



Laser Innovations for Research and Applications

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Breast cancer and laser therapy

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Abstract

Female breast cancer is the most diagnosed cancer globally, and it poses a serious global health threat. Traditional cancer treatments have several undesirable side effects. The most effective therapy for treating breast cancer is doxorubicin (Adriamycin), but it has severe side effects, so developing better therapies for breast cancer is necessary, such as laser therapy which could be a promising treatment option. In this regard, the current review focuses on reviewing the used breast cancer treatments and the progress on using laser therapy.

Keywords: Breast cancer; Doxorubicin; Laser therapy

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1. Introduction

A pulsed laser system with pulse durations in the femtosecond range has several favorable properties (1). The formation of spatially highly focused energy deposition in biological samples is attained by the femtosecond pulses' ability to generate extremely high intensities with little energy. This results in a variety of chemical, mechanical, or thermal processes (2). Femtosecond pulses cause little damage and are regarded as safe since they are too short to transmit heat or trigger inflammation in biological samples (3). The femtosecond pulses produce minimum phototoxicity, confinement, high spatial and temporal resolution, and controllable laser pulses that are non-invasive, clean, and have little absorption by biological samples (4). They have a broad range of wavelengths that can be tuned, which is crucial for determining the ideal parameters of laser (5). Femtosecond lasers have extremely high peak powers and generate free electrons through nonlinear absorption interactions, in contrast to continuous wave (CW) or long-pulsed lasers, which rely on linear absorption of the photon (one photon) and cause more heat accumulation and collateral damage.

The femtosecond laser light is utilized in several medical applications. For example, it is currently used in dental, cataract, and ear surgeries (Krüger et al., 1999; Ryu et al., 2021). Furthermore, the femtosecond laser is becoming a potent tool in fundamental biological research (Gabel, 2008). For example, it exhibits a strong antibacterial effect (Ahmed et al., 2021; El-Gendy et al., 2021). Interestingly, the femtosecond laser has been involved in cancer research. In both developed and developing nations, cancer is the primary cause of disease-related morbidity and mortality [6]. Cancer is characterized by uncontrollable cell division that results in tumor formation and spread to other body parts (Ochwang'i et al., 2014).

Breast cancer is the most prevalent type of cancer in the world. In 2020, there were about 2.26 million cases of breast cancer estimated and it is the primary cause of cancer-related mortality among women (Sung et al., 2021; Wilkinson & Gathani, 2022). Conventional breast cancer therapies such as surgery and radiation therapies are often accompanied by serious long-term side effects such as second non-breast malignancies, pericarditis, and tissue necrosis (Pierce et al.,

1992). Chemotherapy suppresses the spread of cancers but is often accompanied by serious side effects (Karimi et al., 2022). Chemotherapy is frequently employed to treat the symptoms of advanced breast cancer patients as well as to decrease the probability of recurrence in those with localized breast cancer (Dong et al., 2009; Moulder et al., 2008). Doxorubicin is frequently used to treat breast cancer (O'Shaughnessy, 2003). The clinical value of doxorubicin and other anthracyclines is limited by their toxicity. The cumulative dose adverse effects include myelosuppression, acute nausea and vomiting, alopecia, and cardiotoxicity (Hortobagyi, 1997; Tanaka et al., 2009). Furthermore, the limited therapeutic index of cytotoxic treatments and their nonspecific distribution throughout the body are the most significant issues in the development of medicines for breast cancer (Shah et al., 2021). To overcome the side effects of doxorubicin, it can be used in conjunction or replaced with another therapy (Norouzi et al., 2021). Consequently, new therapeutic techniques are urgently needed to overcome the limitations of existing therapies (Apsari et al., 2017).

