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Review Article

Photothermal Therapy For Cancer Treatment

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ABSTRACT

Recent years have seen extensive clinical studies for photothermal treatment (PTT), a very promising anticancer technique that uses near-infrared light-absorbing substances to destroy tumours. The development of mild-temperature PTT, which avoids the drawbacks of traditional PTT (such as thermos resistance and side effects), has considerable promise for upcoming therapeutic applications. However, because to its significantly reduced therapeutic efficiency and lower heat intensity, mild-temperature PTT without adjuvant treatment is unable to entirely destroy malignancies. There is a development of nanomaterials in photothermal therapy of cancer. It is urgently necessary to develop methods that can increase the mild-temperature PTT's anticancer effectiveness. These methods mostly depend on the on-demand manufacturing of functionalized nanoagents. The tactics of mild-temperature PTT promoted by nanoagents are emphasised in this review. Additionally, possibilities and problems in this sector are logically given, and it is hoped that people would be inspired by this potential anticancer therapy. A novel cancer treatment called photothermal therapy has shown positive outcomes in its initial clinical study. This is the first experiment evaluating photothermal therapy's potential as a treatment for cancer patients, despite the fact that it has been widely studied in preclinical models. A cancer treatment known as photothermal therapy (PTT) causes the killing of cancer cells by heating tumour tissue exposed to near-infrared (NIR) light. NIR absorbents are employed to promote effective heat generation. We discuss regarding the challenges, views and certain complications of photothermal therapy and also its future prospects and challenges of its clinical application and uses.

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INTRODUCTION

Attempts to cure a variety of medical illnesses, including cancer, with electromagnetic radiation (often in the form of infrared wavelengths) are known as photothermal therapy (PTT) [1]. The photosensitizer is activated with a particular band of light in this method, which is an extension of photodynamic treatment. The sensitizer gets stimulated as a result of this stimulation and emits vibrational energy (heat), which is what kills the targeted cells [2]. The efficiency of nanoparticle-assisted laser hyperthermia depends on a proper dose strategy of nanoparticle administration, according to a new study of research on plasmonic photothermal treatment (PPT) after intravenous administration of gold nanorods (GNRs) [5,9]. The local heating of the tumour is greatly increased by the buildupof GNRs in the tumour tissue without harming healthy tissues. However, the best GNR intravenous injection (IVI) dosages for tumour accumulation and the best PPT methods have not yet been developed. The objective of the current study is to increase the efficacy of PPT in tumour-bearing rats by administering GNRs multiple fractionally intravenously.

WHAT IS PHOTOTHERMAL THERAPY

Solid tumours can be treated using photothermal therapy, a localised therapeutic paradigm. A photosensitizer is energised throughout the procedure using electromagnetic radiation, often near-infrared. Local hyperthermia is caused when the photosensitizer absorbs the energy and transforms it into heat enabling very precise tumour ablation [1, 2,]. Nanoparticles are the best possible candidates to function as photosensitizers because of their readily modified structure[3,9,11]. They have a high optical absorbance that can be tailored to certain infrared radiation wavelengths, improving the treatment's specificity. Numerous research on photothermal treatment have used a variety of nanoparticle kinds. Due to their high surface area to volume ratio and great biocompatibility, graphene-based particles have been found to be suitable in several investigations. The researchers saw significant photoablation rates and little adverse consequences. The creation of graphene-based nanoparticles with integrated gold nanomaterial has come under scrutiny recently. 2015 saw the use of an aptamer—gold nanomaterial-hybridized graphene oxide as a photosensitizer in a cooperative effort run by the Suzhou Institute of Nano-Tech and Nano-Bionics (China) to trigger a therapeutic response in human breast cancer cell lines. Together, they showed a potent heat-to-energy conversion and elevated anticancer activity.

