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Breast Cancer Early Detection Support Systems CAMI and CAMTP

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Abstract. Breast cancer is one of the main health problems in Mexico; it is currently the main type of cancer suffered by women. Among these neoplasms are triple negative breast cancer (TNBC) and infiltrating breast cancer (IBC). Thesecancers are very aggressive, difficult to diagnose and have high mortality rates. Infiltrating breast cancer is classified into two types: ductal and lobular, the first originates in the cells of the mammary ducts and then invades the surrounding tissues, the second is generated in the lobules of the mammary glands and spreads through the surrounding tissues. Triple negative infiltrating ductal carcinoma isa specific subtype of breast cancer characterized by being negative for hormonereceptors (estrogen and progesterone) and HER2/neu protein. The clinical history is one of the main tools for the early detection of these typesof cancer, so part of the system to be developed is based on a complete clinical history that provides us with important information on the predisposition to present this type of cancer. Another of the hypotheses to be resolved is that the detection of tumor angiogenesis could help us to find tumor formation in its first steps, by identifying a localized increase in temperature in the affected area. To achieve this identification, the construction of a prototype that maps the temperature of the breasts is proposed, to later carry out a thermographic study and that these results, togetherwith the clinical history, can serve as support for health professionals to determine the relevance of imaging studies in young women.

Keywords: Cancer, triple negative, temperature.

1 Introduction

Cancer [1] is a generic term used to designate a broad group of diseases that can affectany part of the body; it is also referred to as "malignant tumors" or "malignant neoplasms". A defining characteristic of cancer is the rapid multiplication of abnormal cells that spread beyond their usual boundaries and may invade adjacent parts of the body or spread to other organs, in a process called "metastasis". The spread of metastases is theleading cause of death from the disease.

Breast cancer according to WHO [1] originates in the cells of the lining (epithelium)of the ducts (85%) or lobules (15%) of the glandular tissue of the

breasts. Initially, thecancerous tumor is confined to the duct or lobule (in situ), where it usually causes no symptoms and has minimal potential for spread (metastasis).

Breast cancer is defined as abnormal and disordered growth of cells of the epithelium of the breast ducts or lobules, which has the ability to spread [2], and triple negative refers to tumors that lack expression of the receptors for estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2/neu) [3].

It is considered one of the major health problems in the world. It is the most frequent malignant tumor in women in developed and developing countries; in our country, it isthe most frequent cause of death from malignant disease in women (15-20%) with prevalence of 20-25% of cases [2].

Breast cancer is classified based on clinical stage, cell morphology and immunohistochemistry analysis. Using c-DNA microarrays, it was determined that there are several subtypes of breast cancer with different gene expression patterns and prognosis[4]. Breast cancer is divided into 2 main groups based on the presence or absence of ER expression.

Gene expression profiling revealed that within ER+ tumors there are 2 subtypes: luminal A and luminal B. ER- tumors also comprise 2 subtypes: HER2 and basal like. These subtypes show short disease-free periods after treatment and a poorer prognosis [5].

HER2 designated by microarray should not be confused with HER2+ tumors by immunohistochemistry or fluorescence in situ hybridization, as of the latter not all showchanges in RNA expression to define the group [4].

The first concepts of triple negative breast cancer (TNBC) were made known around 2006 and, since that date, more than 600 articles have been published on the subject; this highlights the importance of this heterogeneous group of neoplasms, mainly fromthe molecular, pathological and therapeutic points of view [6].

TNBCs are a heterogeneous group of tumors lacking ER, PR and Her2 expression.Because most basal like carcinomas (BTCs) are triple negative and, on the other hand,most TNBCs are CBLs, these 2 entities have been suggested to be synonymous; however, they differ in their clinical, genetic, and immunohistochemical features [5].

TNBC and LBC account for 15% of all invasive carcinomas and are usually high grade, large and nonspecific, occurring more frequently in young black or Hispanic women; on the other hand, more than 75% of tumors occurring in women with mutations in the BRCA1 gene have a triple negative phenotype [6, 7].

In Mexico, triple negative breast cancer accounts for 15 to 23% of all cancers. Its main characteristics include the fact that it mainly affects patients under 50 years of age, black or Hispanic. It usually corresponds to large tumors, poorly differentiated, with high histologic grade and mitotic index and lymph node involvement; it has a higher recurrence rate and lower disease free and overall survival; in addition, visceral and soft tissue metastases to the brain and lung predominate [8, 9].

One of the aspects determined to be of great importance for this study is tumor angiogenesis, which is the growth of new blood vessels that tumors need to grow. This occurs because the tumor and host cells release chemicals near the tumor [10].