The laser light application in oncology is multifunctional with different mechanisms. Laser therapy for breast cancer is intended to be non-invasive and capable of selectively suppressing cancerous cells without harming healthy tissues at specific laser light parameters (Habit et al., 2020). Also, 805 nm laser light was clinically used to ablate small breast cancers depending on the laser ablation technique (Dowlatshahi et al., 2002). It is worth mentioning that laser irradiation, at a power density of 5–150 mW/cm² and a wavelength range of 600–1000 nm, was used to manage chemoradiation-induced side effects in head and neck cancer (Zecha et al., 2016). MCF 7 cell apoptosis was accelerated using a low-level green laser (532 nm) (Suardi et al., 2022). Two breast cancer cell lines (MCF 7 and MB-435) were studied in vitro for their responses to laser wavelengths (830 and 780 nm), and it was found that particular laser dosages up to 5 J/cm² did not promote the growth of cells (Laakso, 2007). Chen et al have reported that femtosecond laser effectively stimulated FePt nanoparticles, which were then able to inhibit the proliferation of EMT-6 breast cancer cells (Chen et al., 2013). Furthermore, as reported in a recent study, aminolevulinate photosensitized by femtosecond laser triggered the death of breast, skin, and bladder cancer cells (Kars et al., 2020).

2. Breast cancer

Breasts are mammary apocrine glands that can develop several benign or malignant diseases. Multiple genetic changes in the breast's milk-producing lobules and milk ducts' epithelial cells increase the chance of cancer (Feng et al., 2018). Women are 100 times more likely than males to get this fatal disease (Gethins, 2012). It is thought that the epithelium lining the breast's terminal ductal lobular unit is where cancerous cells initially appear (Wellings & Practice, 1980).

With an anticipated 2.3 million new cases, or 11.7% of all cancer cases, female breast cancer surpassed lung cancer as the leading cause of cancer incidence globally in 2020 (Sung et al., 2021). In addition, breast cancer is an important global health threat (Wilkinson & Gathani, 2022). It is the most prevalent cancer in women (Sung et al., 2021; Wilkinson & Gathani, 2022).

2.1. Breast cancer types

2.1.1. Based on pathology, invasiveness, and prevalence

There are numerous types of breast cancer. Breast cancer can appear in a variety of places in the breast, including the lobules, the ducts, or the tissue in-between (Weigelt et al., 2010). Breast cancers can be broadly divided into two distinct categories: carcinomas and sarcomas. In most breast cancer instances, epithelial cells found in breast tissues such as glands, milk ducts, and lobules (milk-producing glands) are the source of the malignant cells as shown in Fig.1 (Kiro, 2019). Carcinomas are breast cancer caused by the change of these epithelial cells. However, in rare instances, breast cancers can be sarcomas when breast cancer begins in the cells of the muscles, lipids, or connective tissues of the breast. Sarcomas are a considerably rarer kind of breast cancer. The majority of breast cancers are carcinomas (Feng et al., 2018). Breast cancer is referred to be "in situ" when the affected cells remain confined to the tissues from where they originated and as "invasive" when the cancer cells have migrated to neighboring tissues (Logan et al., 2015; Tsuda, 2020).

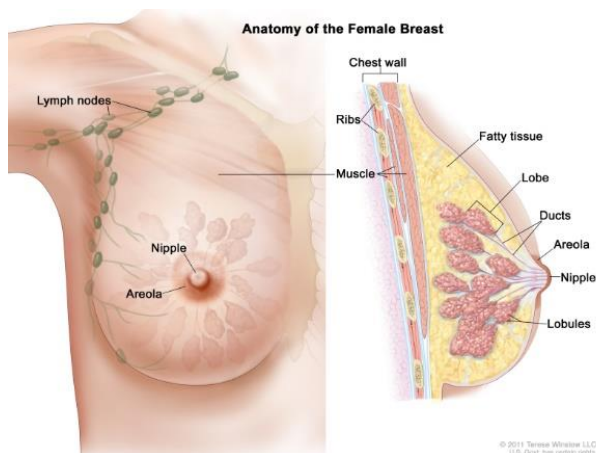


Fig.1. Anatomy of female breast. Cancer can develop from any of the tissues depicted in the diagram and migrate to other parts of the body (Kiro, 2019)

Common breast cancers based on pathological characteristics and invasiveness can be categorized into three main types (SAMINENI et al., 2022):

- 1) In situ or non-invasive breast cancer
- 2) Infiltrating or invasive breast cancer
- 3) Metastatic breast cancers.

2.1.1.1. In situ or non-invasive breast cancer

Breast carcinoma in situ is further classified as ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS). LCIS is thought to be caused by atypical lobular hyperplasia (Simpson et al., 2003). DCIS is a pathological term for the proliferation of neoplastic epithelial cells within the tubulolobular system of the breast (Richie & Swanson, 2003). In situ carcinomas have a high risk of progressing to invasive cancers, even though DCIS is not invasive in itself (Pang et al., 2016).

