Limiting Lung Radiation during Breast Cancer Radiation Treatment Using Machine Learning

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Abstract

The linear accelerator (LINAC) produces x-rays which affect other non-cancerous areas during breast cancer treatment. The lung is highly affected during this process. Many women with breast cancer receive radiation therapy, which may increase the risk of subsequent primary lung cancer, pneumonitis, and lung fibrosis, as some normal or healthy cells in the area can also be damaged by radiation. In breast cancer treatment, breathe adapted radiotherapy enhances minimal effect on healthy tissue on the affected side, especially if the tumour is on the left breast where lung tissue is located. In this research, a prototype was developed to mimic this system. During inhalation, the lung inflates and, if radiation meets the inflated lung, a bigger portion will wear away as opposed to exhalation (when lung deflates). Basically, the principle is to run and turn the beam of the LINAC and radiate during exhalation when the lung is deflated. The input to the system is the pressure sensor which shows the breathing in and out. Outputs are the buzzer, which rings when abnormality occurs; a bulb shows or represents the LINAC and the LCD screen which shows when x-ray is on or off. The system is controlled by an Arduino Nano programmed using C-language. There is a voltage regulator to regulate the voltage and capacitor to filter the voltage. The circuit is based on the atmega328 microcontroller combined with the Arduino nano, and it uses pressure difference to check whether the patient is breathing in or out. Then based on that information the x-ray can then be directed onto the target area on the patient. On the circuit, a small lamp will be used to simulate the x-ray as an x-ray machine is complex to design and it will need more time and resources.

Keywords: Linear accelerator, machine learning, X-ray, breast cancer treatment

Introduction

Breast cancer radiation with a tangential photon field is typically used as an adjuvant to breast-conserving surgery to improve local control and perhaps survival in healthy women (Pedersen *et al.*, 2004). When one has cancer, usually the doctor prescribes a treatment which depends on the type and stage of the disease. The type of treatment is determined by the size and location of the tumour in the breast, as well as the findings of laboratory tests performed on cancer cells and the disease's stage, or extent (Lickiss, 1977). Radiation therapy, which employs high-energy X-rays to destroy cancer cells while limiting damage to healthy cells, is one way to treat breast cancer. It is frequently administered over a period of one to six weeks after a lumpectomy (partial mastectomy) to treat the residual breast tissue. Radiation is applied to the afflicted breast as well as the lymph nodes axillary to the arm and above the supraclavicular region. The majority of women with a tiny, early-stage tumour are ideal candidates for this kind of treatment (Dixon *et al.*, 2001). Using radiation treatment on women with cancer of the left breast poses a risk to the heart and the lung, owing to their proximity with the breast, as they may fall into the radiation field. Women may be at higher risk of coronary heart disease if their hearts are exposed to radiation during breast cancer therapy (Roos *et al.*, 2018). If a patient is also undergoing chemotherapy at the same time, or if they have underlying conditions that put them at risk of heart disease, radiation may increase the danger even more. The overall risk of heart damage owing to radiation is determined by several factors which include the radiation dose and the amount of heart exposed to radiation. This risk; however, is always present whether high or low doses are used (Oliver *et al.*, 2007). Also to note with accurate treatment planning where organs at risk are contoured the risk of exposure to the heart or lungs will be very minimum and will not exceed the dose limit for the organs at risk. However, artificial intelligence (AI) could be the way to go.

Respiratory Gating

Radiation therapy involves giving high doses of radiation beams directly into a tumour. The radiation beams change the DNA makeup of the tumour, causing it to shrink or die. A tumour can sometimes move during treatment, especially if it is in an area of the body that naturally moves because of respiration, such as the breast, abdomen or lungs. Breathe adapted radiotherapy offers a significant potential for improvement in the irradiation of tumour sites affected by respiratory motion such as breast tumours. An example of breathe adapted radiotherapy (BART) is respiratory gating. This is an innovative process that uses advanced computer software to guide the delivery of radiation as a patient breathes.

