body's defense against infection. Only lymph nodes close to the malignancy fall under the N group (regional lymph nodes) [21].

Metastasis (M): Whether the cancer has spread is indicated by the letter M and the number that comes after it. M0 denotes the absence of metastases from cancer. Stage M1 cancer refers to cancer that has spread to other bodily parts [22].

Cancer Stage Grouping

Stage 0: They have not metastasized to nearby tissues. In many cases, cancer can be cured at this point.

Stage 1: At this point, most tumours have not metastasized—that is, they have not greatly spread to other bodily areas.

Stage 2 & 3: Malignancies that have spread farther into surrounding tissue are characteristic of these latter two stages.

Stage 4: This suggests that the cancer has progressed to other bodily regions.

NEWER TECHNIQUES IN MANAGEMENT OF CANCER

It has been observed that using various targeted treatments or "conventional" chemotherapeutics such as taxanes and platinum compounds in combination has a synergistic impact. Recently, there has been a huge advancement in the ability to target various pathways involved in the course of cancer therapy [23]. These routes and characteristics are necessary for the creation of a novel revolution in neoplastic

malignancy or drugs that target particular tumour entities. Chemotherapy is generally considered as the most effective and widely used cancer treatment method, either in combination with radiation therapy or on its own. Chemotherapy drugs typically target tumour cells by producing reactive oxygen species, which are the primary means of tumour cell death. In addition to being widely used for cancer malignancies, hormonal therapies are also known as cytostatic because they stop tumour growth by reducing the amount of hormonal growth factors that act through the hypothalamic-pituitary-gonadal axis (HPGA), obstructing hormone receptors, and reducing the amount of hormones produced by the adrenal glands [24–27].

Approaches in Treatment of Cancer

Stem Cell Therapy

Stem cells in bone marrow are unspecialized cells that can differentiate into any other type of cell in the body. The use of stem cells is another promising approach to treating cancer that has a good chance of being both safe and effective. Blood-forming stem cells can be damaged by high doses of chemotherapy or radiation therapy used to treat some cancers, but these cells can be restored through stem cell transplantation [28].

Autologous Auto Transplant: For an autologous (AUTO) transplant, doctors take healthy stem cells from the bone marrow or blood that are frozen and preserved with great care [29]. Since they are not within your body, they will not be harmed by the chemotherapy and radiation treatments needed to remove cancer cells. When the therapy is complete, the frozen stem cells are reintroduced into circulation by intravenous (IV) injection [30].

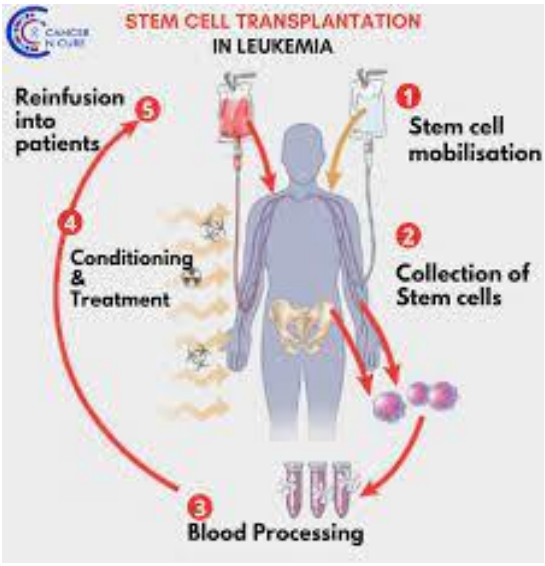

Figure 1. Procedure of stem cell transplantation in human body.

Allogenic Transplant: The healthy stem cells for an allogeneic (ALLO) transplant come from a donor. The donor's bone marrow needs to closely resemble that of the patient. By eliminating own stem cells, this primes the body to receive new stem cells shortly after treatment completion. In a cord blood bank, it can be frozen and kept until its stem cells are required. Before being stored, cord blood is examined. Generally speaking, stem cell therapy employs a range of techniques to treat cancer, including immune effector cell generation, mesenchymal stromal cell (MSC) infusion, therapeutic carriers, hematopoietic stem cell (HSC) transplantation, and vaccine production [31].

Targeted Drug Therapy

Treatment with medications or compounds intended to target cancer cells precisely is referred to as targeted cancer therapy [32]. These medications interfere with growth molecules, preventing cancer

from starting and spreading. Endothelium cells, pericytes, smooth muscle cells, fibroblasts, different inflammatory cells, dendritic cells, and cancer stem cells (CSCs) make up this TM. Small-molecule medications or monoclonal antibodies make up the bulk of targeted treatment [33]. Therapeutic antibodies are a kind of monoclonal antibody—a type of antibody that is synthesized in a laboratory. These proteins were engineered specifically to find their way to targets on cancer. Because of their diminutive size, small-molecule drugs are often used to reach their objectives inside of cells. Certain monoclonal antibodies can specifically target cancer cells, facilitating the immune system's destruction of such cells [34].

Monoclonal Antibodies

Antibodies are synthetic drugs that are injected into the body to attack specific targets on cancer cells. They are essentially proteins of the immune system. Their attack tactics include delivering a lethal payload, such as a radioisotope or poison, to the target cell, binding to ligands or receptors to disrupt essential cancer cell functions and activate the host immune system to attack the target cell. Monoclonal antibody targeting agents have the ability to deliver prodrug activation enzymes, active medications, and toxic chemicals used in chemotherapy. Examples of such antibodies include Blincyto®, which binds to both CD19 (a protein found on the surface of leukaemia cells) and CD3 (a protein found on the surface of T cells) [35–37].

Small Molecule Inhibitors

Due to their small size, small molecule cancer drugs have been used to successfully target intracellular proteins, such as anti-apoptotic proteins, which are essential for delivering downstream signaling for the promotion of cell growth and metastasis, as well as extracellular, cell surface ligand-binding receptors (Figure 2). Receptor tyrosine kinases (RTKs) are frequently chosen as primary targets for anti-cancer medications because their abnormal activation frequently triggers downstream signaling that activates crucial cytoplasmic kinases, most frequently serine/threonine kinases (STKs) [38].