2.1.1.2. Infiltrating or invasive breast cancer

Invasive breast cancers are further divided into the two groups indicated below based on the cells and tissues involved:

a) Invasive ductal carcinoma (IDC):

This form of breast cancer is the most prevalent. Breast milk ducts are where invasive (or infiltrating) ductal carcinoma (IDC) begins (Girish et al., 2014). Medullary carcinoma of the breast, tubular carcinoma of the breast, papillary carcinoma of the breast, mucinous carcinoma of the breast, and cribriform carcinoma of the breast are some of the subtypes included in the IDC classification (Makki, 2015).

b) Invasive lobular carcinoma (ILC):

ILC accounts for 5% to 15% of all breast cancer cases, making it the second most common type (Thomas et al., 2019). ILC can affect women at any age, but older women are more likely to develop it and also ILC usually happens later in life than IDC (Li et al., 2000; Silverstein et al., 1994).

2.1.1.3. Metastatic breast cancers

Breast cancers that have reached a late stage and spread to other body organs are referred to as metastatic or stage IV cancers (Peart, 2017). Breast cancer can spread to distant locations like the lung, liver, bone, and brain as well as to lymph nodes under in the armpit (Feng et al., 2018).

2.1.2. Based on the expression of receptor proteins.

Breast cancers differ in their immunohistochemistry (IHC) characteristics and protein receptor expression depending on their etiology. Thus, they can be clinically divided into four distinct subtypes: luminal A and B, human epidermal growth factor receptor 2 (HER2), and basal-like or triple-negative breast cancers (Tian et al., 2014).

2.1.2.1. Luminal A

The Luminal A subtype of tumors is a low grade subtype and has high expression of the luminal epithelial genes progesterone receptor (PR) and estrogen receptor (ER) and low expression of HER2 (Dai et al., 2015). These tumors are associated with somatic mutations in PIK3CA (phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit α), GATA3 (GATA Binding Protein 3),

MAP3K1 (mitogen-activated protein kinase genes, and often exhibit cyclin D1 overexpression (Norum et al., 2014).

2.1.2.2. Luminal B

When compared to Luminal A tumors, Luminal B tumors are high grade and exhibit lower levels of PR and ER expression (Norum et al., 2014). PIK3CA and TP53 gene mutations, as well as abnormalities in the MAPK and retinoblastoma pathways, are frequently seen in luminal B tumors (Norum et al., 2014). HER2 overexpression is present in some Luminal B tumors, and these HER2-positive Luminal B tumors have a worse outcome than those with HER2-negative status (Guiu et al., 2012). While Luminal B tumors have a worse prognosis than Luminal A tumors, their prognosis is still intermediate when compared to all other subtypes (Fragomeni et al., 2018).

2.1.2.3. HER2-enriched

HER2 gene expression and HER status are not the only factors that determine whether a tumor is HER2-Enriched or not. The EGFR/HER2 signaling pathway (Godoy-Ortiz et al., 2019), which is made up of the four major proteins epidermal growth factor receptor (EGFR), HER2, HER3, and HER4, is what drives HER2-enriched tumors (Moasser, 2007). Proliferative activity is triggered by increased dimerization of HER2 and EGFR (Moasser, 2007). HER2-Enriched tumors typically have high HER2 expression and lack luminal epithelial gene expression (non-luminal). These tumors have a poor prognosis and are highly proliferative (Llombart-Cussac et al., 2017). To assess the efficacy of a treatment that targets the HER2 pathway, the expression of HER2-regulated genes can be used as useful predictive markers (Llombart-Cussac et al., 2017).

2.1.2.4. Basal-like

Genes typically found in basal cells are highly expressed in tumors classified as basal-like (Norum et al., 2014). Specific epidemiological, phenotypic, and molecular characteristics of basal tumors include proliferation, high grade, distinctive genetic alterations, and necrosis. Additionally, the WNT pathway is more active and EGFR expression is higher (Norum et al., 2014). These tumors frequently exhibit TP53 and BRCA1 gene mutations but do not express luminal

genes, ER/PR, or HER2. According to research, basal-like tumors are aggressive, have a poor prognosis, and a high probability of recurring (Dai et al., 2015).