DIBH treatment

Respiratory deep inspiration breath Hold (DIBH) is a specific radiation therapy technique for breast cancer treatment to spare doses to the heart and lungs. Using the DIBH technique, the radiation is delivered only at certain points during the patient's breathing cycle of inspiration and expiration. The patient is asked to take a deep breath in and hold their breath for about 20 seconds. This, in turn, will limit the amount of the heart and lung that is exposed to the radiation beam, since taking a deep breath in will allow these organs to move out of the treatment field. DIBH can be also used to minimise internal organ motion for other body sites such as the stomach, pancreas and liver (Chi *et al.*, 2015). Figure 1 shows the DIBH versus free breathing. One common element of treatment for breast cancer is adjuvant radiation. It has been demonstrated that adding radiation therapy following breast-conserving surgery lowers the local recurrence rate and increases long-term survival. The quality of treatment planning and delivery of radiation therapy depends on the precise delineation of target volumes and organs at risk, which is achieved with innovative technology. This makes it possible to precisely mould the radiation beam to fit the anatomy of every single patient. Target volumes in breast conserving surgery include the surgical bed and mammary gland; in mastectomy, the chest wall; and, if necessary, regional lymph nodes (axillary, supra- and infraclavicular, and internal mammary). Lungs, thyroid, brachial plexus, heart, spinal cord, and oesophagus are among the organs at danger. In this study, the focus is on using machine learning to limit lung consumption during radiation.

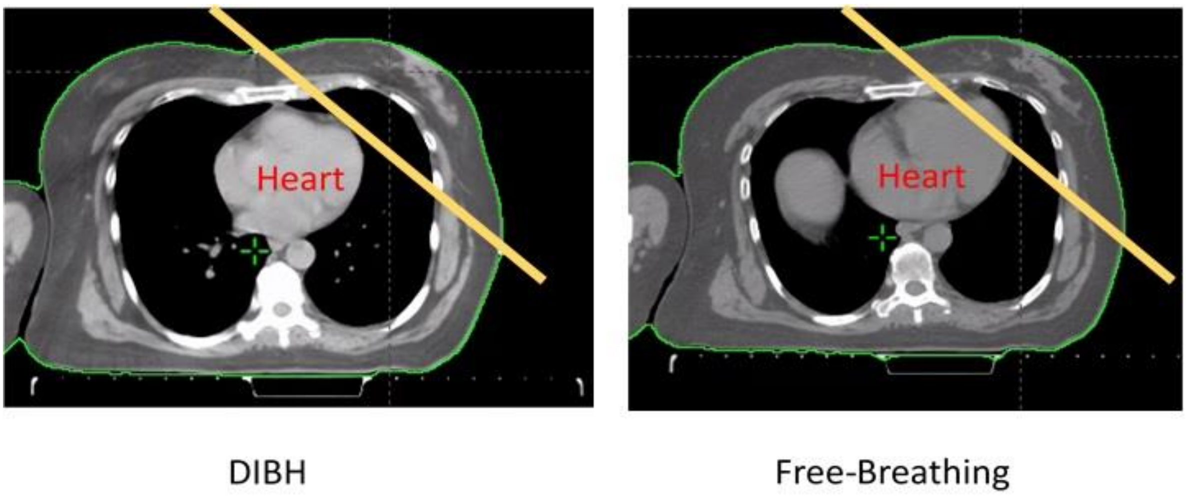


Figure 1: : DIBH vs Free breathing

(Source: Czeremszyńska et al., 2017)

Breast cancer radiation treatment

Broadly speaking, there are two types of radiation therapy used to treat breast cancer: **external beam radiation** and **brachytherapy** (also known as internal radiation therapy) (Chen *et al.*, 2021). In this research, the authors will concentrate on external beam radiation.

Figure 2: External beam radiation, brachytherapy and proton beam therapy(Czeremszyńska et al., 2017) b LINAC being inclined during breast cancer treatment to avoid much tissue damage

Problem statement

During radiotherapy treatment using a linear accelerator, exposing the lungs is unavoidable and this incidental exposure may increase the risk of subsequent primary lung cancer, pneumonitis and lung fibrosis.

Aim

The aim of this study was to develop a machine learning based system that monitors breathing in cancer patients and determines when beam should be applied to spare the lung during breast cancer external beam radiation.

Objectives of the research

The study objectives were to:

i) Create and implement an algorithm that obtains the breathing rate from the voltage signals recorded by the sensor(s),
ii) Establish breathing patterns of patients undergoing treatment,
iii) Develop a microcontroller-based prototype that will demonstrate how the system will work.