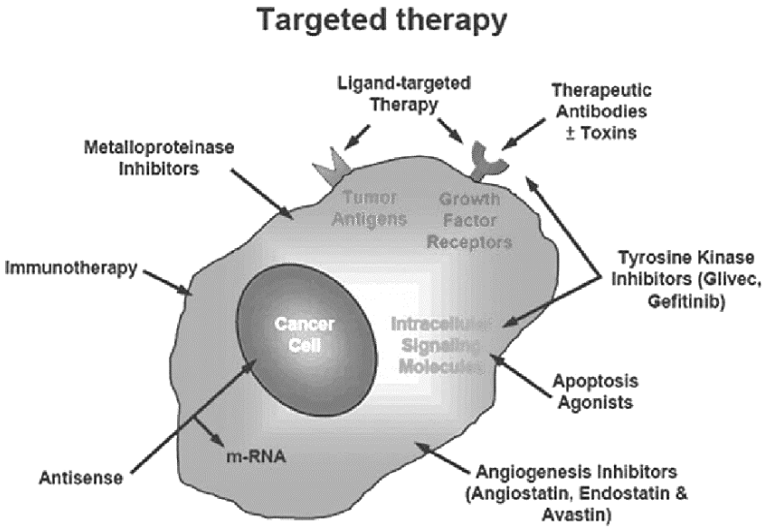

Figure 2. Different types of targeted therapy associated with respective targets for attack.

Gene Therapy

To treat a particular condition, a defective gene is replaced with a healthy copy in a process known as gene therapy (Figure 3). Using a retroviral vector, the adenosine deaminase (ADA) gene was first delivered to T cells in 1990 in individuals with severe combined immunodeficiency (SCID). The synthesis of proapoptotic and chemosensitizing genes, wild-type tumour suppressor genes, genes able to trigger specific anti-tumor immune responses, and targeted silencing of oncogenes are among the techniques being studied for cancer gene therapy [39].

Some of the ways in which gene therapy may be used to treat cancer include.

a. *Expressing* a gene to trigger apoptosis or to make tumours more sensitive to standard drug or radiation therapy.
b. *Substituting* the introduction of a wild-type version of a tumour suppressor gene for a deregulated or absent one.
c. *Employing* an antisense (RNA/DNA) method to stifle the expression of an oncogene.
d. *Boosting* the tumor's immunogenicity to bring in more immune cells.

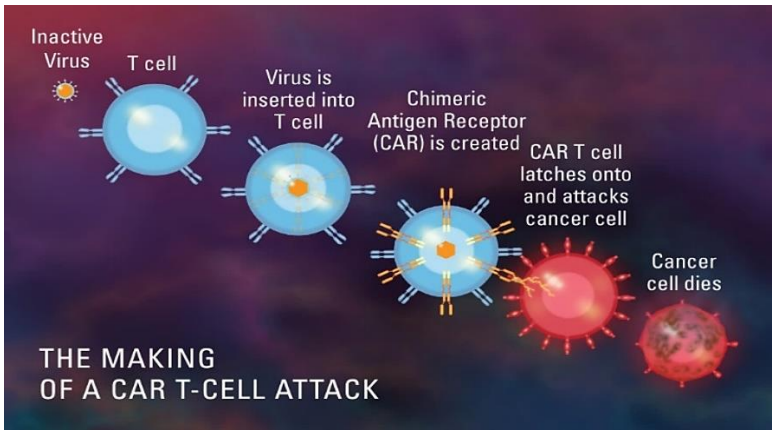

Figure 3. CAR T-cell therapy targets cancer cells more precisely by using T cells that have undergone specific alteration.

Ablation Therapy

This procedure is typically used for small tumours that are less than 3 cm in size. For bigger tumours, ablation is additionally combined with embolization. Treatment for solid tumours is accomplished using this minimally invasive surgical approach. Using specialist probes, malignancies are "burned" or "frozen" instead of undergoing the standard operation. The needle probe is guided and positioned inside the tumour using computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound [40–42].

Cryoablation Therapy

A tumour is eliminated during cryoablation by being frozen with a thin metal probe. After being guided into the tumour, the probe is filled with extremely cold gases that freeze the tumour and kill the cancer cells. One ablation technique, known as cryoablation, destroys large amounts of tissue by freezing it to a fatal temperature, causing liquid to form, and leaving behind no trace of the formerly large amounts of tissue [43].

Thermal Ablation

Similar to surgery, thermal ablation eliminates the tumour along with a margin of tissue that appears to be normal and is 5–10 mm thick, but that tissue is actually killed in situ and eventually absorbed by the body. The placement of the ablation probes during thermal ablation may be assisted using CT, ultrasound, or MRI technology [44].

Microwave Ablation

Heat is produced at the probe's tip when energy is applied. Over time, the dead tumour cells are gradually replaced by scar tissue, which eventually shrinks. Heat is produced during microwave ablation via the utilisation of dielectric hysteresis. Tissue damage occurs when an applied electromagnetic field, usually at 900–2500 MHz, heats tissues to fatal temperatures. The polar molecules in the tissue, primarily H_2O, are forced to realign constantly by the shifting electric field, which raises both the temperature of the tissue and their kinetic energy. Electromagnetic waves in the microwave frequency spectrum are used for microwave ablation [45].

Radiofrequency Ablation

High-energy radio waves are used. The physician inserts a small, needle-like probe into the tumour through the skin. The tumour is subsequently heated and the cancer cells are killed by a high-frequency current that is then fed via the probe's tip. It is a modified electrocautery technique. Radiofrequency ablation (RFA) has been used for many years to treat osteoid osteoma, prostate enlargement, chronic discomfort, and cardiac dysrhythmias caused by abnormal conduction pathways [46].

Ionic currents are fueled by radiofrequency electric fields in tissue, which results in resistive heating. RFA can be used with a variety of techniques to increase coagulation volume. The internal electrode cooling, multiprobe array electrodes, gradual or pulsed heating, and saline infusion are the most effective of these methods [47].