WHAT IS CANCER

Cancer is an uncontrolled cell proliferation that poses a threat to life. Some cells' uncontrolled cell division results in the build-up of abnormal cell populations that endanger life by interfering with essential bodily processes. These abnormal cell populations produce solid tissues in the majority of tissues. Tumours are masses with that name. benign tumours do not pose a threat to life, whereas cancerous tumours pose a life-threatening threat. A malignant tumour is a cancer; however, a cancer is not always a malignant tumour (for example, leukaemia). The classic definition of cancer is a condition brought on by unchecked cell proliferation and tissue invasion. The phrase benign tumour is frequently used to describe tumours that remain at their original location. According to these conventional classifications, patients with non-metastatic brain tumours who pass away would pass away from benign tumours rather than cancer because their tumour cells do not spread. When cancerous cells invade surrounding or distant tissues, life is frequently at danger. However, in other circumstances, the buildup of aberrant cell populations in particular tissues poses a threat to life even in the absence of metastasis (e.g., leukaemia, some brain cancers,

and any non-metastatic cancer originated in vital organs or tissues). An unchecked cell proliferation that poses a threat to life can be used to categorise all malignancies.

TYPES OF CANCERS

There are several different forms of cancer [22], including

a Carcinomas:

They begin in the skin or tissue that covers the surface of the glands and internal organs. A solid tumour is created. Cancers of the breast, prostate, colorectal, and lungs.

b **Sarcomas:**

The tissues that bind and support the body are where it begins. It can develop in blood vessels, bone, lymphatic vessels, muscles, cartilage, tendons, nerves, and joints.

c Leukaemia's:

A blood malignancy is called leukaemia. Healthy blood cells start to alter and grow out of control at this point. There are four different kinds of it: acute myeloid leukaemia, acute lymphocytic leukaemia, chronic myeloid leukaemia, and chronic lymphocytic leukaemia.

d Lymphomas:

The lymphatic system, which is a network of glands and tubes that aids in the fight against infection, is where lymphoma, a disease, first develops. There are two types of lymphoma: Hodgkin and non-Hodgkin.

e Central Nervous System Cancers:

Brain and spinal cord tumours are cancers that originate in the brain and spinal cord, along with primary CNS lymphomas, vestibular schwannomas, gliomas, pituitary adenomas, primitive neuro-ectodermal tumours, meningiomas, and gliomas.

f Multiple Myeloma:

Plasma cells, another type of immune cell, are the origin of multiple myelomas, a cancer. In the bone marrow, plasma cells called myeloma cells multiply and cause malignancies to form in the bones. There are two names for it: Kahler disease and plasma cell myeloma.

g Melanoma:

It begins in the precursor cells to melanocytes. These cells are specialised cells that produce melanin, the pigment responsible for the skin's colour. Melanomas typically appear on the skin, but they can also appear in other pigmented tissues, such as the eye.

h Other Types of Tumours:

i Germ Cell Tumours:

It is the kind of tumour that develops from the cells that produce eggs or sperm. This could be benign or cancerous, and it could happen anywhere in the body.

ii. **Neuroendocrine Tumours:**

Cells that release hormones into the blood in response to a signal from the nervous system are the source of neuroendocrine tumours. It is made up of the cells that release hormones into the blood in response to nerve signals. These tumours can produce higher than usual levels of hormones, which will result in a wide range of symptoms. It could either be benign or cancerous.

iii. **Common Cancers:**

Humans can develop more than 100 different types of cancer, but the most common ones are bladder, breast (female-malele), endometrial, thyroid, colorectal cancer, leukaemia, lung (including bronchi), melanoma, kidney (renal cell and renal pelvis), non-Hodgkin lymphoma, prostate, and pancreatic cancer.

EVOLVING CANCER TREATMENTS:

Depending on the type of cancer and how far along it is, there are several forms of cancer therapies. Many cancer patients receive a combination of treatments, such as surgery and radiation therapy, rather than just one cancer treatment.

The different sorts of therapies include[23]

1. Surgery:

A surgeon might remove lymph nodes to stop or slow the progression of the disease and get cancer out of the body.

2. Radiation therapy:

High doses of radiation are utilised in this therapy to reduce tumours and kill cancer cells while treating cancer.

3. Chemotherapy:

Chemicals are used in this therapy to shrink tumours and destroy cancer cells, but it comes with serious side effects.

