

# Analysis of Different Treatment Methods for Breast Cancer

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**Abstract.** This research discusses the mechanisms of current medical treatments for breast cancer and a brief analysis of the treatments. The aim of this research is to present the different cancer therapies and to select the most promising and promising therapies for breast cancer based on the performance of each therapy, where chemotherapy, radiotherapy, and immunotherapy for breast cancer are discussed. By analyzing the various therapies, it is concluded that all three therapies selected for discussion have shown a significant increase in efficacy over their traditional counterparts, but at the same time, the risks and potential shortcomings of the newer therapies have been demonstrated in experimental trials. Through the analysis of this research, it is hoped that there will be a combination of techniques and breakthroughs in therapies for breast cancer. Each therapy has its own shortcomings, and the combination of chemotherapy, radiation, and immunotherapy with current cancer therapies will be the future of cancer breakthroughs.

**Keywords:** breast cancer; radiation therapy; immunotherapy; chemotherapy.

## 1. Introduction

Whenever people talk about a disease that is highly lethal, widespread and difficult to treat, the topic of cancer never escapes them. However, its incidence still continues to increase worldwide. Among all the cancer types, breast cancer has been extensively studied, and various therapeutic options have been developed to control it worldwide. Breast cancer has been one of the most common diseases in women population. The occurrence of breast cancer has shown an upward trend in the majority of the last forty years. In recent years, with available data (selected between 2010-2019) provided, the incidence rate is about increasing by 0.5% [1]. Breast cancer has taken a toll on the body, including symptoms such as pain, fatigue, and psychological distress.

In order to control cancer and mitigate its negative impact on human health, various treatment options have been developed throughout human history. These include therapies such as surgical resection, radiotherapy, chemotherapy, immunotherapy, and targeted therapy. Despite significant advances in cancer treatment, there is still a need for more effective and less toxic therapies. For example, immunotherapy is a relatively new approach that has shown promise in the treatment of various cancers. Targeted therapy, which involves the usage of drugs which specifically target cancer cells or specific molecules involved in cancer growth and progression. In the case of breast cancer, HER-2 constitutes a well-recognized treatment focus for a significant portion of population diagnosed. Targeting antibodies, such as trastuzumab and pertuzumab have already gained approval for dealing with breast cancer cases characterized by HER-2 positivity [2]. In addition, it has laid the foundation of correspondence for future targeted drug treatment of cancer. Despite the success of targeted therapies in treating breast cancer, there is still a need for more effective and less toxic treatments for other types of cancer. The state of research on cancer therapies is evolving, and ongoing studies are exploring new targets, drugs, and method combinations.

This research has been chosen to discuss radiotherapy, chemotherapy, and immunotherapy since they have received much attention in recent years due to their potential to provide more effective and less toxic treatments for cancer patients and have already led to breakthroughs and successes in the treatment of breast cancers. In detail, this research is about the mechanism and analysis of radiotherapy, chemotherapy and immunotherapy for the treatment of breast cancer. One means of each of the three therapies has been chosen to be specifically analyzed in this research.



## **2. Mechanism and Therapeutic Effects for Breast Cancer**

### **2.1. Chemotherapy**

Chemotherapy is a standard treatment that kills cancer cells by certain medical drugs. Chemotherapy drugs work by targeting rapidly dividing cells, mostly to limit their ability to divide, grow, and kill mutated cells. There are many different types of chemotherapy drugs, each with a unique mechanism of action. The function of chemotherapy drugs is to inhibit DNA synthesis of mutated cells. Doing so can help inhibit mutated cells from replication and spreading. Other chemotherapy drugs disrupt cell division by targeting the microtubules that help separate chromosomes during cell division.

Chemotherapy can be a successful cancer treatment, but it also has risks. They are including but not limited to nausea, vomiting, exhaustion, and increasing various infections. Depending on the particular chemotherapy medications used and the patient, these side effects may differ. To manage side effects, healthcare providers may prescribe medications to alleviate symptoms or make recommendations for lifestyle adjustments. Research has shown that chemotherapy for breast cancer, including anthracyclines and targeted agents, has a toxic influence on multiple body systems, particularly causing the risk of cardiotoxicity [3]. Recent studies have provided a promising approach, which will be explained below. To address this problem, the first thing we need to do is target breast cancer cells. The first step for almost every cancer treatment will always be targeting the mutated cell. For most breast cancer diagnoses HER-2 has always been the biomarker for targeting since HER-2 is present in around 20 to 30% of breast cancer cells [4]. Thus, cancer cells will be targeted successfully. The second thing is to deliver the drugs. So far, there are many cancer drugs available: doxorubicin (DOX), colchicine, 5-fluorouracil, cisplatin, actinomycin D, and methotrexate [5].