Ethanol (Alcohol) Ablation

Alcohol is used in the minimally invasive interventional radiology procedure known as "ethanol ablation" to kill malignancies (Figure 4). The location of a tumour is determined via CT imaging. The next step involves one of our interventional radiologists carefully manipulating a thin probe into the tumour via the skin. In order to harm cancer cells, pure alcohol is directly injected into the tumour during this operation [48].

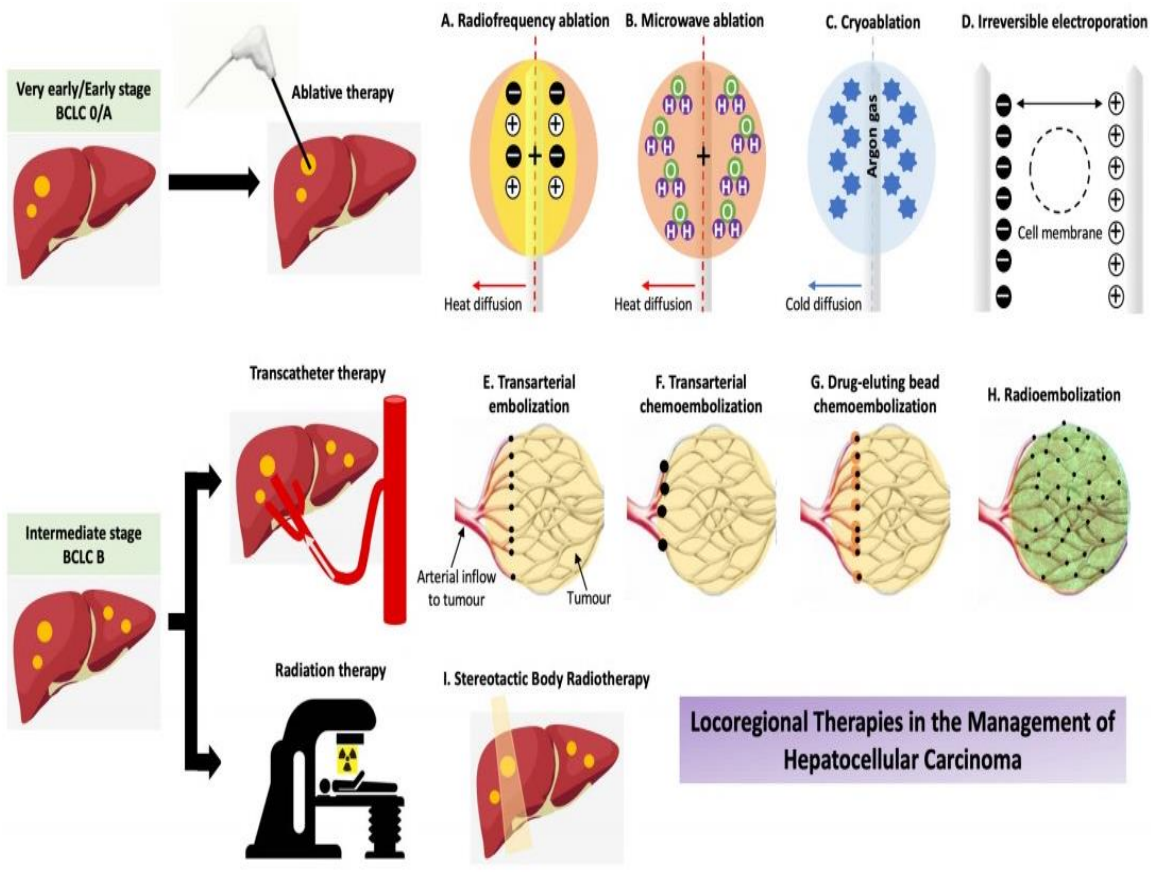

Figure 4. Locoregional therapies in the management of hepatocellular carcinoma.

Natural Antioxidants

Vitamins, polyphenols, and bioactive compounds derived from plants are used as preventive and therapeutic drugs against toxic molecules that damage the body because of their inherent anti-inflammatory and antioxidant properties. Numerous compounds, including vitamins, alkaloids, flavonoids, carotenoids, curcumin, berberine, quercetin, and others, have been evaluated as natural

antioxidants both in vitro and in vivo. Brussels sprouts, kale, broccoli, cabbage, collard greens, and cauliflower are examples of cruciferous vegetables. A generated particle, a tiny negatively-charged particle present in atoms, is what happens when an electron is gained or lost by an atom or molecule (a compound made up of two or more atoms). The body naturally produces free radicals, which are essential for many normal cellular processes. Free radicals can harm the body in excessive concentrations and harm all significant cellular components, including DNA, proteins, and cell membranes. In order to stop free radicals from doing harm, antioxidants interact with them and neutralize them [49].

Nanoparticles

Passive Targeting: Nanoparticle (NP)-based drug delivery systems have demonstrated promise in the treatment and management of cancer due to their accurate targeting, favourable pharmacokinetics, minimal side effects, and absence of drug resistance. Particles with a single dimension of less than 100 nm and unique characteristics that are usually missing from bulk samples of the same material are referred to as NPs. It was found that deep tissue penetration increases the enhanced permeability and retention (EPR) effect of NPs [50].

Targeting particular markers that are overexpressed by cancerous cells requires the attachment of biorecognition molecules to the surface of the nanovectors. These tactics have received the label "active targeting," which indicates greater specificity and effectiveness in reaching the targeted result. One of the most effective pharmacological classes used to treat cancer is the taxane family. A wide range of malignancies have demonstrated the remarkable potency of paclitaxel [51].

Active Targeting: Particular ligands or substances, such as transferrin and folate, which bind to molecules or receptors that are preferentially expressed or overexpressed on the target cells, are necessary for the ability to target cells (diseased organs, tissues, cells, or subcellular domains). This targeting technique is known as ligand-mediated targeting (Figure 5). To boost affinity in this case, the target needs to be in close proximity to the NPs that have ligands with particular actions, such as retention and uptake. By raising the possibility that NPs will bind to cancer cells, this strategy boosts the uptake of medication. In 1980, its first proof was discovered through the grafting of antibodies onto the liposome surface [52].

