Evaluation of Cardiac Toxicity in Breast Cancer Radiotherapy Utilizing Flexible Patch Heart Sound Sensor

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Abstract. This study focuses on the evaluation of cardiotoxicity during radiotherapy for breast cancer. The background of the study is that radiotherapy is widely used in the treatment of breast cancer but may cause cardiotoxicity, especially radiation myocarditis, which poses a threat to the long-term quality of life of patients. The subject of this study is the monitoring of heart health using a flexible patch heart sound sensor. The research methods include selecting radiotherapy patients as research objects, collecting heart sound signals and using Matlab software for feature extraction, and exploring the relationship between heart sound signals and heart function through statistical analysis. The results show that the heart sound signals of patients undergo important changes during radiotherapy, and indicators such as heart rate, heart sound intensity, and heart sound interval can be used to evaluate heart function. Moreover, the heart sound classification model based on the KNN classification algorithm can accurately identify abnormal heart sounds, providing an effective guarantee for predicting radiation myocarditis. The flexible patch heart sound sensor has an important value in the evaluation of cardiotoxicity in breast cancer radiotherapy, which can effectively predict the risk of heart injury and provide an important reference for clinical decision-making.

Keywords: Flexible electronics, radiotherapy, cardiotoxicity, heart sounds.

1. Introduction

Radiotherapy plays an important role in the treatment of breast cancer, especially in postoperative adjuvant therapy, local control, metastatic breast cancer treatment, neoadjuvant therapy, and in combination with other treatments [1]. However, cardiotoxicity, especially radiation myocarditis, which may be induced during radiotherapy, poses a serious threat to patients' long-term quality of life. The mechanism of radiation myocarditis involves direct damage to the DNA of myocardial cells, inflammatory response, damage to vascular endothelium leading to ischemia and hypoxia, and myocardial fibrosis resulting from long-term inflammation [2]. In order to effectively monitor and predict the occurrence of radiation myocarditis, this study focuses on the application of a flexible patch heart sound sensor. As a direct reflection of heart activity, heart sound signals contain abundant physiological information. With the high-precision and high-sensitivity flexible patch heart sound sensor, the heart sound signal can be collected in real-time and non-invasively, providing continuous monitoring of the heart health of patients with breast cancer radiotherapy.

The purpose of this study is to explore the practical application value of flexible patch heart sound sensors in breast cancer radiotherapy. This study predicted the occurrence of radiation myocarditis by monitoring the changes of heart sound signals and provided a key basis for clinical decision-making.

2. Research Background and Theory

Radiotherapy is widely used in the treatment of breast cancer, but cardiotoxicity is a side effect that cannot be ignored. Radiation myocarditis is one of the cardiac complications caused by radiotherapy, and its mechanism involves many aspects. Direct cell injury leads to apoptosis and necrosis of cardiomyocytes, inflammation exacerbates myocardial injury, vascular injury leads to ischemia and hypoxia, and fibrosis affects cardiac systolic and diastolic functions [3]. To effectively assess the effects of radiotherapy on the heart, a reliable, real-time monitoring method is needed. The acquisition technology of heart sound signals has attracted much attention because of its non-invasive, real-time and high sensitivity. As a new type of acquisition equipment, the flexible patch heart sound sensor has the advantages of high sensitivity, miniaturization design, strong anti-interference ability and real-time monitoring, and can accurately capture small change of heart sound signal [4].

The flexible patch heart sound sensor is an innovative medical device based on advanced flexible piezoelectric materials and technologies designed to improve the accuracy and comfort of heart sound detection. The relevant theories mainly focus on the piezoelectric effect, the selection and performance optimization of flexible piezoelectric materials, and the application principle of sensor in heart detection. Firstly, the piezoelectric effect is the core theoretical basis of the flexible patch heart sound sensor. The piezoelectric effect means that when some crystal materials are deformed by external forces, their internal positive and negative charge centers will be relatively displaced, resulting in a potential difference, that is, mechanical energy can be converted into electrical energy. Conversely, when an external electric field is applied, these materials also deform, which is an inverse piezoelectric effect. In the flexible patch heart sound sensor, the positive piezoelectric effect is mainly used to convert the weak mechanical vibration generated by the heart beat into electrical signals. Secondly, the choice of flexible piezoelectric material is crucial to the performance of the sensor. Poly (vinylidene fluoride-trifluoroethylene) (P(VDF-TrFE)) is one of the preferred materials for flexible piezoelectric sensors because of its excellent piezoelectric properties, good biocompatibility and softness. In order to further improve the piezoelectric properties of the sensor, researchers usually add fillers such as zinc oxide (ZnO) and graphene (GR) to the P(VDF-TrFE) matrix and prepare composite flexible piezoelectric nanofilms through processes such as high-pressure electrospinning. These fillers can significantly improve the piezoelectric properties of the film, allowing it to capture heart sound signals more sensitively. In addition, the design of the flexible patch heart sound sensor also fully considers the ergonomic principle. The outer layer of the sensor is usually made of soft and biocompatible materials, such as edible grade silicone, to ensure that the sensor can be tightly fitted to the skin and improve wearing comfort. The structure of the sensor also adopts a sandwich structure, that is, the piezoelectric film is packaged between two layers of conductive material to form a complete circuit system. In the process of heart sound detection, the soft patch heart sound sensor captures the weak vibration generated by the heartbeat, converts it into an electrical signal, and finally presents the heart sound signal in the form of visual graphics on the electronic device through signal amplification, filtering and other processing steps. This not only facilitates doctors conduct real-time analysis and diagnosis, but also forms a personal heart sound library to provide reference for the treatment and follow-up of cardiovascular diseases [5].