Literature review

Breasts are a pair of structures on the pectoral region of the anterior thoracic wall (Swanson, Kim and Glucksman, 2010). They can be found in both males and females; however, they are more pronounced in females after puberty. The mammary glands; the most important tissues in lactation, an auxiliary gland of the female reproductive system, are found in the breasts of females (Barret *et al.*, 2016). The breast is placed on the anterior thoracic wall, it runs horizontally from the sternum's lateral border to the mid-axillary line and vertically between the 2nd and 6th costal cartilages (Academy et al., 2016). It superficially connects the pectoralis major, serratus anterior and the external oblique muscles. The breast can be divided into two sections: the upper and lower portions. The largest and most visible component of the breast is the circular body. The nipple, which is largely made up of smooth muscle fibres, is located in the centre of the breast. The areolae are a pigmented patch of skin that surrounds the nipple. Within the areolae, there are numerous sebaceous glands, which increase during pregnancy and secrete an oily material that serves as a protective lubricant for the nipple (Academy et al., 2016).

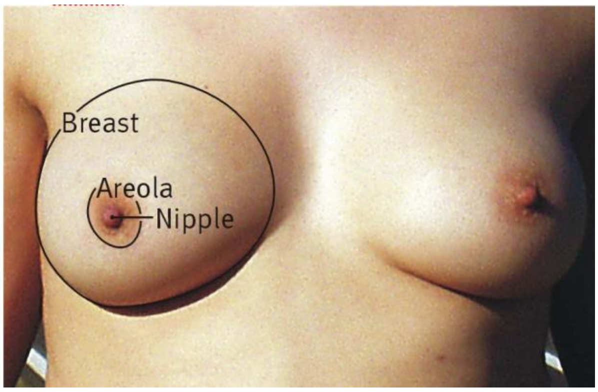


Figure 3: Surface anatomy of the breast

As the nipple grows, it appears as bilateral bands of thickened epidermis called the mammary lines or mammary ridges. In the 7th week the lines extend from the base of the forelimb to the region of the hindlimb on both sides of the body(Losi *et al.*, 2018). Greater part of the mammary lines disappears as soon as the nipple forms, leaving a small portion in the thoracic region and penetrates the underlying mesenchyme. It then forms 16-24 sprouts which are canalised to form lactiferous ducts by the end of the prenatal life. Initially, the lactiferous ducts open into a small epithelial pit which shortly after birth is transformed into a nipple by proliferation of underlying mesenchyme. At birth, lactiferous ducts have no alveoli therefore no secretory apparatus. At puberty; however, increased concentration of oestrogen and progesterone stimulate branching from the ducts to form alveoli and secretory cells (Atun *et al.*, 2015).

Table 1: Breast composition

	Gland part	Drainage
1	Central and lateral parts	75% drain into pectoral group of axillary nodes then into apical
2	Upper part	Drains into apical group (directly) of axillary lymph nodes
3	Medial part	Drains into internal thoracic (parasternal) lymph nodes, forming a chain along the internal thoracic vessels
		Some lymphatics from the medial part of the gland pass across the front sternum to anastomose with that of opposite side. So, cancer can spread from one breast to another.
4	Inferomedial part	Anastomose with lymphatics of rectus sheath and linear alba, and some vessels pass deeply to anastomose with the sub-diagrammatic lymphatics.

Machine learning in breast cancer treatment

Utilising machine learning algorithms for classification of illness qualities and anticipating medical endpoints (for example, tumour recurrence hazard) relies vigorously upon imperatives to the classifier model itself. Generally, machine learning algorithms are organised to investigate training information, distinguish examples and connections, and devise models that relate the information to estimated results. As a rule, machine learning algorithms are prepared to discover the connection between the independent variable(s) "X" and result/dependent variable(s) "Y." The independent variables (that is, "X" variables) are known as descriptors, provisions, or attributes and are retrieved from estimated perceptions or models. In the radiomics setting, these may incorporate surface elements and shape descriptors. Right names of information tests (that is, factor "Y") are alluded to as the ground truth and are bound to exact results, classes, or occasions. These might incorporate clinical endpoints, for example, tumour recurrence, death, or proportions of medication obstruction. Ground facts may likewise be tissue characterisations, for example, harmless versus dangerous sorts. Ground truth names are otherwise called "gold standard' classifiers and frequently require manual assessment or contribution from human (expert) partners (Tran *et al.*, 2019).