4. Immunotherapy:

In this therapy, drugs or other therapies are used to strengthen the immune system. Consider the use of adoptive cells and checkpoint inhibitors.

5. Targeted therapy:

This treatment also boosts immune system alterations in cancer cells that aid in their growth, division, and dissemination. Monoclonal antibodies and small-molecule medications are two examples.

6. Hormone therapy:

Hormones are utilised in this therapy to stop and reduce the growth of cancers like prostate and breast.

7. Stem cell transplants:

In this treatment, cancer patients' stem cells that have been killed by extremely high radiation or chemotherapy dosages are restored.

8. Precision medicine:

It is a more recent strategy in which genetic testing is used to decide a patient's best course of action.

Adverse effects of various treatments:

1. Surgery:

Infection:

Following surgery, infection is a possibility that can be avoided by taking antibiotics.

Pain:

One of the most frequent issues with surgery is pain at the site of the operation on the body[24]

2. Radiation therapy:

Radiation therapy has a number of potential side effects, which are typically manifested by the radiation-damaged normal cells[25,26 ,27,28]

3. Chemotherapy:

While chemotherapy kills cancer cells, it also kills normal cells. Healthy cells are damaged, which results in side effects. The side effects include: hair loss, mouth sores, nausea, and fatigue, thus a patient at least needs child care on the day of chemotherapy[29,30,31].

4. Immunotherapy:

Skin responses at the needle site are the most typical side effects. The following side effects are also possible: Diarrhoea, Low and High Blood Pressure, Headache, Risk of Infection, Organ Inflammation, Heart Palpitations, Sinus Congestion, Pain, Swelling, Redness, Soreness, Rash, Chills, Fever, Dizziness, Nausea and Vomiting, Fatigue, Muscle or Joint Aches, Trouble Breathing, Headache, Low and High Blood Pressure. Although rare, these therapies can occasionally result in serious or deadly allergic responses.[32,33,34,35,36]

5. Targeted therapy:

Diarrhoea and liver issues are frequent side effects. Fatigue, mouth sores, hair loss, nail changes, high blood pressure, and skin issues like dry skin and rash are some other side effects.

- Issues with blood clotting and wound healing
- Rare side effects include the possibility that a whole will form through the small intestine, oesophagus, large intestine, or stomach wall. Medicines may be used to treat or prevent certain side effects.[37,38]

6. Hormone therapy:

Depending on the individual, the side effects vary. Unwanted side effects result from this therapy because it inhibits hormone production or interferes with hormone function. Depending on the individual, the side effects vary. In men: Bone deterioration, Hot flashes, Diarrhea, Nausea, Fatigue, Loss of desire or ability to engage in

sexual activity, Tender and swollen breast. In women: Changes in menstruation if not yet in menopause, Dry vagina, Nausea, Mood swings, Loss of interest in sex, Hot flashes.[39,40]

7. Stem cell transplants:

The issues brought on by cancer therapies prior to a stem cell transplant include bleeding and an increased risk of infection. Graft-versus-host disease, which can occur after an allogeneic transplant, occurs when the WBC from the donor (the graft) recognises cells in the body (the host) as foreign and attacks them. As a result, the skin, liver, gut, and other organs are injured. To treat graft-versus-host disease, the immune system is suppressed with steroids or other medications.[41]

Emerging Photothermal treatment for cancer

The history of cancer treatment has been marked by ups and downs due to the promise and reality of total remission and cure in many cases, as well as the ineffectiveness of medicines and adverse effects. Radiation and anticancer medications, which have occasionally been the preferred course of treatment, are part of the therapeutic arsenal together with surgery in the case of solid tumours. Immunotherapy has emerged as a significant therapeutic alternative in recent years and is currently the treatment of choice in many situations. With the advent of nanotechnology, there are now novel therapeutic options available. These include using nanostructures for guided target therapy, combining imaging and treatment, controlled drug administration, and using heat. These treatments may be used independently or in conjunction with other elements (antibodies, peptides, folic acid, etc.). Gene therapy is also presenting potential new therapeutic approaches [43].