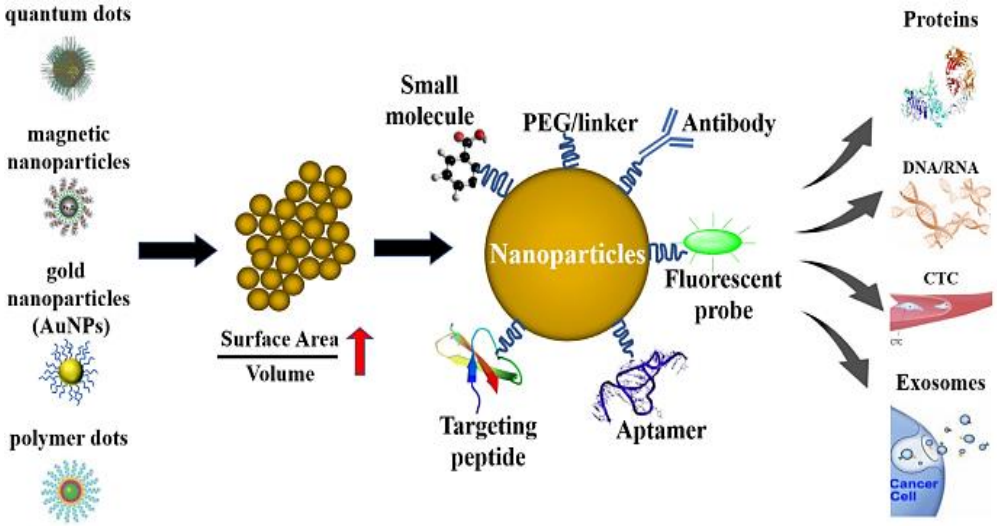

Figure 5. Cancer diagnosis and detection are improved by nanotechnology.

Radionics

Disease can be detected and cured by exposing the body to electromagnetic radiation (EMR), such as radio waves, using an electrically driven instrument. Radionics is a technique for delivering precisely

targeted healing energy to individuals, animals, or plants anywhere in the world. Radionics is an excellent instrument for measuring and balancing these energies. Over the past 80 years, its usage has been supported by hundreds of controlled trials. Additionally, it can be used to elicit knowledge and wisdom from the collective unconscious, which has the power to change the lives of those who employ it. It is a tool for identifying and treating illnesses in people, pets, and even plants [53].

Chemodynamic Therapy

Chemodynamic therapy (CDT) differs from many other proof-of-concept reactive oxygen species (ROS)-related cancer therapy strategies, including conventional chemotherapy, radiotherapy, photodynamic therapy (PDT), and sonodynamic therapy (SDT). CDT uses chemodynamic therapeutic agents to convert internal hydrogen peroxide (H_2O_2) into toxic hydroxyl radicals (\OH) for the purpose of killing cancer cells [54].

This could be attributed to its:

1. Higher specific response to H_2O_2.
2. No external field penetration depth restriction.
3. Fewer side effects on normal tissues.
4. More desirable ROS generation ability.
5. No drug-resistance, device limitations, external stimulation.

Sonodynamic Therapy

A non-toxic sonosensitizer is used in sonodynamic therapy (SDT)—a non-invasive method that targets the generation of hazardous ROS using ultrasonic in the presence of molecular oxygen (Figure 6). Treatment method combines sonosensitizers, which are specific chemical agents, with low-intensity ultrasound. It was discovered when triggered with ultrasound, a number of hematoporphyrin (HP) derivatives (HPDs) utilised in PDT also caused considerable cell damage. Since then, it has been shown that a number of recently created HPDs have the potential to be employed as sonosensitizers for tumour treatment in conjunction with ultrasound 2–4, which is known as SDT 5. The energy source utilised to activate the sensitizers is the main distinction between SDT and PDT (ultrasound versus light) [55].

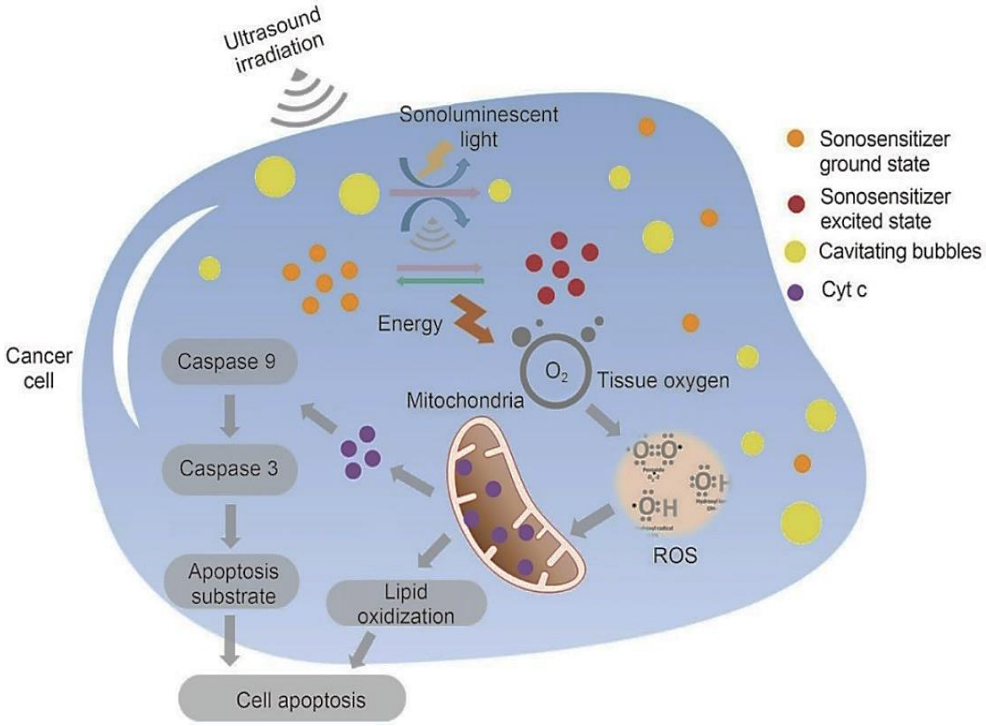

Figure 6. Potential SDT mechanisms.