2.2. Breast cancer therapy

2.2.1. Surgery

The breast cancerous tissues removal can be achieved through mastectomy and breast-conserving surgery (BCS), which are the two main surgical techniques. BCS, also known as partial or segmental mastectomy, lumpectomy, wide local excision, or quadrantectomy, allows for the simultaneous removal of malignant tissue and preservation of healthy breast tissue, frequently in conjunction with oncoplastic techniques in plastic surgery. When a breast is completely removed during a mastectomy, rapid breast reconstruction is commonly done next. Sentinel lymph node biopsy (SLNB) and axillary lymph node dissection (ALND) are procedures used to remove the affected lymph nodes. Despite the fact that BCS seems to be more advantageous

for patients, individuals who have had it commonly show a propensity for a need for a total mastectomy in the future (Morrow et al., 2001). The European Society for Medical Oncology (ESMO) has guidelines for patients with early breast cancer that depend on the patient's willingness to preserve the breast, tumor size, surgical feasibility, clinical phenotype, and type of therapy (Cardoso et al., 2019).

2.2.2. Chemotherapy

Chemotherapy is a systemic treatment for breast cancer. The best option is chosen specifically for each patient based on the characteristics of the cancer; chemotherapy may also be employed in cases of secondary breast cancer.

The current course of treatment involves the administration of 2 to 3 combinations of the following drugs: 5-fluorouracil/capecitabine, carboplatin, cyclophosphamide, anthracyclines (doxorubicin, epirubicin), and taxanes (paclitaxel, docetaxel). Choosing the right medication is crucial since various molecular breast cancer subtypes respond differently to preoperative

chemotherapy (Rouzier et al., 2005). In comparison to postoperative chemotherapy, preoperative chemotherapy is more effective (Fisher et al., 1998). Even though chemotherapy is effective, it frequently causes several side effects such as nausea/vomiting, hair loss, diarrhea, fatigue, mouth sores, higher risk of infection, bone marrow suppression, paired with anemia, leucopenia, and easier bruising or bleeding. Less frequently but still possible side effects include neuropathy, cardiomyopathy, impaired mental functions, and hand-foot syndrome (Łukasiewicz et al., 2021). Reproductive difficulties and menstrual cycle irregularities may also appear in younger women (Łukasiewicz et al., 2021). The most clinically-used drug for management of breast cancer is doxorubicin (Czeczuga-Semeniuk et al., 2004). The mechanism of action of doxorubicin includes several pathways including its ability to induce DNA damage through DOX–DNA adducts formation and DNA Intercalation (Lipscomb et al., 1994; Yang et al., 2013; Zlatanova & Victor) or Topoisomerase Trapping (Pommier et al., 2010; Ross et al., 1978), cause the creation of ROS by binding to cardiolipin on the inner mitochondrial membrane, which starts the process of apoptosis (Gilliam et al., 2012; Goormaghtigh et al., 1990; Gorini et al., 2018), and stimulate senescence in cancer cells (Joyner et al., 2006). A significant dose-dependent toxicity limits the use of doxorubicin (Dong et al., 2009). Doxorubicin toxicity can be decreased by combining it with another more tumor-specific treatment to reduce the dosage.

2.2.3. Radiation therapy

Following surgery and/or chemotherapy, radiotherapy is a common local treatment for breast cancer. It was developed to prevent the spread of breast cancer by ensuring that all malignant cells were killed. Radiation treatment is also advantageous for metastatic or not curable breast cancer (Yang & Ho, 2013). There are several distinct forms of breast radiation therapy, including: (1) 3D-conformal radiotherapy (3D-CRT), (2) intraoperative radiation therapy (IORT), (3) intensity-modulated radiotherapy (IMRT), and (4) Brachytherapy. Irritation and discoloration of the radiation-exposed skin, coupled with fatigue and lymphedema, are some of the most prevalent adverse effects of radiation therapy for breast cancer patients. However, radiation therapy has a strong correlation

with increased patient overall survival rates and decreased recurrence risk (Joshi et al., 2007).