Machine learning algorithms to obtain breathing rate from voltage signals

Machine learning is the consequence of trend acknowledgment and the assumption that computers can figure out how to execute an assignment. As a field of AI, machine learning is the capacity of a machine to learn, distinguish, and group from being presented to explicit information in an intuitive manner, and to learn and settle on dependable choices as well as to adjust when presented with new information. This method can be helpful for automatic trend acknowledgment in respiratory signals, for example, sleep apnoea, respiratory trend, and talking recognition (Hu *et al.,* 2020).

Feature extraction

To begin with, for machine learning characterisation, a few elements should be given to the arrangement algorithm. These components should be retrieved from the original signal, and they should be picked for better outcomes.

For instance, when working with a wearable acoustic sensor (Rahman, 2017) meaning to perceive action designs like sitting, eating, and drinking and respiratory examples like murmuring, deep breath, and coughing, the elements retrieved from the sensor signals were identified with time, frequency, and cepstral.

Microcontrollers and opto-coupling

Opto-isolators or Opto-couplers, are comprised of a light transmitting gadget, and a light acute gadget, all enveloped within one package; however, with no electrical association between the two, simply a light emission (Hanna, 2021). The light emitter is almost consistently a LED. The light acute gadget might be a photodiode, phototransistor, or more recondite gadgets, for example, thyristors, TRIACs and so on. The optocoupler typically found in switch mode power supply circuit in numerous electronic hardware. It is associated in the middle of the essential and auxiliary part of force supplies. The opto-coupler application or capacity in the circuit is to:

1) Monitor high voltage
2) Output voltage sampling for regulation
3) System control micro for power ON/OFF
4) Ground isolation

Biosensors and breast cancer treatment

Regardless of the developing benefits of distinguishing breast cancer biomarkers, generally utilised symptomatic tests are ineffectively acute, confounded, tedious, expensive, just as high danger of false positive and negative (Jain, 2014). There is thusly yet a basic requirement for basic and quick acute and explicit strategies. Until this point, the distinguishing proof of oncogenetic biomarkers has been founded on the investigation of natural material gained through tumour tissue biopsy. Chemically changed cathodes were unmistakable in investigations with biosensors and electroanalysis. It is a moderately present-day strategy for anode frameworks that has a wide range of examination and clinical applications. For breast cancer identification, various kinds of nanoparticles have been secured to electrochemical biosensors utilising distinctive explicit biomarkers, for example, c-erbB-2 oncogene, and various antigens and antibodies. The review by Chen et al. (2014) alludes to the grouping of the oncogene c-erbB-2 in the saliva of ladies with breast cancer. In any case, because of the low centralisation of this biomarker, various tests were expected to work on a biosensor dependent on a fluorogenic arrangement, just as to plan a sign intensification plot utilising a sign transducer test equipped for recognising the oncogene in the example of DNA present in saliva.

Materials and methods

The research was done at one central hospital using the current LINAC machine for radiotherapy. Objectives 1, 2 and 3 were prepared and done. MATLAB was used to prepare the algorithm and check how the lung blows high and low. The demonstration used to show the system comprises the components below.

Table 2: Components to make the prototype.

	Name of component	Specification
1.	LCD	To show X-ray on / off
2.	Arduino Nano controller	To control the circuit
3.	Pressure sensor	As input to get the patient information whether breathing in or out
4.	Buzzer	To show the abnormality of the patient
5.	Bulb	Turns on when the radiation passes and off when it does not pass

Suggested solution

The lung is always a concern when treating breast cancer and it should only receive 65Gy or less of dose, which, if exceeded, could highly affect it (Appendix 1). An algorithm is to be developed that determines breathing patterns and pattern of ECG to be followed. Table 2 shows the different components used to test the system.

Parameters to control: Radiation beam

Parameters to measure: Breathing rate

Signal and data processing

To process data and signals to detect and establish breathing patterns, MATLAB was used in the project to analyse the ECG signal.