Combination of PTT with existing treatment

Both basic science research and clinical investigations have demonstrated the significant potential of combining several therapeutic approaches in the treatment of cancer.

- PTT in combination with radiotherapy
- PTT in combination with chemotherapy
- PTT in combination with immunotherapy

PTT in combination with radiotherapy:

It has been demonstrated that hyperthermia enhances radiation, making the combination of PTT and radiotherapy a viable and alluring method for treating metastatic cancer[50,51,65]. For this application, only copper sulphide (CuS) nanoparticles have been used thus far. CuS/[131I] I nanoparticles were created by Liu et al. by combining 131I with iodine-doped CuS nanoparticles. These particles were then functionalized with PEG to provide a single nanoagent for PTT and radiation therapy of metastatic cancers [52]. By combining the doped 131I-radioactivity and the intrinsic increased NIR absorbance, synergistic therapeutic efficacy might be attained. A possible technique for combination therapy of metastatic cancers was provided by the remarkable inhibition of lung metastasis and significant extension of animal survival caused by the combined PTT/radiotherapy. Similar to this, Li et al. created 64Cu labelled CuS ([64Cu] CuS) nanoparticles for combined PTT and radiation therapy of metastatic breast cancer by removing tumour-initiating cells [51]. The combination of radiation and PTT therapy dramatically slowed the growth of the tumour and increased animal survival. Additionally, the combination therapy with [64Cu] CuS nanoparticles significantly decreased the amount of lung metastatic nodules and tumour mammosphere development in the 4T1-induced metastatic breast cancer model.

PTT in combination with chemotherapy:

Chemotherapy, which can be effective in treating both the primary tumour and metastatic lesions in distant locales, is one of the most often utilised modalities in cancer metastasis treatment [52,53]. PTT and chemotherapy have received the most attention recently because of their ability to have synergistic effects on cancer spread[54,55,56].

The most often used combination for PTT/chemotherapy is doxorubicin (DOX) and the gold nanostructure. There, DOX was used as an anticancer medicine for chemotherapy while gold nanoclusters or nanorods were used as photothermal agents for PTT, enabling their synergistic combination therapy. A DOX-loaded DNA wrapped gold nanorod (GNR@DOX) for combination therapy of metastatic breast cancer was recently developed[57,65]. Following NIR radiation, the combined therapy with GNR@DOX nanoparticles significantly slowed the growth of the main tumour and the lung metastasis of breast cancer. Additionally, mesoporous magnetic gold nanoclusters coated with DOX are being developed for PTT/chemotherapy of metastatic breast cancer (Qian et al) [57]. The 4T1 breast cancer model's tumour locations could be successfully targeted by the nanoclusters with the aid of extra-magnetic field. The effective prevention of pulmonary and mediastinal metastases under the combination therapy significantly increased animal survival. A thermo- and pH-sensitive polymer functionalized mesoporous silica coated gold nanorods loading DOX for NIR laser-induced targeted cancer therapy was specifically designed by Chen et al[59]. With easy control over the area, time, and dosage, the nanocomposite could simultaneously deliver heat and anticancer drugs to tumour sites by a single nano-agent in a laser-motivated mechanism, effectively eradiating tumour growth and lung metastasis. Additionally, a combination therapy using SV119-gold nanocage conjugates loading DOX could efficiently and specifically eliminate breast cancer stem cells. Despite these promising efforts, the nonbiodegradable gold nanostructure safety issues may significantly impede any further clinical translation that may be achieved [60]

PTT in combination with immunotherapy:

The most effective method of treating cancer has long been thought to be immunotherapy, which works by using the immune system of the patient to identify and destroy cancer cells [61]. Upon local NIR laser irradiation, PTT can cause tumour cell death, and the dying cancer cells can leak tumour antigens into the environment to trigger an immune response against the tumour[61,62,65]. Most significantly, PTT and immunoadjuvant combined with laser immunotherapy could result in an in situ autologous cancer vaccine (inCVAX) [63]. While the semi-synthetic glucosamine polymer of N-dihydro-galacto-chitosan (GC) was optimised as an immunoadjuvant with effective immunological stimulated functions, the FDA-approved NIR probe of ICG was chosen as the best candidate for PTT. The combination of ICG and GC may have long-lasting curative effects and anti-tumour immune responses after NIR laser irradiation, eliminating the remaining primary and metastatic cancer cells. Preclinical research and clinical metastatic breast cancer and melanoma pilot trials have demonstrated the therapeutic efficacy. Additionally, PTT in conjunction with immunotherapy can enhance therapeutic efficacy in a complementary way on both primary tumour and metastatic cancer cells in distant regions. Dendritic cells (DC) within tumour-draining lymph nodes might mature and produce proinflammatory cytokines and chemokines, which would prime antitumour CD8+ effector T cell responses. This is possible with gold nanoshell-based PTT (Foster et al). PTT and adoptively transferred tumour-specific T cells worked together to effectively stop lung metastases from developing and tumour growth at distant sites [64].

Table1. Typical nanoparticles utilized in combination therapy as PTT agents.

Nanomaterials	Combination Therapy	Mechanism	Ref.
CP-TPP/Au/PEG nanospheres	PTT + PDT	LTH (808 nm) and ROS (630 nm)	[68]
GNc-HyNA	PTT + PDT	LTH (808 nm) and ROS (690 nm)	[69]
GNS-PEG-Ce6	PTT + PDT	LTH (671 nm) and ROS (671 nm)	[70]
Te-NDs	PTT + PDT	LTH and ROS (785 nm)	[71]
UCNPs-NGO/ZnPC	PTT + PDT	LTH (808 nm) and ROS (630 nm)	[72]
CDAuNs	PTT + CT	LTH (808 nm) and CDR	[73]
DINPs	PTT + CT	LTH (808 nm) and CDR	[74]
HPSN-Pax/PdPc	PTT + CT	LTH (730 nm) and CDR	[75]
Polydopamine-rGO-MSN	PTT + CT	LTH (808 nm) and CDR	[76]
Polypyrrole@MIL-100/DOX	PTT + CT	LTH (808 nm) and CDR	[77]
HCuSNPs-CpG	PTT+IT	LTH (900nm)andusing small-molecule inhibitors	[78]
OVA-ICG	PTT+IT	LTH (808nm)andSI as cancer vaccine	[79]
PCN	PTT+IT	LTH (808 nm) and SI as immune agonist	[80]
PEGylated SWNT	PTT+IT	LTH (808 nm) and SI as immune checkpoints blockades	[81]
piTRLs	PTT+IT	LTH (808 nm) and SI using immunostimulant	[82]
CSA	PTT + RT	LTH (808 nm) and X-ray	[83]
Dox-HGNP	PTT + RT	LTH (808 nm) and X-ray	[84]
mPEG@HGNPs	PTT + RT	LTH (808 nm) and X-ray	[85]
PtNP	PTT + RT	LTH (808 nm) and X-ray	[86]
WS2QDs	PTT + RT	LTH (808 nm) and X-ray	[87]

Complications and its solutions for PTT

Thermal damage caused by photothermal therapy to the normal cells and tissues and its solution:

The effective photothermal therapy is based on photosensitizers' excellent tumour site specificity. The highest agglomerative thermal impact is only produced by high concentrations at the tumour location and the lack of localization of photosensitizer in healthy tissues, which allows for a rise in temperature at a set point and subsequent "heating" of the tumour without causing harm to healthy tissues. Two methods that ensure both the tumour-abusing impact and the security of healthy tissues have been put forth by researchers. The first involves enhancing photosensitizers' targeting capabilities, while the second involves using low-temperature PTT [67]. The tumor site should have a high concentration of photosensitizing substances. To improve the targeting ability. Only the tumour location, which contains the photosensitizers, would produce a significant quantity of heat energy unlike normal tissues, under NIR light stimulation. Nevertheless, low temperature photothermal therapy aims to enhance the effects of photothermal therapy on tumours and lower the temperature needed for the procedure, it also aims to decrease the by inhibiting the production of heat shock protein (HSPs), tumor cells become more resistant to heat. This idea was created by Liu and colleagues and several subsequent scientific investigations reinforced and optimized it in order to get a stronger tumour suppression impact and

significantly minimize heat injury to normal tissues.