2.2.4. Hormonal (endocrine) therapy

Endocrinal treatment can be used as either neoadjuvant or adjuvant therapy in patients with the Luminal-molecular subtype of breast cancer and is beneficial in cases of metastasis or recurrence of breast cancer. Since ER expression is a prevalent characteristic in breast cancer patients, inhibiting ERs with hormone therapy is commonly used as one of the potential therapeutic strategies. The goal of hormonal therapy is to lower estrogen levels or prevent estrogen from stimulating the growth of breast cancer cells (Lumachi et al., 2011). Selective estrogen receptor degraders (SERDs) (fulvestrant) and selective estrogen receptor modulators (SERMs) (tamoxifen, toremifene) are medications that block ERs. Also, aromatase inhibitors (AIs) (letrozole, anastrozole, and exemestane) are treatments that aim to lower the levels of estrogen (Lumachi et al., 2011; Tremont et al., 2017). However during such treatment, about 50% of hormone receptor-positive breast cancers are resistant to hormonal therapy (Drăgănescu & Carmocan, 2017).

2.2.5. Phototherapy

Phototherapy is a broad word for any therapy that utilize various wavelengths of light (colors) for therapeutic objectives (Martel, 2018). Light therapy for various diseases has a very long history dating back to antiquity (Daniell et al., 1991). Phototherapy was used by many ancient civilizations, but it wasn't until the early 20th century that it was reappeared (Ackroyd et al., 2001). Four thousand years ago, sunlight and color were utilized in temple rituals and as a Divine healing agent in the ancient healing temples of Greece (at Heliopolis: "helios" meaning Sun, "opolis" meaning city) and Egypt. During healing rituals, the priests split white light into each of the seven colors of the rainbow/spectrum using various colored crystals to shine it on a sick person. According to what was necessary for their recovery, sick persons were bathed in a specific color. It is believed that the priests primarily treated the spiritual problems that a patient presented with, which would later cure the mental and physical ailments. The Greeks named sunbathing of the body heliosis, after their sun god Helios, and used to take sand

baths in the sun to treat a variety of ailments of the body and soul (Heinrich, 2008). The Egyptians, Chinese, and Indians employed light to treat a variety of diseases such as vitiligo, rickets, psoriasis, and skin cancer (Spikes, 1985). Heliotherapy, which was presented by the Greeks 3000 years ago, was one of the oldest documented reports of the sun as a therapeutic approach. The Greeks favored a type of heliotherapy in which participants lay nude in specially designated sites and were subjected to whole body exposure to the sun. The father of heliotherapy was Herodotus, a prominent physician from the second century BC. His teaching highlighted the importance of sun exposure for health restoration (Hopper, 2006). The physician Cauvin declared in 1815 that sunlight might be a curative agent for scurvy, rheumatism, scrofula, rickets, paralysis, swellings, dropsy, and weakness of muscle (Koorengel & Meesters, 2002).

Niels Finsen, a Danish physician, introduced phototherapy as a science. He claimed in 1893 that applying red light to smallpox lesions may prevent suppuration and subsequently proved that sunlight's ultraviolet photons are the reason for their bactericidal effects. This prompted him to develop a way for treating lupus vulgaris with carbon arc phototherapy, for which he was awarded the Nobel Prize in 1903 (Urbach et al., 1976). Finsen is also known for establishing the Medical Light Institute in Copenhagen, and Denmark, and for using an electric carbon arc torch to treat over 800 patients with lupus vulgaris using ultraviolet radiation in 1896. Finsen's work resulted in the establishment of the "School of the Sun" in the Swiss Alps for tuberculosis patients (Roelandts & Photomedicine, 2005). Princess Alexandra introduced phototherapy to England and prompted doctors at the London Hospital to apply it. Phototherapy is still used to treat newborn jaundice today (Hopper, 2006).

2.3. Laser therapy as a specialized field of light therapy

One of the most well-known and well-researched light therapy modalities is laser therapy (Azadgoli & Baker, 2016). The use of laser therapy has been approved by scientific and medical authorities (Heinrich, 2008).