In summary, the flexible patch heart sound sensor is a new medical device based on the piezoelectric effect and flexible piezoelectric materials. The theoretical basis covers the piezoelectric effect, the selection and performance optimization of flexible piezoelectric materials, and the application principle of sensor in heart sound detection. This sensor has the advantages of high sensitivity, high comfort, easy to wear, and real-time monitoring, and has broad application prospects in the field of heart sound detection and cardiovascular disease diagnosis.

3. Research Method

The aim of this study was to evaluate the effects of radiation therapy on the heart of breast cancer patients, in particular by monitoring the occurrence of radiation myocarditis with a flexible patch heart sound sensor.

3.1. Verify the Value of Heart Sound Signals in Cardiac Evaluation

The study selected patients who received radiotherapy in the Radiotherapy Department of the Cancer Prevention and Treatment Center of Sun Yat-sen University between October 2022 and October 2023 as the study subjects. By collecting echocardiographic parameters of these patients and strictly dividing them into normal diastolic function group (G0 group) and left ventricular diastolic dysfunction group (G group) according to the 2016 ASE and EACVI Diagnostic guidelines for diastolic function. Group G is further subdivided into three diastolic dysfunction subgroups (group G I, group G II, and group G III).

In terms of data acquisition, the research team collected and recorded the patients' heart sound signals and used Matlab software to precisely extract a key heart sound parameter, the diastolic to systolic duration ratio (D/S).

In the aspect of statistical analysis, various statistical methods were used to ensure the accuracy and reliability of the results. Firstly, the relationship between the different indicators between the two groups and the identification of left ventricular diastolic dysfunction was explored through one-way Logistics regression analysis. Then, the single factor index with $P<0.05$ was incorporated into the multi-factor Logistics regression model to establish a diagnostic model for recognizing left ventricular diastolic dysfunction. In addition, the model's effectiveness in identifying left ventricular diastolic dysfunction was evaluated by plotting an ROC curve.

Through the analysis of the study results, it was found that compared with the normal diastolic function group, the D/S ratio of patients with left ventricular diastolic dysfunction was significantly lower, and this difference was highly statistically significant. Further analysis also showed that in the subgroup of left ventricular diastolic dysfunction, the D/S ratio decreased with the severity of diastolic dysfunction. In addition, the D/S ratio was well correlated with echocardiographic parameters such as E peak, E/e', LAVI, and TR, which further confirmed the potential value of the D/S ratio of heart sound signals in assessing left ventricular diastolic function.

3.2. Study the Value of Heart Sound Signal in the Evaluation of Radiation Toxicity

3.2.1. Selection of subjects

Inclusion criteria were patients over 18 years of age who were diagnosed with malignant tumors requiring radiotherapy, such as breast cancer, or lung cancer, and had no prior history of cardiovascular disease. Exclusion criteria included recent heart surgery or other interventions, the presence of severe comorbidities (such as liver and kidney insufficiency), and pregnant or lactating women. 100 patients were included to ensure the validity and reliability of the study results.

3.2.2. Formulation of radiotherapy program

Three-dimensional conformal radiotherapy (3D-CRT) or intensity-modulated radiotherapy (IMRT) was used to improve the accuracy of target irradiation and reduce the damage to surrounding normal tissue. The radiotherapy dose is determined according to the type and stage of the tumor, usually 50-60 Gy, divided into 25-30 doses of 2 Gy each. Imaging tests are performed prior to radiotherapy and a radiotherapy plan is developed through the radiotherapy planning system to ensure maximum protection of the heart.