Nanoparticles have been used in the treatment of breast cancer to reverse medication resistance and act as drug carrier systems for chemotherapy medicines [5]. In this instance, a novel medication delivery system is used to lower the potential for cardiotoxicity. To be more precise, the studies to test the efficacy of the DOX were conducted using graphene-based yolk-shell magnetic nanoparticles (GYSM-NPs), a stimuli-responsive platform with a good drug loading capacity of about 91 percent. The results showed that the amount of DOX released by GYSM-NPs showed different variations, with values ranging from 6.8% to 45.6%, and a large part of the reason for this is the variable PH in the human body. The benefits are apparent; a study has shown that breast cancer cells can interact with healthy cardiac cells as well as decrease the levels and the rate of HER-2 expression with the addition of free DOX. The study shows the excellent news that GYSM-NPs can be a good and effective drug delivery platform. As a result, the new suggested platform has shown promising to treat breast cancer with a fresh approach as well as reduce the risks of cardiotoxicity inducement. The advantages of using GYSM-NPs in breast cancer treatment include their high biocompatibility, low toxicity, and ability to target cancer cells more precisely. Moreover, the magnetic properties of the nanoparticles enable drugs to be guided to the tumor site using an external magnetic field, which improves accuracy and reduces side effects on the human body.

Chemotherapy is an essential and effective treatment option for many types of cancer, and it also has a long history and well-established technology among all the existing cancer treatments. While it can cause side effects, which can often be managed with appropriate care and support, the cost and availability of chemotherapy can vary depending on several factors. Still, efforts are being made to improve access to this vital treatment option for all needy patients. As the evidence has shown, there is no denying that chemotherapy is one of the optimal cancer treatment choices available for breast cancer. However, the side effects mentioned above have put patients into concerns. As a result, it is eager to find another cancer treatment.

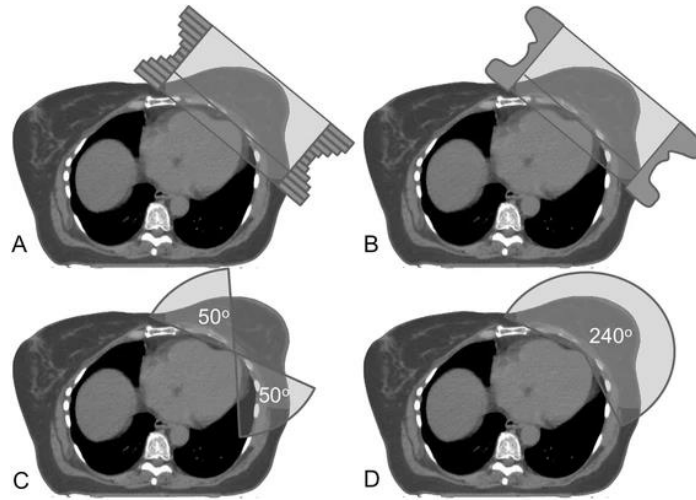
### **2.2. Radiation Therapy**

Radiation therapy is another common and effective treatment for cancer, by applying high-energy radiation to kill mutate cells. Data supported that approximately half of all cancer patients receive

radiotherapy during their courses. Radiotherapy has contributed to 40 percent of curative treatment for cancers. Like the chemotherapy mentioned above, radiation therapy also has a high reputation and reliability among cancer treatments. The explanation is clear given that radiotherapy is both a very effective palliative treatment option and a curative treatment that may be used to cure cancers and other illnesses and reduce their symptoms in patients [6]. One thing that needs to be clarified is that cancer cells with a high ability to generate are more vulnerable under exposure to radiation, which further suggests that normal healthy cells are more likely to repair after radiation damage. Radiation therapy could be successfully applied in this situation. The aim of radiotherapy can be achieved through various mechanisms, including direct DNA damage or indirectly generating free radicals, which could further interfere with cancer cell division. Thus, by damaging the DNA of cancer cells, they are not able to repair and eventually die.