Increasing Photothermal Materials' Targeting Capability:

Most photothermal materials' ability to target tumours without the addition of tumour-specific targeting agents would rely on the phenomenon known as the increased permeability and retension (EPR) effect, which indicates that macromolecules and particles of particular size(such as liposomes and vesicles) have a higher chance of permeating tumor tissues through the EPR effect and staying there for a predetermined period of time. According to research, tumour cells release vascular endothelial growth factor because they require more nutrients and oxygen to continue their rapid pace of development. The tumour would be extremely reliant on the nourishment and oxygen supplies that tumour blood channels give, particularly when the tumour reaches 150-200 m in size. The shape and architecture of the freshly formed tumour blood vessels now differ significantly from those of normal blood vessels. The blood artery wall's smooth muscle layer is lacking, there is a significant endothelial cell gap, and the angiotensin receptor is not functioning. Additionally, the absence of lymphatic capillaries in tumour tissues inhibits lymph fluid from returning. These elements make it possible for macromolecular chemicals to easily get through blood vessel walls and accumulate in tumor cells. These compounds remain in the tumor tissues for a considerable amount of time because the lymph fluid that returns cannot eliminate them.

If the photothermal materials' composition, porosity, size, qualities, surface traits, and targeting ligands are all optimal.

Photothermal Therapy at Low Temperature:

The low-temperature PTT is suggested as a solution to the issue of thermal harm to normal tissues caused by thermal distribution throughout the therapeutic process, as was stated above. However, the most pressing problem in this particular field of study is how to guarantee the tumour-abusing impact even at comparatively moderate temperatures (43–45 °C).

Low Photothermal Effect Solutions:

The major issue with PTT is the shallow depth to which light can penetrate, which causes tumours outside of the radiation field to only partially be cured. The majority of the time, monotherapy is insufficient to totally eradicate the tumour, and PTT is no exception. Even while PTT has a strong therapeutic impact, its inherent limits may still cause only partial cancer cell eradication, which in turn causes the tumour to return and spread. The total effectiveness of the treatment would increase if PTT was combined with other therapeutic modalities. In many instances, combining various therapy modalities results in a more effective treatment than simply a basic complement.

Concurrent Therapy:

Combining PTT with chemotherapy is a typical tactic. For instance, Zhang and colleagues were successful in molybdenum telluride nanosheets functionalization (MoTe2-PEG-cRGD) and loading them with the chemotherapy medication doxorubicin (DOX) for the detection and treatment of tumours. The developed MoTe2-PEG-cRGD/DOX demonstrates good cell abusing capabilities under NIR it is highly efficient in converting light into heat under irradiation. The cyclic arginine-glycine-aspartate (cRGD) motif's particular tumour targeting enables MoTe2-PEG-cRGD/DOX to effectively accumulate in tumours and provide potent cauterising effects. It's significant to note that MoTe2-PEG-cRGD can deteriorate when stimulated by NIR light.It can be used as a food that encourages bacteria at the tumour location to continue reproducing. They incorporated PD-1 immune checkpoint inhibitor added to the phase-change gel of phospholipids to better apply this therapeutic approach to big tumours that are challenging to conquer (P-

AUNP). Through a single subcutaneous injection, a drug depot may be created, and the slowly released PD-1 antagonist can persist for up to 42 days. This prolongs the anticancer impact of the nanosystem by continually altering the immunosuppressive milieu of the tumour. This three-pronged therapeutic approach—bacteria, heat, and immunity—offers a novel approach to tumour immunotherapy.

Bioactive Nanoagents:

The effectiveness of PTT can be impacted by a variety of variables in the very complex tumour microenvironment, including acidity, alkalinity, glutathione level, and oxygen content. As a result, different photothermal materials that take into account the tumour microenvironment and other bioenvironments are continually being created.