Filtering: A capacitor is used to minimise high-frequency noise, preserving the sensor signal
Amplification: To amplify low amplitude signals for example, high-impedance voltage amplifiers.

Results and discussion

In this study the researchers managed to come up with breathing rate using ECG pattern. This helped to tell whether the pressure was high or low, and therefore objective 1 fulfilled. After the breathing rate, patterns were obtained, and the signals were done thereby fulfilling objective 2. Objective 3 was to come up with a micro-controller-based system and this was done with pictures attached.

Create and implement an algorithm that obtains the breathing rate from the voltage signals recorded by the sensor(s), process data and signals that detect and establish breathing patterns

- The voltage signal used for this research was from an ECG machine. An electrocardiogram (ECG) is a simple test that can be used to check heart's rhythm and electrical activity of the heart.
- The sensors used to record the signal were taken to be electrode pads attached to the skin. Electrical leads carry the signal from the patient to the ECG monitor. The ECG machine stores the information about the heart electronically, which could be analysed by a professional when the test is complete.
- MATLAB was used in the project to analyse the ECG signal
- The signal data was acquired by a health care professional and uploaded to phyiso.net.org and, to bring it to be used in MATLAB, it was copied and pasted from the site and saved it as a txt. file in the working directory of MATLAB as shown below:

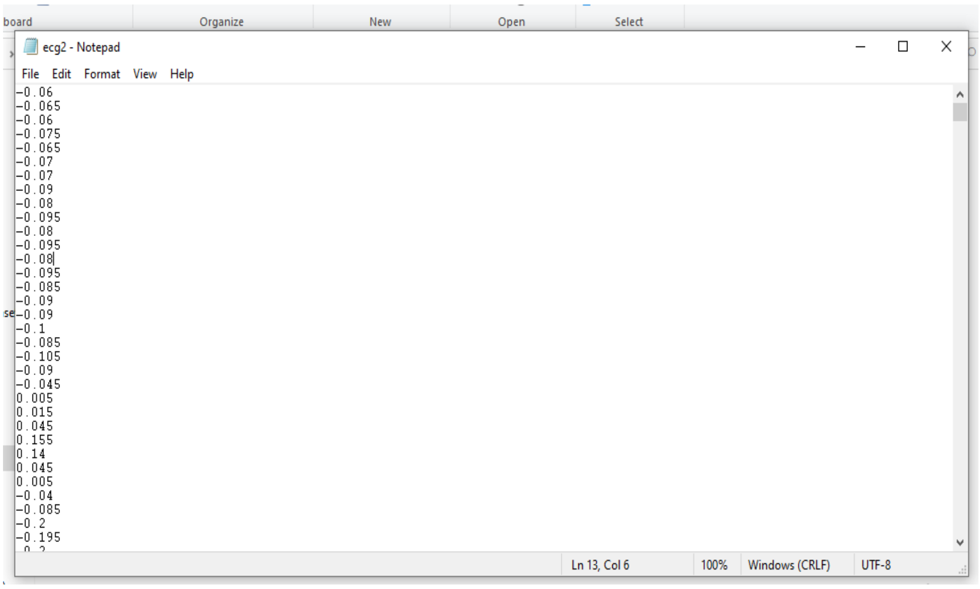


Figure 4: 6000 ECG machine data samples captured by a professional to be analysed using MATLAB

(Source: https://eleceng.dit.ie/dorran/matlab/ecg.txt)

- ➢ After bringing the data into MATLAB, process data and signals that detect and establish breathing patterns using the following algorithm. A heart rhythm plot should result with an accurate count of the sampling data.