The surface of cancer cells becomes cavitated when exposed to ultrasound radiation. Cancer cells begin to produce sonoluminescent light when cavitating bubbles burst, releasing energy in the process. As a result, the sonosensitizer is aroused from its ground state. The energy released when the activated sonosensitizer returns to its ground state can be transferred to the surrounding oxygen to create a significant amount of ROS, such as oxygen ions, peroxide, and singlet oxygen. These ROS then cause damage to the mitochondrial membrane and the release of cytochrome c, which in turn mediates the mitochondrial-dependent cell apoptosis (Figure 6).

Ferroptosis-Based Therapy

Mistakes in the metabolism of iron and lipids lead to ferroptosis, which is marked by a build-up of ROS and lipid peroxidation. Unbound intracellular ferrous ions react with hydrogen peroxide through Fenton reactions to activate lipoxygenase (LOX), which in turn causes polyunsaturated fatty acids (PUFAs) in cell membranes to peroxide (1). The toxic free radicals that the oxidised lipids produce lead to more oxidised lipids and more oxidative damage. Ferroptosis can be suppressed by iron sequestration, polyunsaturated fatty acid (PUFA) synthesis inhibition, or ROS scavenging. The two parallel systems that primarily control ferroptosis and phospholipid peroxidation are the glutathione (GSH)/glutathione peroxidase 4 (GPX4) and ferroptosis suppressor protein 1 (FSP1)/ubiquinone (CoQ10)/NAD(P)H axes [56].

Chemotherapy

Chemotherapy is the most common method of treating cancer because of the rapid growth and division of cancer cells. Chemotherapy slows or inhibits cancer cells' rapid growth and division. Chemotherapy can be used to alleviate the distressing side effects of cancer by shrinking the tumours at their source. When used in conjunction with other treatments, chemotherapy can reduce the size of a tumour prior to radiation therapy or surgery (preoperative chemotherapy), kill any remaining cancer cells after radiation therapy or surgery (adjuvant chemotherapy), and boost the efficacy of other therapies by eliminating cancer cells that have returned or spread elsewhere in the body [57, 58].

Chemotherapy can be given in various ways.

1.Injecting medication into the region around the brain and spinal cord is the earliest method of intrathecal delivery.
2.The second kind, intraperitoneal (IP), is inserted into the abdominal cavity, where vital organs such as liver is present.
3.Thirdly, oral medications can be taken by mouth in the form of tablets, capsules, or liquids.
4.Another way is via intravenous (IV) injection. It is a type of injection that is administered straight into a vein.
5. It can be administered by injection using a needle placed into a muscle of the arm, thigh, or hip.
6.It can be given through intra-arterial route given via injection into the artery thought to be responsible for the malignancy.
7. Another method is topical application or used on the skin.

Oncologists use a variety of chemotherapy techniques, such as:

Adjuvant Therapy: After radiation therapy or surgery, chemotherapy is used to treat cancer as an adjuvant therapy.

Curative Therapy: Chemotherapy totally eradicates cancer, guaranteeing that it won't return. It may also involve radiation and/or surgery.

Neo-adjuvant Therapy: Chemotherapy reduces a tumor size prior to radiation therapy or surgery.

Palliative therapy: While chemotherapy cannot cure cancer, it can reduce tumours and symptoms.

Surgery

The aberrant tissue is destroyed with the help of liquid nitrogen or argon gas, during a procedure known as cryosurgery. Cryosurgery is a treatment option for retinoblastoma, precancerous growths on the skin and cervix, and early-stage skin cancer. Cryotherapy is another term for cryosurgery. In an open procedure, the surgeon makes a single, substantial cut to remove the tumour, some surrounding good tissue, and possibly some lymph nodes.

One of the tiny apertures is used to insert a tiny camera that is at the end of a long, thin tube. The tumour is removed and some good tissue using specialised surgical tools that are put through the other tiny wounds. The recovery period is shorter after minimally invasive surgery than it is after open surgery because smaller cuts are used [59].

Mechanism of Surgery

Destroy the Whole Tumour: Cancer that is localised is removed with surgery.

Remove a Tumour: Surgery only completely removes a portion of a cancerous tumour.

Reduces the Signs of Cancer: Tumors that are uncomfortable or pressing on nearby organs are surgically removed.

Laser Surgery

This method shrink or destroy tumours, activate medications to kill cancer cells, or remove very small malignancies (without harming surrounding tissue) without the use of equipment. Laser surgery is a very accurate method that can be used to treat hard-to-reach body parts such as skin, cervix, rectum, and throat [60].

Electrosurgery

Electrosurgery can be used to treat oral and skin cancer. This method destroys cancer cells using electrical current.

Microscopically Controlled Surgery

This surgery is beneficial when cancer affects delicate body components, such as the eye. Skin layers are taken off and examined under a microscope until no malignant cells are visible.

Biomarker Testing

Biomarker testing is a way of looking for indicators of cancer, such as genes, proteins, and other substances (biomarkers or tumour markers).

In medical parlance, a biomarker test is called a "companion diagnostic" when it is used in tandem with a particular therapy.

EGFR inhibitors are a class of drugs that target specific mutations in the EGFR gene and are used to treat people with cancer. By testing biomarkers, doctors can learn whether or not a patient's cancer is caused by a mutation in the EGFR gene and hence amenable to treatment with an EGFR inhibitor [61].

Hormone Therapy

Hormone therapy is a cancer treatment that slows or stops the growth of cancer that uses hormones to grow.

Hormone therapies alter the amount of hormones in your body in various ways :

1. Prevent the body from producing a hormone.
2. Modify the way a hormone functions in the body.
3. Preventing a hormone from binding to cancer cells.

Examples include Aromatase inhibitors (AIs), such as anastrozole, exemestane, and letrozole in treating breast cancer; CYP17 inhibitors, such as abiraterone and ketoconazole in treating prostate cancer; Progestins, such as medroxyprogesterone acetate or megestrol acetate in treating endometrial cancer etc.

Immunotherapy

Immunotherapy is a type of cancer treatment that works to boost the body's natural defenses against the disease. The immune system is a key defensive mechanism for the body, helping to ward off foreign invaders and diseases. It is composed of several white blood cells, organs, and parts of the lymphatic system.