Applications of PTT:

1. In order to achieve thermal ablation, clinical PTT therapies now require laser technology. This is because endogenous tissue chromophores can be excited to produce thermal ablation. This tactic lessens the difficulty of regulation and the expense of PTT agent development.
2. For example, endobronchial tumors can be treated using endoscopic ND. A YAG laser is used for photocoagulation treatment.
3. The tumour tissue is thermally destroyed by laser photocoagulation, which targets the blood arteries that surround and deliver oxygen and nutrition to the tumours.
4. For example, Nd: YAG laser therapy for instance, demonstrated therapeutic effects in 603 patients with colorectal carcinoma that had spread to their liver (5 cm in diameter) and 500 patients with hepatocellular carcinoma (3 cm in diameter). This led to an 81 % ablation efficacy for primary liver cancer and a 2% recurrence rate for tumour metastasis.
5. In 899 individuals with malignant liver tumours treated with laser, there were very few problems (1% of patients).
6. The Visualise Thermal Therapy® (150 w, 980-nm laser) and Neuroblasts® laser ablation systems were authorized by the US Food and Drug Administration (FDA) in the 2000s to perform stereotactic laser ablation of high-grade gliomas (12W, 1064-nm laser) using MRI guidance.
7. Indocyanine green (ICG), an FDA-approved medical contrast agent, has generated a lot of interest as a phototherapeutic agent due to its photothermal impact and lethal ROS generation during NIR laser irradiation. ICG in particular has been used to treat cancer as a potent NIR- absorbing PTT agent with high light-to-heat conversion efficiency.
8. Although laser-based PTT has low regulatory barriers and development costs, PTT-agent enhanced thermal ablation offers significant improvements, such as greater selectivity to the target tissue and simple device design by using lower-power lasers.

Current guidelines of PTT:

Photothermal therapy (PTT) has shown promise in treating cancer metastases because of its unique features, which include low invasiveness and useful specificity. PTT can be used in addition to existing medications, in conjunction with multimodal imaging, or alone for the most effective therapy of cancer metastases. A range of photothermal nanotherapeutics (PTN) have been developed with encouraging therapeutic efficacy on metastatic cancer in multiple preclinical animal trials. Near- infrared (NIR) laser photo absorbers are used in photothermal therapy (PTT), a recently identified and potential therapeutic method, to generate heat for the thermal ablation of cancer cells after NIR laser irradiation [88,89,90]. PTT has several advantages over existing therapeutic approaches for the treatment of cancer, including

as precise spatial-temporal selectivity, low invasiveness, and high specificity. [91,92] PTT has the ability to directly destroy cancer cells in the primary tumor or locally spread the cancer to nearby lymph nodes in order to treat the initial stage of cancer metastasis. Additionally, it can be utilized in conjunction with the other therapeutic approaches to treat cancer cells that have spread to other areas. [93,94] The therapeutic efficacy of photothermal therapy (PTT) is largely dependent on the ability of photothermal agents—especially nanoscale agents—to efficiently convert light into sufficient heat. Several photothermal nanotherapeutics (PTN) have been comprehensively studied up to this point, such as organic nanoagents, transition metal sulfide/oxide nanomaterials, noble metal nanostructures, and nanocarbons. [95,96] PTT may eliminate all cancer cells from the primary tumor or local lymphatic metastases in the superficial tissues, stopping the cancer cells from spreading to other distant organs. However, due to the uneven heat distribution throughout these tissues, PTT is not enough to eliminate all cancer cells and stop the tumor from spreading or regenerating. PTN should be developed with deep penetration and specific targeting in tumor tissues to increase its therapeutic effectiveness. Moreover, PTN's significant selectivity for cancer stem-like cells, metastatic cells, and normal tumor cells must be considered in imaging-guided PTT. The imaging guidance provided by the current PTN is rarely employed to image distant metastatic lesions in deep tissues and is often limited to seeing primary tumor or lymph node metastases. PTN should be designed with valuable imaging and high targeting to metastatic disease in order to provide significant imaging advice for PTT alone or additional combination treatment. Combining PTT with immunotherapy, systemic chemotherapy, or stereotactic radiation may be an efficient alternative treatment for metastatic cancer. Concerns about the co-administration of PTN increase since a synergistic interaction between the photothermal agents and combination therapeutic agents is required for the combined therapeutic benefits to be achieved.