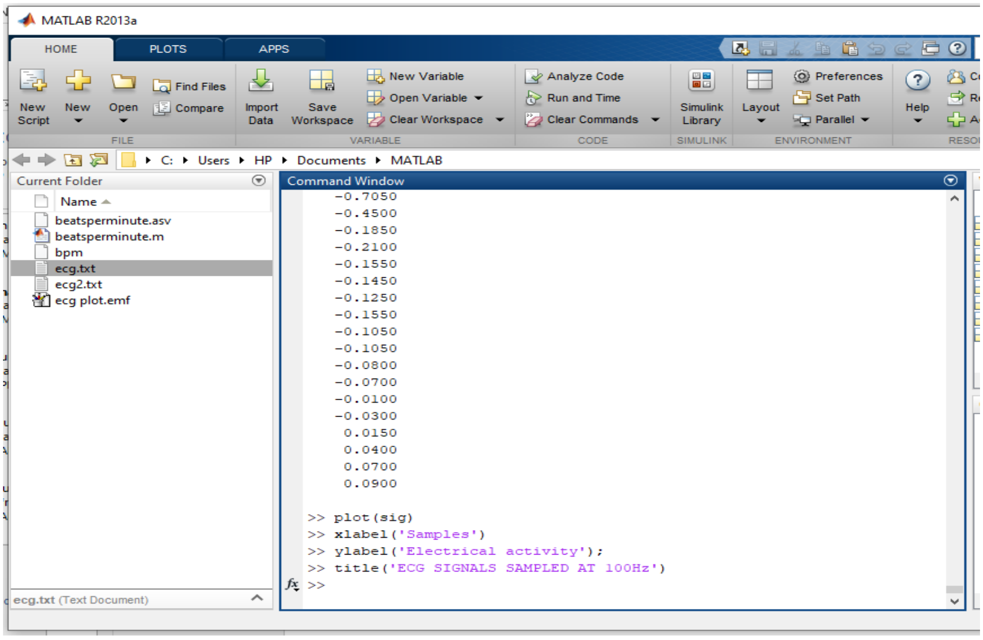


Figure 5: Algorithm for processing data signals

- ➢ The heart rhythm plot from the ECG data that shows 6000 samples was processed.

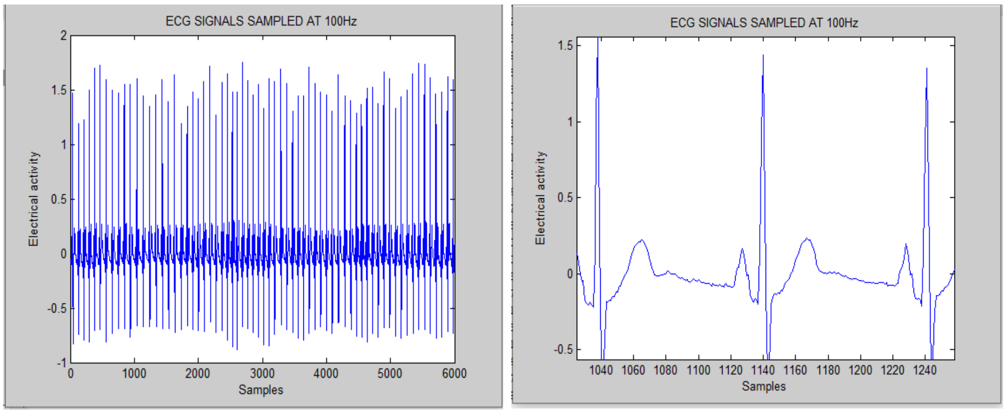


Figure 6: Established breathing patterns plot b. ECG signals sampled at 100Hz

- The zoomed showing clearer indication of heart rhythm is shown in Figure 6b:
- After processing the data signals use the following algorithm to determine the beats per minute from the electrical leads voltage signals as shown below.
- This algorithm counts the dominant peaks in the signal and corresponds them to heart beats. Peaks are defined to be samples greater than their nearest neighbour on both sides and greater than 1. *A for loop is used* in MATLAB
- After determining the dominant peaks (distinguishable heart beats); divide the beats by the signal duration (in minutes). Use the variable N to store the length of the signal so that you can divide N by the sampling rate fs(Hz) and by 60 to get duration in minutes
- Finally, to obtain the breathing rate from the signal divide beat count by duration in minutes.
- The MATLAB code is shown below:

beatsperminute.m

```
%program to determine BPM of an ECG signal

%count the dominant peaks in the signal (these correspond to heart beats)
% - peaks are defined to be samples greater than their nearest neighbour
% and greater than one

%identify the peaks by using a for loop to go through each sample of the signal
%peaks are equivalent of beat count

beat_count = 0
for k = 2 : length(sig)-1
    if(sig(k) > sig(k-1) & sig(k) > sig(k+1) & sig(k) > 1)
        k
        disp('prominent peak found');

        beat_count = beat_count + 1
    end
end
%divide the number of beats counted by the signal duration (in minutes) use the variaable N to store the duration of the signal
 N = length(sig);
fs = 100
%where fs is th variable used for sampling rate
duration_in_seconds = N/fs;
duration_in_minutes = duration_in_seconds/60;
bpm = beat_count/duration_in_minutes
```