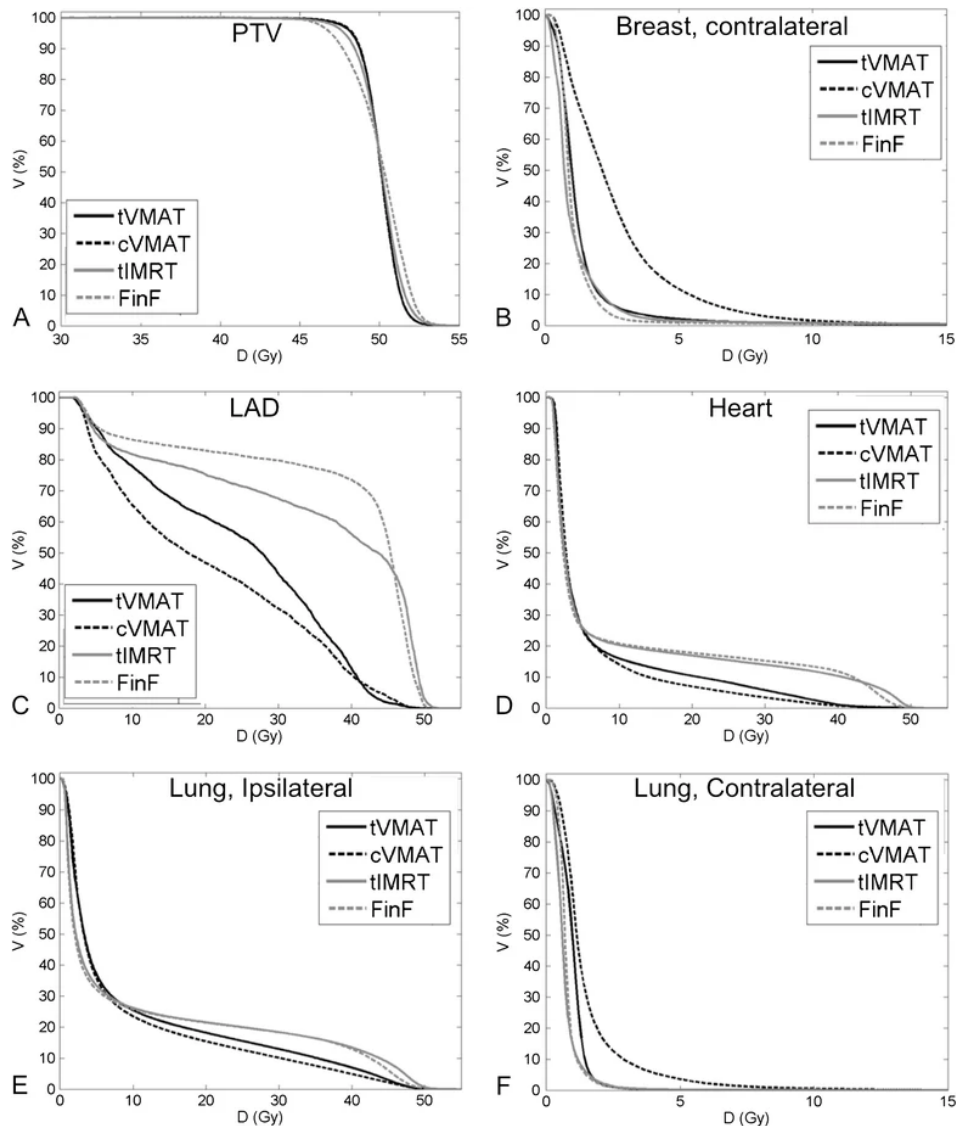
Radiation therapy is more promising to cure cancers and prevent further cancer cell growth when treating cancer in a relatively early stage. There are two ways that radiotherapy can be employed: internally and externally. The external approach is aiming high-energy rays at the tumor's location from points outside human bodies. As for internal therapy, which also refers to brachytherapy, it targets the tumor sites and inserts radioactive sources into the sites where cancer cells are generated and spread. This treatment is carefully planned to deliver the radiation precisely to the tumor site, considering several factors such as tumor size, location, and sensitivity. Throughout several treatment sessions, radiation therapy can effectively shrink tumors, control their growth, and alleviate symptoms associated with cancer. Radiation therapy side effects might vary based on the type of cancer being treated, the amount and length of treatment, as well as the particular patient. Common side effects of radiation therapy include fatigue, skin irritation, and hair loss in the area being treated. More severe side effects can occur in some cases, such as damage to nearby organs or tissues. This damage could be severe in some cases. To manage side effects, healthcare providers may prescribe medications to alleviate symptoms or make recommendations for lifestyle adjustments. One thing that needs to be explained is the risk of radiation affecting normal cells and tissue. Fortunately, radiation could be highly controlled to minimize the damage in this way. Prostate cancer, breast cancer, lung cancer, and brain tumors are just a few of the many malignancies that can be effectively treated with radiation treatment. Radiation therapy may be used to treat cancer as the main course of treatment in some circumstances, while it may also be used in conjunction with other therapies like surgery or chemotherapy.