Immune Checkpoint Inhibitors

Certain medications disable immunological checkpoints. These immune system checkpoints prevent overly powerful immune responses and are a typical component of the immune system [62].

T-cell transfer Therapy

This treatment involves taking immune cells out of the tumour and using them against the tumour itself.

T-cell transfer therapy is also known as immune cell therapy, adoptive immunotherapy, and adoptive cell treatment.

Monoclonal Antibodies

These are artificial proteins from the immune system that have been engineered to attach to specific sites on malignant cells. Some monoclonal antibodies can be used to "tag" cancer cells, alerting the immune system to the fact that they should be attacked.

Treatment Vaccines

They combat cancer by strengthening body’s immune system response to cancer cells. There are vaccines that help prevent and treat diseases.

Immune System Modulators

The immune system modulators strengthen the body's defense against cancer.

Radiation Therapy

Radiation treatment often uses X-rays; however, protons and other kinds of energy can be utilised as well. In this type of radiation, high-energy beams are produced by an external device and focused on a particular area of the body. An injection of radiation is given into the body during brachytherapy—a unique kind of radiation treatment [63].

Radiation treatment is harmful because it destroys cells by removing DNA, which controls cell growth and division. Radiation treatment, in conjunction with chemotherapeutic medicines and surgical techniques, is one of the most successful methods to treat cancer.

External Beam Radiation Therapy

The tumour is exposed to high-energy radiation beams using external beam radiation therapy (EBRT). X-rays, electrons, or protons are the three possible types of energy.

Forms of EBRT

i. *3-D Conformational Radiation Therapy:* The equipment guides radiation beams toward the cancer site while avoiding healthy tissue using the model as a reference.

ii. *Intensity modulated radiation therapy (IMRT):* Numerous radiation beams with varying dose intensities are used in IMRT. This therapy gives the tumour a higher radiation exposure while giving lesser exposure to the healthy tissues.
iii. *Arc-based Therapy:* Energy beams of varied intensities are directed by it in a rotating arc-like pattern. Arc-based radiation includes tomotherapy and volumetric modulated arc treatment (VMAT).

Internal Radiation Therapy

i. *Brachytherapy:* A tumour is implanted with a solid radioactive source, or "seed," inside it or close to it. To destroy cancer cells, the source emits radiation in a restricted space.
ii. *Systemic Therapy:* Radionuclide treatment is one of the therapies (radioimmunotherapy). During radioimmunotherapy, a radioactive protein detects certain cancer cells, binds to them, and then radiates the cancer cells to death.

Photodynamic Therapy

In PDT, light is used to activate a chemical called a photosensitizer or photosensitizing agent, which is then utilised to kill cancer cells. There are several possible sources of illumination, including lasers and LEDs.

Over time, the cancer cells absorb the medication. Following treatment, the affected region is illuminated. A special type of oxygen molecule is produced as a result of the medicine's reaction to light, which then kills the cells. Blood supply of cancer cells is cut off and the immune system is triggered into action by PDT, making it a potentially effective treatment option [64].

PDT has a number of advantages:

1. PDT only targets the cancer cells, not healthy cells.
2. Unlike radiation therapy, it can be used again in the same place.
3. It less risks than surgery.
4. Compared to many other cancer therapies, it is quicker and less expensive.

Since PDT does not leave scars, it is beneficial for those who have skin cancer and precancers.

Another novel PDT variant being developed by researchers is known as photoimmunotherapy (PIT). This treatment involves the use of a photosensitizer as well as an immune protein that transports the photosynthesizer to cancer cells. When light is supplied, the photosynthesizer destroys the cancer cells.

Hyperthermia

Cancer patients who receive hyperthermic intraperitoneal chemotherapy (HIPEC) have heated chemotherapy medicines injected into their abdominal cavities. HIPEC, also referred to as "hot chemotherapy," is carried out after the surgeon removes abdominal tumours or lesions.

The chemotherapy medication cisplatin is heated to 103°F (42 °C) and delivered through the abdominal cavity after all visible malignancies have been removed. To keep their body temperature steady, the patient is allowed to rest on a cooling blanket that has been specially made for them [65].

Compared to traditional chemotherapy, HIPEC provides a number of benefits:

1. Instead of many treatments spaced out over several weeks, it is a single therapy performed in the operating room.
2. Drug absorption from the rest of the body is reduced by 90% because it remains in the abdominal cavity.
3. It permits a higher dose of chemotherapy.

DISCUSSION

The present article was aimed to provide an overview of the development and history of the most popular cancer treatments now in use, as well as recent advancements in therapy. Apart from medical procedures such as surgery, chemotherapy, radiation therapy, PDT, or immunotherapy, novel therapies are currently at various phases of research with the goal of reducing drug toxicity in healthy tissues and increasing efficacy through the use of novel nanostructures for diagnostic or therapeutic reasons, cell and gene therapy, or targeting tumour angiogenesis. Due to their inherent qualities, new products made possible by nanotechnology can be utilised either alone to target cancer cells or in combination with other biomolecules such as folic acid, albumin, anti-tumoral medicines, antibodies, and aptamers [66].

CONCLUSION

Many malignancies are resistant to traditional treatments, and the only method to eradicate tumour cells is typically to use a variety of medication and therapy combinations (such as surgery combined with radiation and chemotherapy). This might also be the case for the recently introduced novel treatments. Although much more research is needed, still these innovative treatment approaches are giving hope to many patients who have been waiting for a successful therapy.

Conflict of Interest

The authors declared no conflict of interest regarding this paper.