Figure 7: MATLAB algorithm coding for determining breathing rate in beats per minute

➢ The results were displayed as follows:

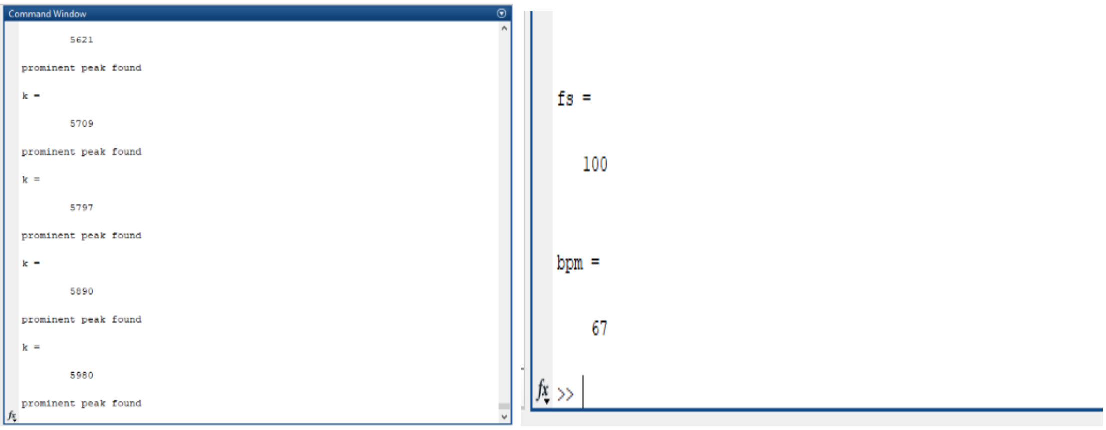
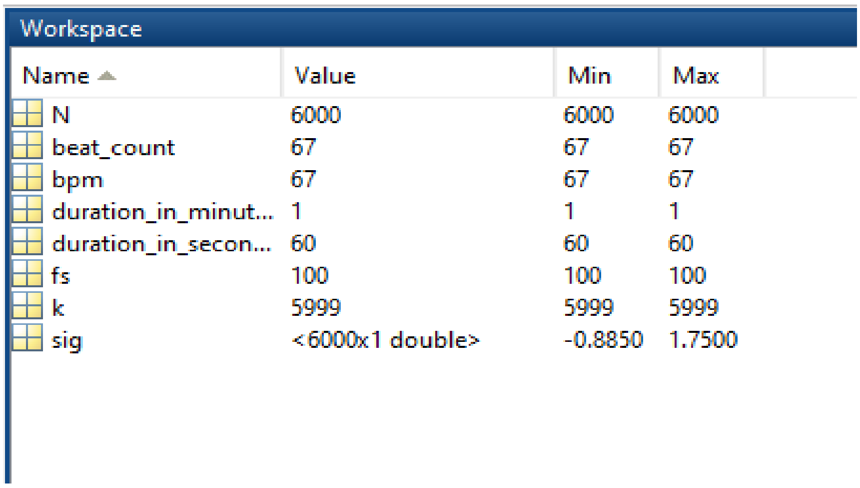


Figure 8: Results of the coding

In conclusion, the analysis of the ECG signal is shown below:



Workspace

Name	Value	Min	Max
N	6000	6000	6000
beat_count	67	67	67
bpm	67	67	67
duration_in_minut...	1	1	1
duration_in_secon...	60	60	60
fs	100	100	100
k	5999	5999	5999
sig	<6000x1 double>	-0.8850	1.7500

Figure 9: Workspace for the BART

BART Summary

Breathe adapted radiotherapy techniques benefit many developments in breast cancer treatment. However, appropriate methods customised to each patient must be developed. These techniques are essential to reduce acute and late toxicity including cardiac and pulmonary during breast cancer treatment.