FUTURE PROSPECTIVE

Preclinical studies have tested a number of PTT-based strategies, and the results have been encouraging for some cancer treatments. In this field, many nanomaterials have been developed to cause localized hyperthermia in response to NIR light irradiation. In addition, combining PTT with different conventional therapies may be able to cure cancers that are not amenable to laser irradiation and produce better therapeutic results than PTT alone. This could lower the dose of PTT agents needed to destroy tumours and minimise any potential adverse effects. Tumors have been effectively removed from the body using photothermal ablation, which is based on an external laser device. However, due to the heat-sink effect, which causes heat loss and, consequently, lower photothermal effectiveness, it is challenging to efficiently treat lesions close to significant vascular systems utilising laser treatment without PTT drugs [104]. Additionally, the only tissues that laser light-induced thermal ablation is used to treat are superficial tumors due to human tissue's high absorption coefficient in the visible light spectrum and the possibility of harming non-cancerous cells. For successful clinical translation, improvements in light delivery are just as important as improvements in PTT agents themselves. The minimal depth of laser light penetration in biological tissues (less than 1 cm), for example, is a difficulty to the clinical translation of PTTs and leads to inadequate treatment for deep-tissue cancers. Because NIR lasers have a lower tissue absorption and dispersion than visible light, they can penetrate deeper than visible light, making them a highly recommended option for PTT. Therefore, the

following new generation technologies are part of the present approaches:

1. Reaching tumors using fiber-optic NIR lasers
2. Using PTT in conjunction with laser-irradiated surgery on a surgical table
3. Creating PTT compounds in the NIR II (1000-1700 nm) range, which has a greater maximum allowable exposure and a longer penetration depth than NIR I (700-1000 nm), in order to achieve deep tissue tumor imaging and treatment.

In conclusion, next-generation technologies such as appropriate PTT agents with optimal optical characteristics, safety, and tumor-specific targeting, as well as enhanced laser fiber devices (multiple interstitial fibers) can be developed to provide superior cancer therapy. In order to optimize the therapeutic results, PTT should be properly matched with subsequent treatments. Innovative design and advancements in PTT platforms have a significant possibility of transferring from the lab to the clinic and expanding in clinical use.

CONCLUSION:

Photothermal therapy is now able to treat both local tumours and advanced metastatic malignancies, having evolved from a technique for ablating small tumours. From a functional viewpoint, we have evaluated the main nanoparticles employed in PTT of cancer in this paper. PTT is capable of completely eliminating cancer cells from the initial tumour or local lymphatic metastases in the superficial tissues, preventing them from spreading to other distant organs. However, PTT by itself is not enough to completely eradicate cancer cells in order to stop tumor recurrence and spread due to the uneven heat distribution inside these tissues. To increase the treatment efficacy, PTN should be created with precise targeting and deep penetration capabilities in tumour tissues. Additionally, PTT cannot be used to treat metastatic cancer cells at deep remote areas because to NIR light's low depth of penetration, which is a key contributing factor to the high mortality of cancer metastasis. An effective alternate treatment for metastatic cancer may involve combining PTT in conjunction with systemic chemotherapy, immunotherapy, or stereotactic radiation. The development of co-administered PTN poses extra questions since, in order to achieve the desired combined therapeutic effects, it is necessary to administer photothermal agents and combination therapeutic agents in a synergistic manner. In conclusion, PTT has shown considerable potential for treating cancer metastasis both on its own and in conjunction with existing medicines or imaging guidance. These advantages, nevertheless, have only just begun to be seen in animal experiments, and few have been verified in human clinical trials. To better their further clinical translation, significant efforts are required in the development of a therapeutically effective PTT that is biocompatible The PTT or their combination therapy, in our opinion, can offer a very promising therapeutic approach and renew hope for the future battle against cancer metastasis.

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