The effectiveness of radiotherapy is dependent on several different factors, including but not limited to tumor types, treating stage, the sites of the tumor, and the patient's overall general health condition. The disease of choice in this instance to further demonstrate the novelty of radiation therapy is breast cancer. Among all the disadvantages suggested in the previous context, one of the main concerns of radiation therapy is that the radiation dose could be too high to affect surrounding healthy organs, in this case, around the breast, the lungs, and the heart. This result is not expected since the side effects of radiation are potential mutation occurrence and unnecessary additional treatment requirements. Tangential volumetric modulated arc treatment (VMAT) is suggested here as an alternative to traditional tangential field-in-field and tangential intensity-modulated radiotherapy. The ipsilateral lung dose is reduced while VMAT produces excellent target coverage and uniformity. In order to optimize VMAT and IMRT plans and avoid skin overload, PTV<sub>in</sub> was also used in this comparative experiment. According to a variety of scientific studies, the experiment's recommended dose was 50 Gy given in 25 pieces. 98 percent of the treatment area was supposed to be covered by 47.5 Gy in the PTV [7]. For the Elekta Infinity® accelerator, the testing led to the development of a 5 mm Agility® MLC treatment plan. Careful consideration is given to the size of the PTV while selecting the energy, which are either 6 or 10 MV. As shown in Figure 1 below, four distinct treatment plans using the same isocenter were suggested. The four possibilities are: standard tangential; dynamic IMRT with two static tangential fields; tVMAT with two tangential dual arcs of 50 degrees, and cVMAT with one dual arc 240 degrees.



**Figure 1.** Typical beam arrangements for FinF, tIMRT, tVMAT and cVMAT [7].

The study's findings indicate that VMAT offers three main benefits over other treatments, as shown in Fig. 1. Firstly, the tVMAT technique demonstrated an apparent reduction in high lung dose-volume compared to tIMRT and FinF. Secondly, the VMAT techniques provided significantly better dose coverage about V47.5 Gy than FinF and tIMRT techniques [7]. Lastly, VMAT techniques achieved significant cardiac dose sparing in the heart and LAD graph compared to FinF or tIMRT.



**Figure 2.** Average cumulative DVHs for different techniques studied [7].

The most effective arc configuration for the VMAT plans while accounting for the various testing situations was found by creating a range of plans with diverse qualities, such as the choosing arcs angles that were previously described. The study depicted above used the beam arrangement that produced the best results. Despite the fact that VMAT has shown promising results in tests, it is important to be aware of the hazards and restrictions this medical technology may carry. When cVMAT and tVMAT are compared, the latter is more encouraging since cVMAT has raised low-dose volume in the lungs and contralateral breasts compared to tVMAT, even if the latter has successfully decreased high-dose volume in the cardiac LAD and ipsilateral lungs, as shown in Fig. 2. When contrasting the two methods, it is important to note that they both have the same concern: boosting low-dose volume to the contralateral breast and lung. The volume of each approach is the subject of the aforementioned experiment. The rise in low-dose volumes continues to be the primary cause of the delay in the practical application of IMRT and VMAT technologies in full breast irradiation. These radiation dosage increases have no therapeutic advantage and might lead to further treatments that are not essential. To solve these difficulties, more thorough research is still needed. In conclusion, radiation therapy is an essential and effective treating option for breast cancer. As for the side effects, these still need to be highly concerned but can often be managed with appropriate care and support. Efforts still need to be made to improve access to this critical treatment modality for all needy patients.

### **2.3. Immunotherapy**

Immunotherapy is another option of treatment different from the traditional one. Immunotherapy focuses on harnessing the power of human immune system to fight against cancer cells. Unlike the two traditional therapies which has been mentioned above, they directly target cancer cells more or less. Immunotherapy works by activating and enhancing the body's own immune response to recognize and destroy cancer cells. Several different approaches are used in current treatments. The strategy employed in immunotherapy is often to add to or stimulate the immune system with a large number of cells, proteins, medications, and vaccination elements in order for the body's immune system to be able to once again detect and eliminate the sick cancer cells [8].