3.2.3. Acquisition of heart sound signal

The flexible patch heart sound sensor is used to collect heart sound signals. Heart sound signals are collected periodically before, during, and after radiotherapy, each time lasting 5-10 minutes to ensure stable heart sound data. During collection, the patient should keep quiet to avoid interference from external noise. The collected heart sound signal is transmitted to the computer in real-time through the USB interface for subsequent analysis. In the process of heart sound signal acquisition, the flexible patch heart sound sensor is chosen because its miniaturization and high sensitivity are ideal for long-term and dynamic monitoring of heart sound signals. The collection sites were selected at the 4th costal space at the left margin of the sternum and the 5th costal space at the left papillary line, which could better capture the main sounds of the heart. Collection time points included baseline collection (before radiotherapy), weekly collection during radiotherapy, and follow-up collection at 1, 3, and 6 months after radiotherapy.

3.2.4. Analysis method of heart sound signal

Use Matlab software to extract the characteristic parameters of the heart sound signal, such as the frequency, amplitude, and timing of the first heart sound (S1) and the second heart sound (S2). To evaluate the relationship between the changes in heart sound signal and cardiac function during radiotherapy, compare the characteristics of heart sound signal at different time points by statistical methods, and explore the correlation with the changes in radiotherapy dose and cardiac function. The structural and functional changes of the heart were evaluated comprehensively with traditional detection methods such as electrocardiogram and echocardiography.

3.2.5. Data analysis

The preprocessing of heart sound signals includes noise removal, signal normalization, and artifact removal to improve signal quality. Feature extraction can extract meaningful information from preprocessed heart sound signals, including the time domain feature, frequency domain feature and time-frequency feature. The KNN classification algorithm was used to analyze the heart sound signals to predict the occurrence of radiation myocarditis. Data analysis plays a key role in predicting radiation myocarditis, enabling early identification of risk, quantitative assessment of changes in cardiac function, individualized treatment, and integrated monitoring.

4. Result

During radiotherapy, heart sound signals in breast cancer patients undergo a series of important changes that are monitored and evaluated by key indicators such as heart rate, heart sound intensity, and heart sound interval. Heart rate, as the number of heartbeats per minute, is usually maintained within the normal range of 60-100 beats per minute before radiotherapy. However, as radiotherapy progresses, patients may experience an increase in heart rate to 70-110 beats per minute due to psychological stress, pain, or physiological responses to radiotherapy itself. After the end of radiotherapy, the heart rate of most patients is able to gradually return to the baseline level, but for those who develop heart complications, the heart rate may remain high.

Heart sound intensity, the loudness of heart sounds, is usually between 50-70 decibels at baseline before radiotherapy. However, during radiotherapy, the intensity of heart sounds may fluctuate due to the effects of radiation on the heart, decrease reflect a weakening of heart function, or may be enhanced due to complications such as pericardial effusion. Heart sound intensity recovers somewhat after radiotherapy, but may remain persistently low in patients who have already developed heart disease.

Heart sound interval refers to the time interval between the first heart sound (S1) and the second heart sound (S2), usually between 300 and 400 milliseconds before radiotherapy. During radiotherapy, the interval between heart sounds is prolonged, which may be related to impaired cardiac function or affected cardiac electrical conduction system, especially ventricular diastolic dysfunction. After the end of radiotherapy, the heart sound interval gradually returns to the normal range, but in patients who develop radiation myocarditis, the heart sound interval continues to be prolonged.

In addition, the heart sound classification model based on the KNN classification algorithm can accurately identify normal heart sounds and abnormal heart sounds, which provides an effective guarantee for the prediction of radiation myocarditis by heart sound signals and is also an important aspect of evaluating the impact of radiotherapy on patients' hearts.

5. Discussion

This study shows that the flexible patch heart sound sensor has an important value in the evaluation of cardiotoxicity in breast cancer radiotherapy. The change in heart sound signal is closely related to the occurrence of radiation myocarditis. By monitoring the heart sound signal regularly, the risk of heart injury can be effectively predicted. This finding provides an important reference for clinicians to develop individualized radiotherapy regimens and optimize cardiac protection measures.

However, there are some limitations in this study. The acquisition time of heart sound signal mainly focuses on the short-term follow-up during and after radiotherapy, which may not fully capture the change in long-term heart health status. Future studies will need longer follow-ups to assess the long-term effects on heart health.

6. Conclusion

This study focuses on the application of flexible patch heart sound sensors in cardiotoxicity assessment of breast cancer radiotherapy. By monitoring changes in heart sound signals, we can effectively predict the risk of radiation myocarditis. This finding not only highlights the importance of flexible patch heart sound sensors in heart health monitoring but also provides strong support for cardiac protection in breast cancer radiotherapy patients.

Future research should continue to optimize the heart sound signal acquisition technology to improve the accuracy and real-time performance of the sensor. At the same time, a multi-center, large-scale clinical trial will be conducted to verify the association between changes in heart sound signals and radiation myocarditis and to evaluate its applicability in different patient populations. In addition, multi-modal data analysis combined with other physiological indicators will help to comprehensively evaluate the heart health status of patients and provide a more accurate basis for clinical decision-making.

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