REFERENCES

1. Olsson M, Zhivotovsky B. Caspases and cancer. Cell Death & Differentiation. 2011; 18(9): 1441–1449p.
2. Weinberg RA. How cancer arises. Scientific American. 1996; 275(3): 62–70p.
3. Mantyh PW. Cancer pain: causes, consequences and therapeutic opportunities. In: Wall and Melzack's Textbook of Pain. USA: Saunders; 2006.1087–1097p.
4. Doll R, Peto R. The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. Journal of the National Cancer Institute. 1981; 66(6): 1192–1308p.
5. Clapp RW, Jacobs MM, Loechler EL. Environmental and occupational causes of cancer: new evidence 2005–2007. Reviews on Environmental Health. 2008; 23(1): 1–38p.
6. Vogelstein B, Kinzler KW. Cancer genes and the pathways they control. Nature medicine. 2004; 10(8): 789–799p.
7. Stephens PJ, Tarpey PS, Davies H, Van Loo P, Greenman C, et al. The landscape of cancer genes and mutational processes in breast cancer. Nature. 2012; 486(7403): 400–404p.
8. Lawrence MS, Stojanov P, Mermel CH, Robinson JT, Garraway LA, et al. Discovery and saturation analysis of cancer genes across 21 tumour types. Nature. 2014; 505(7484): 495–501p.
9. Lawrence MS, Stojanov P, Mermel CH, Robinson JT, Garraway LA, et al. Discovery and saturation analysis of cancer genes across 21 tumour types. Nature. 2014; 505(7484): 495–501p.
10. Wodarz A, Näthke I. Cell polarity in development and cancer. Nature Cell Biology. 2007; 9(9): 1016–1024p.
11. Frederic EM, Lathrop TG. Modes of spread of cancer of skin. AMA Archives of Dermatology and Syphilology. 1952; 66(4): 427–439p.
12. Kirchner JA, Carter D. Intralaryngeal barriers to the spread of cancer. Acta Oto-Laryngologica. 1987; 103(5–6): 503–513p.
13. Brossart P. The Role of Antigen Spreading in the Efficacy of Immunotherapies Epitope Spreading in Cancer Immunotherapy. Clinical Cancer Research. 2020; 26(17): 4442–4447p.
14. Kapałczyńska M, Kolenda T, Przybyła W, Zajączkowska M, Teresiak A, et al. 2D and 3D cell cultures–a comparison of different types of cancer cell cultures. Archives of Medical Science. 2018; 14(4): 910–919p.
15. Glinsky GV, Berezovska O, Glinskii AB. Microarray analysis identifies a death-from-cancer signature predicting therapy failure in patients with multiple types of cancer. The Journal of Clinical Investigation. 2005; 115(6): 1503–1521p.

16. Patel P, Hanson DL, Sullivan PS, Novak RM, Moorman AC, et al; Adult and Adolescent Spectrum of Disease Project and HIV Outpatient Study Investigators. Incidence of types of cancer among HIV-infected persons compared with the general population in the United States, 1992–2003. Annals of Internal Medicine. 2008; 148(10): 728–736p.
17. Saunders CM. The care of the terminal stages of cancer. Annals of the Royal College of Surgeons of England. 1967; 41(Suppl): 162p.
18. Qi F, Zhao L, Zhou A, Zhang B, Li A, et al. The advantages of using traditional Chinese medicine as an adjunctive therapy in the whole course of cancer treatment instead of only terminal stage of cancer. Bioscience Trends. 2015; 9(1): 16–34p.
19. McMahon KW, Karunasena E, Ahuja N. The roles of DNA methylation in the stages of cancer. Cancer Journal. 2017; 23(5): 257p.
20. Rami-Porta R, Crowley JJ, Goldstraw P. Review the revised TNM staging system for lung cancer. Ann Thorac Cardiovasc Surg. 2009; 15(1): 5p.
21. Puppa G, Sonzogni A, Colombari R, Pelosi G. TNM staging system of colorectal carcinoma: a critical appraisal of challenging issues. Archives of Pathology & Laboratory Medicine. 2010; 134(6): 837–852p.
22. Patel SG, Shah JP. TNM staging of cancers of the head and neck: striving for uniformity among diversity. CA: A Cancer Journal for Clinicians. 2005; 55(4): 242–258p.
23. Lababede O, Meziane M, Rice T. Seventh edition of the cancer staging manual and stage grouping of lung cancer: Quick reference chart and diagrams. Chest. 2011; 139(1): 183–189p.
24. Detterbeck FC, Boffa DJ, Tanoue LT. The new lung cancer staging system. Chest. 2009; 136(1): 260–271p.
25. Hajj C, Goodman KA. Role of radiotherapy and newer techniques in the treatment of GI cancers. Journal of Clinical Oncology. 2015; 33(16): 1737–1744p.
26. Lipsett MB. Newer techniques and some problems in cooperative group studies. In: Conference on Experimental Clinical Cancer Chemotherapy; USA: National Cancer Institute; 1960.18: 277p.
27. Schnitt SJ. Classification and prognosis of invasive breast cancer: from morphology to molecular taxonomy. Modern Pathology, 2010; 23: S60–S64.
28. Herberts CA, Kwa MSG, Hermsen HPH. Risk factors in the development of stem cell therapy. J Transl Medicine. 2011; 9(1): 1–14p.
29. Biehl JK, Russell B. Introduction to stem cell therapy. The Journal of Cardiovascular Nursing. 2009; 24(2): 98p.
30. Sagar J, Chaib B, Sales K, Winslet M, Seifalian A. Role of stem cells in cancer therapy and cancer stem cells: a review. Cancer Cell International. 2017; 7(1): 1–11p.
31. Jenq RR, Van den Brink MR. Allogeneic haematopoietic stem cell transplantation: individualized stem cell and immune therapy of cancer. Nature Reviews Cancer. 2010; 10(3): 213–221p.
32. Vasir JK, Labhasetwar V. Targeted drug delivery in cancer therapy. Technology in Cancer Research & Treatment. 2005; 4(4): 363–374p.
33. Pérez-Herrero E, Fernández-Medarde A. Advanced targeted therapies in cancer: Drug nanocarriers, the future of chemotherapy. European Journal of Pharmaceutics and Biopharmaceutics. 2015; 93: 52–79p.
34. Jain KK. Targeted drug delivery for cancer. Technology in Cancer Research & Treatment. 2005; 4(4): 311–313p.
35. Roth JA, Cristiano RJ. Gene therapy for cancer: what have we done and where are we going?. Journal of the National Cancer Institute. 1997; 89(1): 21–39p.
36. Schmitt TM, Gunnar BR, Greenberg PD. T cell receptor gene therapy for cancer. Human Gene Therapy. 2009; 20(11): 1240–1248p.
37. Rosenberg SA. Gene therapy for cancer. JAMA. 1992; 268(17): 2416–2419p.
38. Mauri G, Nicosia L, Xu Z, Di Pietro S, Monfardini L, et al. Focused ultrasound: Tumour ablation and its potential to enhance immunological therapy to cancer. The British Journal of Radiology. 2018; 91(xxxx): 20170641.