The mechanism of action of immunotherapy varies depending on the specific type of treatment. One common form of immunotherapy is immune checkpoint inhibitors, which block proteins that inhibit the immune response. These proteins, known as checkpoints, can also help prevent immune cells from attacking healthy cells and tissues as well as allowing the re-activation of immune system, to be specific, T killers cells to recognize and attack cancer cells. Immunotherapy has shown remarkable efficacy in treating various types of cancer. In the case of breast cancer, immune checkpoint inhibitors have revolutionized breast cancer treatment by significantly improving overall survival rates and reducing cancer cells. They have also shown promising results in other types of cancer, such as lung, bladder, and kidney. The mechanisms of immunotherapy for breast cancer are explained here. It is common knowledge that activated CD8 positive cells are in charge of identifying and eliminating pathogen-infected and abnormal cells, such as cancer cells. The majority of the body's cell-mediated immune effectors are thought to be CD8 positive. Since they may boost B cell production of antibodies and increase antibody responses by acting as T-helper cells to protect the altered cells, CD8-positive T cells have become essential for starting and controlling the immune response. Inhibitors are implanted because there is a link between cancer cells and T-cell activators, and some breast cancer cells inhibit the immune system by suppressing the production of T-cells, which in turn prevents the immune system from attacking and eliminating the cancer cells. This is why it is necessary to stimulate the proliferation and maturation of T-cells by promoting the binding of T-cell receptors to antigen-presenting cells, under the combined influence of co-stimulatory and antigen-specific signals [9].

Both the programmed cell death protein 1 (PD-1) or programmed cell death protein 1 ligand (PD-L1) and cytotoxic T-lymphocyte-associated antigen 4 (CTLA4) pathways have been identified as effective targets for developing new cancer treatments due to their critical roles in the immune response and peripheral tolerance. Checkpoint inhibitors can prevent T-cell fatigue and restore anti-

tumor immune responses, although co-stimulatory signals are essential for controlling T-cell activation [10]. These two pathways have allowed several checkpoint inhibitors to be approved. T cell activation, which is triggered by antigen-presenting cell receptors, is regulated by co-stimulatory signals like CD28 and CTLA-4. T-cell activation and cytokine release are dependent on CD28 signals, whereas CTLA-4 signaling suppresses T-cell activation. Therefore, it is not difficult to conceive that CTLA-4 inhibitors might avoid unnecessary T-cell depletion and significantly enhance anti-tumor T-cell responses by preventing the interaction between CTLA-4 and CD80/86 (antigen presenting cells receptor) ligands. When the ratio of CD28 compare to CD80/CD86 is high, CD80 and CD86 ligands generated on active APCs can trigger CD28 and CTLA-4, which leads to the synthesis of growth cytokines and T-cell proliferation and differentiation. Due to CTLA-4's high affinity for CD80/86 and competition with CD28, it contributes to immunosuppression by removing CD80/86 from antigen-presenting cells' surfaces. Therefore, employing CTLA-4 inhibitors can prevent T-cell depletion and improve the anti-tumor T-cell reaction by cutting the interaction between CTLA-4 and CD80/86 ligands.

The following scenario also occurs in a comparable manner: In the final phases of an immune response, PD-1 controls previously activated T-cells. When it binds to the ligand PD-L1, it prevents T-cells from proliferating, surviving, producing cytokines, and performing other effector activities. Inhibitors have shown useful in prolonging the average lifespan of metastatic cancer patients. When PD-1 binds to PD-L1, T-cell receptor signaling pathways governed by protein kinases are inhibited by the dephosphorylation of T-cell receptor signaling components. This inhibition has an effect, as seen by decreased T-cell survival, proliferation and cytokine generation. Checkpoint inhibitors can thereby reestablish the immune response against malignancies and aid in the removal of malignant cells by disrupting the connection between PD-1 and PD-L1. However, the response rates of blocking medicines range from 20 to 38% for various tumor types, emphasizing the significance of timing for immunotherapy success. What is most enlightening and reassuring is that the PD-L1 antibody atezolizumab is used with other therapies like chemotherapy after receiving FDA approval. This combination can be used to treat patients with triple-negative metastatic breast cancer who are positive for PD-L1 protein expression [11].