Microcontroller based system

An Arduino Nano based system was developed as shown in Figure 10 below.

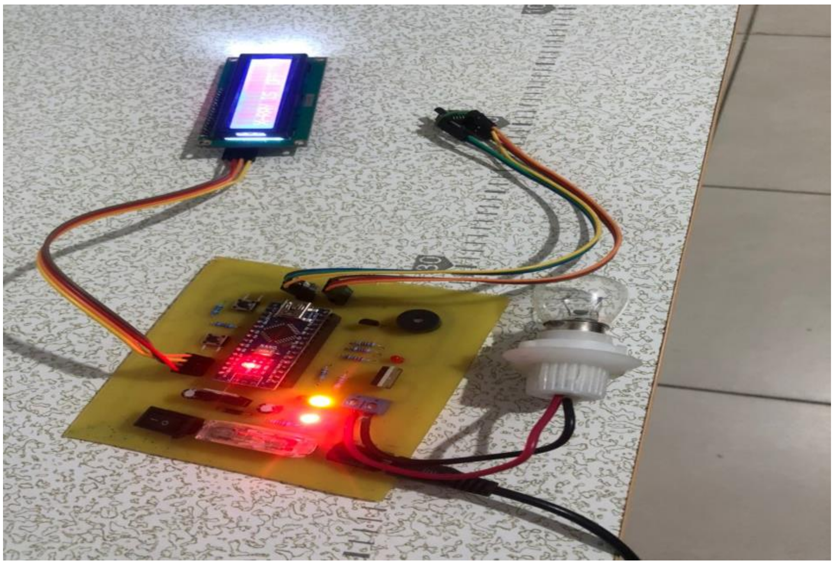


Figure 10: Micro-controller-based system

How the system works

The circuit is based on the atmega328 microcontroller combined with the Arduino nano, and it uses pressure difference to check whether the patient is breathing in or out. Based on that information, the x-ray can then be directed onto wherever it is to be directed on to the patient. On the circuit, a small lamp will be used to simulate the x-ray. This is mainly because the x-ray machine is complex to design, and it will need more time and resources. The system has proved to work in the prototype stage, and it will be a good idea if resources are in place to do this research in detail. The Arduino nano was used because the data to be stored is not much and it performs well. The ECG was only used as demonstration to show rhythmic movements of the breathing in and out of any person which gives an idea for the design.

Recommendations and conclusion

The system was done as prototype and the researchers highly recommend further investigation to implementation stage. This system will be very useful if used in breast cancer treatments and ECG measurements. This will be helpful to know rhythmic contractions and expansions of the human body. The bulb will be a sign that shows radiation is going on and shows accepted radiation that does not affect the lung.

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List of Appendices

Appendix 1

Table 4.1 Estimated tolerance doses for various organs expressed as different parameters with dose delivered with 2 Gy/fraction. These have wide confidence limits and vary with age, individual sensitivity, vascular status and with other treatments given

OAR	TD5/5 (Gy)	TD50/5 (Gy)	DVH Vx % or mean dose in Gy	Tolerance dose (Gy)
Spinal cord	5 cm 50 10 cm 50 20 cm 47	70 70		45–50 40–44 (>15 cm) EUD = 52.5
Brain	Whole 45 <1/3 60			50–60
Brainstem	1/3 60 2/3 53 3/3 50	65	V60 < 0.9 mL	54 1% up to 60
Peripheral nerves				60
Pituitary gland (hormone production)				20–24
Permanent hair loss				45–55
Optic nerve				50–55
Optic chiasm				50
Lacrimal gland				32–35
Lens				10
Retina	Whole 45			45–50 Small volume <60
Cornea				<48
Cochlea				50
Parotid	2/3 32 3/3 32	46 46	V30 <45%	24
Epiphyses before fusion in children				10
Femoral heads			V50 <50	
Heart	1/3 60 2/3 45 3/3 40	70 55 50	V40 <30 V30 <40–45 V20 <50	D_{max} <60
Lung	1/3 45 2/3 30 3/3 17.5	65 40 24.5	V30 <10–15 V20 <25 Mean 10	
Kidney	1/3 50 2/3 20–30 3/3 23	40 28	Mean 17.5 Gy	

Individual organ tolerances