2.3.1. Origin of laser

Laser stands for Light Amplification by Stimulated Emission of Radiation (Takac & Stojanović, 1999). Physicist Albert Einstein described the laser principle for the first time in 1917, when he described the theory of stimulated emission (Gross & Herrmann, 2007). Microwave amplification of the stimulated emission of radiation was discovered by Townes in 1957. The MASER principle was applied to the optical component of the electromagnetic field by Schawlow and Townes in 1958 (Schawlow & Townes, 1958). Theodore Hurold Maiman performed the first successful laser operation with a synthetic ruby made of aluminium oxide doped with chromium oxide in 1960 (Bernatskyi et al., 2021). Peter.P.Sorokin and Mirek Stevenson invented the first Uranium laser in 1960 [158]. Helium Neon (He-Ne) laser was invented in 1961 by Ali Java William, Bennet Jr, and Donald Herriot (Natarajan et al., 2011). Geusic, Markos, and Van Uiteit created the first working Nd:YAG laser in 1964 (Joshi et al., 2022). Kumar N Patel invented the CO2 laser in 1964 (Patel, 1964). Also, William Bridges invented the Argon Ion laser in 1964 (Bridges, 2000).

2.3.2. How does laser work?

An active lasing medium is energized to produce laser energy. The active medium can be gas, solid, or liquid. Normally, the atoms in the lasing medium are found in a resting state. Around the nucleus, the electrons are in lower orbits. The external pumping system runs in parallel with the active medium (Van Pelt, 1970).

When energy is introduced from an external source (a pumping source), the atom absorbs the energy, which causes the electron to rise to a higher or excited state. Flashlamps, other lasers, and electrical discharge are all examples of this external power source (Goebel, 1994). The electron remains in the excited state for a very short time before the atom attempts to regain equilibrium by returning to the ground state. Atoms emit radiation when an electron falls in orbit. Normally, this is done in random directions and at random times. As a result, incoherent light is produced, with many photons travelling in different directions. This is known as spontaneous emission of radiation (Heinrich, 2008).

As the photon travels through the medium, it collides with another excited atom. The photon is absorbed, resulting in a faster decay to the ground state. Two

identical photons are emitted during the electron's return to equilibrium. The first photon absorbed, and the second produced by the decaying atom. The preceding atomic process is referred to as "Stimulated Emission of Radiation." (Silfvast, 2004).

The process is advanced by stimulated emission, which greatly increases or amplifies the photon number. Photons generated by stimulated emission make a pattern in the resonator by reflecting back and forth across the axis of two aligned mirrors. One mirror is 100% reflecting, while the other is only 90% reflective. Reflections between the parallel mirrors increase the intensity of intracavity energy. For Stimulated Emission to produce light amplification, the number of excited atoms must exceed the number of atoms or molecules in the ground state. This is known as "Population Inversion." (Goebel, 1994).

2.3.3. Laser light properties

There are various light sources that can be used for therapy with different parameters (wavelength, output power, continuous wave or pulsed operation modes, and pulse parameters). These parameters are typically specified in the operating manual (Karu, 2009).

A laser's light output differs from that of ordinary light sources. The output of the laser is characterized by three properties: directionality, monochromaticity, and coherence. These three characteristics are what make the laser so valuable and account for the laser's ever-expanding list of applications (Kim et al., 2020; Silfvast, 2004).

- a) Directionality: laser light is emitted in a specific direction as a relatively narrow beam. Ordinary light is emitted in a variety of directions away from the source such as that emitted by a light bulb. This property is a direct result of the active medium being placed in a resonant cavity.
- b) Monochromaticity: This property results from the following two factors:
 - (1) An electromagnetic wave with
 - c) frequency ν_0 can only be amplified. (2) Because the two-mirror arrangement creates a resonant cavity, oscillation can occur only at the cavity's resonance frequencies.

- d) Coherence: Laser light is said to be coherent when the wavelengths of the laser light are in phase in space and time.

2.3.4. Femtosecond laser as a Pulsed laser

Pulsed lasers are lasers which emit light not in a continuous mode, but rather in the form of optical pulses (light flashes). Both continuous and pulsed wave (CW/PW) modes of laser therapy is available. According to recent studies, PW has different biological and clinical effects than CW. It is claimed that PW is more effective than CW Because CW has no quench intervals (no pulse-off durations) which increase tissue heating. Numerous studies have demonstrated that low level laser therapy (LLLT) in PW mode may more effectively breakthrough skin boundaries like melanin, proving the idea that pulse is effective in penetrating deep organs (Ando et al., 2011; Hashmi et al., 2010). In this work, the used two pulsed laser systems which are femtosecond laser systems (Inspire HF 100 and Mai Tai HP) from Spectra-Physics. Laser pulses delivered by the Inspire HF100 laser system (Spectra-Physics), which is pumped by a mode-locked femtosecond Ti: sapphire Mai Tai HP laser (Spectra-Physics).