Immunotherapy can have negative effects, just like any other cancer treatment. Despite this significant achievement, the treatment's success in this case is still hindered by the low complete response rates and immune-mediated severe adverse consequences that can lead to treatment discontinuation [12]. These factors support the need for new therapeutic approaches. The particular adverse effects observed can change according on the type of immunotherapy administered, among other malignancies. Fatigue, a skin hives, diarrhea, and flu-like symptoms are typical adverse reactions. In some cases, more severe immune-related side effects can occur, such as inflammation of organs like the lungs or liver. It is essential for healthcare providers to closely monitor patients receiving immunotherapy and manage any side effects promptly. Immunotherapy is considered a relatively safe treatment among current treatments since it does not involve entering foreign drugs or other radiation. However, by harnessing immune power, there is the possibility that the immune system will attack cells indiscriminately, including healthy, normal cells. It requires patients to improve self-tolerance meanwhile accepting treatments.

By utilizing the immune system's capacity to combat cancer cells, immunotherapy is a ground-breaking method of treating cancer. With different mechanisms of action and varying efficacy across different types of cancer, immunotherapy has shown remarkable potential in improving patient outcomes. However, managing side effects and ensuring access to affordable immunotherapy remain important considerations. Continued research, investment in healthcare infrastructure, and global collaboration are crucial for maximizing the benefits of immunotherapy in the fight against cancer.

### 3. Conclusion

It can be concluded that the innovations in each therapy have undoubtedly led to significant improvements in efficacy, including but not limited to chemotherapy, which has led to increased efficacy and a significant reduction in the potential side effects of cardiac disease. For radiotherapy, it meets the need for tumor intervention while also allowing for a reduction in the crucial effects of radiation on the thoracic cavity, cardiac organs, and in the deposition of radiation. For immunotherapy, this treatment method can be achieved through specific analysis and understanding of the targeting of immune cells and receptors to be stimulated, as well as blocking the receptors that inhibit immune cells from attacking tumors. It is important to note that all three therapies have made significant contributions to the field, but what cannot be ignored are still the side effects and shortcomings that come with each therapy. The various therapies prove to us the disadvantages of a single cancer treatment. Therefore, combining multiple cancer therapies will be the future trend and a fundamental and necessary tool for potentially eradicating cancer.

### References

- [1] Giaquinto A N, Sung H, Miller K D, et al. Breast cancer statistics, 2022. *CA: a cancer journal for clinicians*, 2022, 72 (6): 524 - 541.
- [2] Wang J, Xu B. Targeted therapeutic options and future perspectives for HER2-positive breast cancer. *Signal transduction and targeted therapy*, 2019, 4 (1): 34.
- [3] Volkova M, Russell R. Anthracycline cardiotoxicity: prevalence, pathogenesis and treatment. *Current cardiology reviews*, 2011, 7 (4): 214 - 220.
- [4] Ishikawa T, Ichikawa Y, Shimizu D, et al. The Role of HER-2 in Breast Cancer. *Journal of surgery and science*, 2014, 2 (1): 4 – 9.
- [5] Harker W G, Sikic B I. Multidrug (pleiotropic) resistance in doxorubicin-selected variants of the human sarcoma cell line MES-SA. *Cancer research*, 1985, 45 (9): 4091 - 4096.
- [6] Baskar R, Lee K A, Yeo R, et al. Cancer and radiation therapy: current advances and future directions. *International journal of medical sciences*, 2012, 9 (3): 193.
- [7] Virén T, Heikkilä J, Myllyoja K, et al. Tangential volumetric modulated arc therapy technique for left-sided breast cancer radiotherapy. *Radiation Oncology*, 2015, 10 (1): 1 - 8.
- [8] Koury J, Lucero M, Cato C, et al. Immunotherapies: exploiting the immune system for cancer treatment. *Journal of immunology research*, 2018, 2018.
- [9] Fontana M F, Vance R E. Two signal models in innate immunity. *Immunological reviews*, 2011, 243 (1): 26 - 39.
- [10] Jeong S, Park S H. Co-stimulatory receptors in cancers and their implications for cancer immunotherapy. *Immune Network*, 2020, 20 (1).
- [11] Twomey J D, Zhang B. Cancer immunotherapy update: FDA-approved checkpoint inhibitors and companion diagnostics. *The AAPS journal*, 2021, 23: 1 - 11.
- [12] García-Aranda M, Redondo M. Immunotherapy: a challenge of breast cancer treatment. *Cancers*, 2019, 11 (12): 1822.