39. Friedman M, Mikityansky I, Kam A, Libutti SK, Walther MM, et al. Radiofrequency ablation of cancer. Cardiovascular and Interventional Radiology. 2004; 27(5): 427–434p.
40. Ashikbayeva Z, Tosi D, Balmassov D, Schena E, Saccomandi P, et al. Application of nanoparticles and nanomaterials in thermal ablation therapy of cancer. Nanomaterials. 2019; 9(9): 1195.
41. Block KI. Antioxidants and cancer therapy: Furthering the debate. Integrative Cancer Therapies. 2004; 3(4): 342–348p.
42. Valadez-Vega C, Delgado-Olivares L, Gonzalez JAM, Garcia EA, Ibarra JRV, et al. The role of natural antioxidants in cancer disease. In: Oxidative stress and chronic degenerative diseases-A role for antioxidants. IntechOpen; 2013.
43. Brigger I, Dubernet C, Couvreur P. Nanoparticles in cancer therapy and diagnosis. Advanced Drug Delivery Reviews. 2012; 64: 24–36p.
44. Aghebati-Maleki A, Dolati S, Ahmadi M, Baghbanzhadeh A, Asadi M, et al. Nanoparticles and cancer therapy: Perspectives for application of nanoparticles in the treatment of cancers. Journal of Cellular Physiology. 2020; 235(3): 1962–1972p.
45. Tansley DV. Radionics & the subtle anatomy of man. USA: Random House; 2011.
46. Andreadis E, Saliangas K, Economou A, Nikoloudis N, Manna I, et al. Application of radionics on primary and metastatic tumours of the liver. Techniques in Coloproctology. 2004; 8(1): 184–186p.
47. Wang X, Zhong X, Liu Z, Cheng L. Recent progress of chemodynamic therapy-induced combination cancer therapy. Nano Today. 2020; 35: 100946.
48. Li SL, Jiang P, Jiang FL, Liu Y. Recent advances in nanomaterial-based nanoplatforms for chemodynamic cancer therapy. Advanced Functional Materials. 2021; 31(22): 2100243.
49. Chen H, Zhou X, Gao Y, Zheng B, Tang F, et al. Recent progress in development of new sonosensitizers for sonodynamic cancer therapy. Drug Discovery Today. 2014; 19(4): 502–509p.
50. Xu M, Zhou L, Zheng L, Zhou Q, Liu K, et al. Sonodynamic therapy-derived multimodal synergistic cancer therapy. Cancer Letters. 2021; 497: 229–242p.
51. Umemura S, Kawabata K, Sasaki K, Yumita N, Umemura K, et al. Recent advances in sonodynamic approach to cancer therapy. Ultrasonics Sonochemistry. 1996; 3(3): S187–S191.
52. Shen Z, Song J, Yung BC, Zhou Z, Wu A, et al. Emerging strategies of cancer therapy based on ferroptosis. Advanced Materials. 2018; 30(12): 1704007.
53. Michael M, Tannock IF. Measuring health-related quality of life in clinical trials that evaluate the role of chemotherapy in cancer treatment. CMAJ. 1998; 158(13): 1727–1734p.
54. Coffey JC, Wang JH, Smith MJF, Bouchier-Hayes D, Cotter TG, et al. Excisional surgery for cancer cure: Therapy at a cost. The Lancet Oncology. 2003; 4(12): 760–768p.
55. Hayes DF. Biomarker validation and testing. Molecular Oncology. 2015; 9(5): 960–966p.
56. Lim C, Tsao MS, Le LW, Shepherd FA, Feld R, et al. Biomarker testing and time to treatment decision in patients with advanced nonsmall-cell lung cancer. Annals of Oncology. 2015; 26(7): 1415–1421p
57. Kuhle CL, Kapoor E, Sood R, Thielen JM, Jatoi A, et al. Menopausal hormone therapy in cancer survivors: a narrative review of the literature. Maturitas. 2016; 92: 86–96p.
58. Abraham J, Ocen J, Staffurth J. Hormonal therapy for cancer. Medicine. 2022; 44(1): 30–33p.
59. Kirkwood JM, Butterfield LH, Tarhini AA, Zarour H, Kalinski P, et al. Immunotherapy of cancer in 2012. CA: A Cancer Journal for Clinicians. 2012; 62(5): 309–335p.
60. Melief CJ, Toes RE, Medema JP, Burg SHV, Cornelis JM, et al. Strategies for immunotherapy of cancer. Adv Immunol. 2000; 75: 235–282p.
61. Dougherty TJ, Gomer CJ, Henderson BW, Jori G, Kessel D, et al. Photodynamic therapy. JNCI: Journal of the National Cancer Institute. 1998; 90(12): 889–905p.
62. Agostinis P, Berg K, Cengel KA, Foster TH, Girotti AW, et al. Photodynamic therapy of cancer: an update. CA: A Cancer Journal for Clinicians, 2011; 61(4): 250–281p.
63. Hahn GM. Hyperthermia and cancer. Germany: Springer Science & Business Media; 2012.
64. Baronzio GF, Hager ED, eds. Hyperthermia in cancer treatment: A primer. Germany: Springer Science & Business Media; 2008.

65. Wan GY, Liu Y, Chen BW, Liu YY, Wang YS, et al. Recent advances of sonodynamic therapy in cancer treatment. Cancer Biology & Medicine. 2016; 13(3): 325p.
66. Zhang Y, Li M, Gao X, Chen Y, Liu T. Nanotechnology in cancer diagnosis: progress, challenges and opportunities. Journal of Hematology & Oncology. 2019; 12(1): 1–13p.