2.3.5. Laser applications in oncology

Laser-assisted mucosal ablation techniques were widely and successfully used to treat superficial gastrointestinal cancers such as superficial esophageal cancer, early gastric cancer, colorectal adenoma, and high-grade Barrett's oesophagus (Muguruma et al., 2012). Through its photomechanical, photochemical, and photothermal effects, direct laser ablation has been used to damage the cells of cancer (Chen et al., 1995; Thomsen & photobiology, 1991).

Lasers were being used safely to treat cancers in a variety of organ systems. Laser interstitial thermal therapy (LITT), for example, is a preferred treatment option in neurosurgery for patients who were not ideal surgical candidates (Sherman et al., 2011). Lasers have been successfully used to treat unresectable gliomas, as well as hard and hemorrhagic tumors such as tumors of the deep skull base, meningiomas, , and tumors deep in the ventricles (Hawasli et al., 2014; Takeuchi et al., 1982).

Laura et al reported that 380 nm was used to obtain photo switchable inhibitors of protein-protein interactions, and these inhibitors were then applied to living cells such as HeLa, HEK293, and MCF7 and caused inhibition to these cell lines (Nevola et al., 2013). A previous study also reported that 405 nm blue laser induced high levels of intracellular ROS in lung cancer cells while 664 nm or NIR (808 nm) did not affect ROS levels (Kushibiki et al., 2013). previous study in which MCF 7 and MB-435, two breast cancer cell lines, were studied in vitro for how they responded to lasers with common wavelengths (780 and 830 nm), and it was observed that laser dosages up to 5 J/cm² did not stimulate cell proliferation (Laakso, 2007). Also, 805 nm laser beam was clinically used to ablate small breast cancers depending on the laser ablation technique (Dowlatshahi et al., 2002). MCF 7 cell apoptosis was accelerated using a low-level green laser (532 nm) (Suardi et al., 2022). Two breast cancer cell lines (MCF 7 and MB-435) were studied in vitro for their responses to lasers of wavelengths (780 and 830 nm), and it was found that particular laser doses up to 5 J/cm² did not promote cell growth (Laakso, 2007).

Photodynamic therapy (PDT) was developed to more precisely target the desired tumor cells and improve this process (Mroz et al., 2011). In 1995, Sibille et al treated 123 esophageal cancer patients with PDT using a 630 nm dye laser (Sibille et al., 1995). PDT has been used successfully in the treatment of tumors for example, laser was used for intraocular tumors using localized red light (635± 5 nm; 40 to 400 milliwatts/sq cm) generated by a free running rhodamine B dye laser pumped by a 5-watt argon laser (Gomer et al., 1983). A 652 nm diode red laser with a fluence (energy) rate of 25mW/cm² was also used to assess the potential of PDT as a tool for head and neck cancer treatment (Sharwani, 2006). Chen et al have reported that femtosecond laser effectively stimulated FePt nanoparticles, which were then able to inhibit the proliferation of EMT-6 breast cancer cells (Chen et al., 2013). Furthermore, as reported in a recent study, aminolevulinic acid photosensitized by femtosecond laser triggered the death of breast, skin, and bladder cancer cells (Kars et al., 2020).

3. Conclusion

Laser Innovations for Research and Applications

The femtosecond laser light is utilized in several medical applications. The laser light application in oncology is multifunctional with different mechanisms. Laser therapy for breast cancer is intended to be non-invasive and capable of selectively suppressing cancerous cells without harming healthy tissues. From the studies covered in this review it appears that laser therapy for breast cancer is likely to be a promising treatment in the future. Research must be conducted in this point to explore the optimum laser parameters that can be used alone or in combination with another drug for breast cancer therapy.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors declare no conflict of interest.

Competing interests The authors declare no competing interests.

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