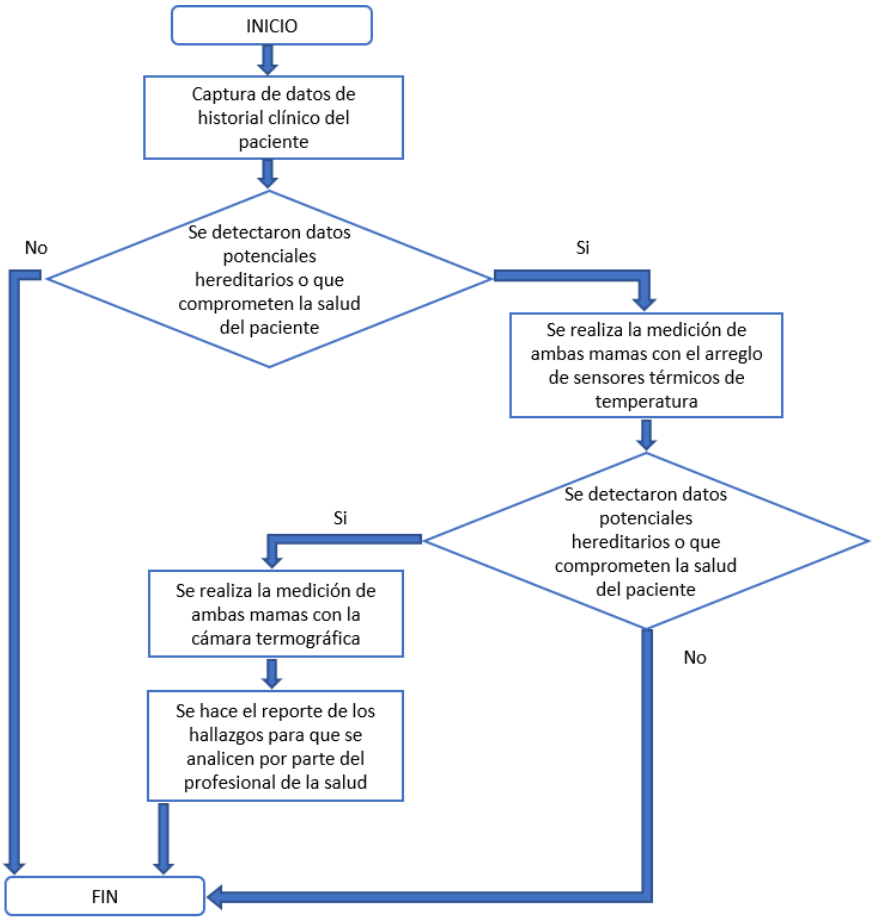

Fig. 1. Diagrama de flujo de la solución.

2 Methodology and Development

During the present work a documentary research was carried out to establish the limitations of the project, determining that the type of cancer on which the prediagnosis process will focus is triple negative infiltrating breast cancer, since this variation affects young women in which nuclear medicine studies are not indicated because of their age, and the diagnosis is usually late, hence the low survival rate for this type of neoplasia.

The process will include three stages, the first is the integration of a clinical history,which is recommended for all women over 20 years of age in order to detect those whomay develop this type of disease at some point. Once the data from the clinical history has been analyzed, it will be possible to determine those patients who, according to their state of health or history of diseases, havea higher percentage of risk. This group will be evaluated for tumor angiogenesis activity.

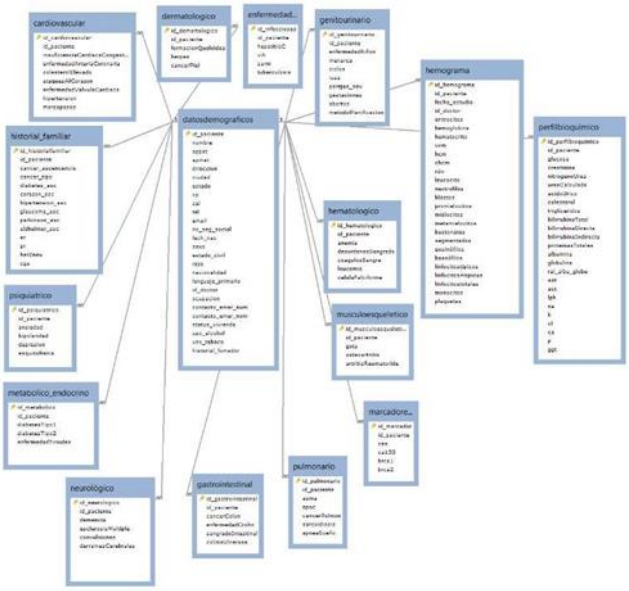

Fig. 2. Database structure.

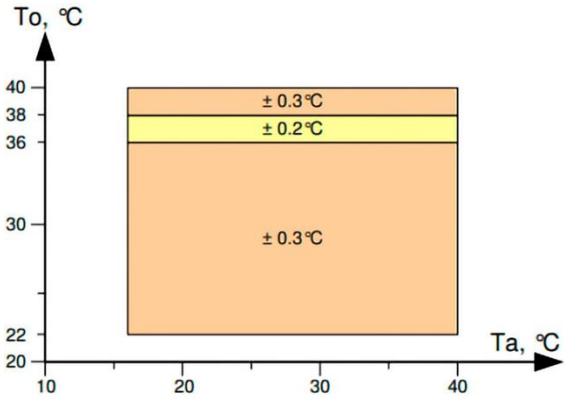

Fig. 3. Medical grade sensor temperature range.

During tumor angiogenesis, the growth of new blood vessels can generate a localized increase in temperature in the affected area. This is because the process of new blood vessel formation involves an increase in blood flow and an increase in the metabolic activity of the cells involved in angiogenesis.

This increase in blood flow and cell metabolism can result in an increase in temperature in the region where angiogenesis is occurring. However, it is important to note that this temperature increase may be very small and difficult to detect with the nakedeye or with conventional temperature measurement techniques.

For this reason, a prototype will be used to map the temperature of both breasts by means of an array of infrared temperature sensors, in the search for variations as

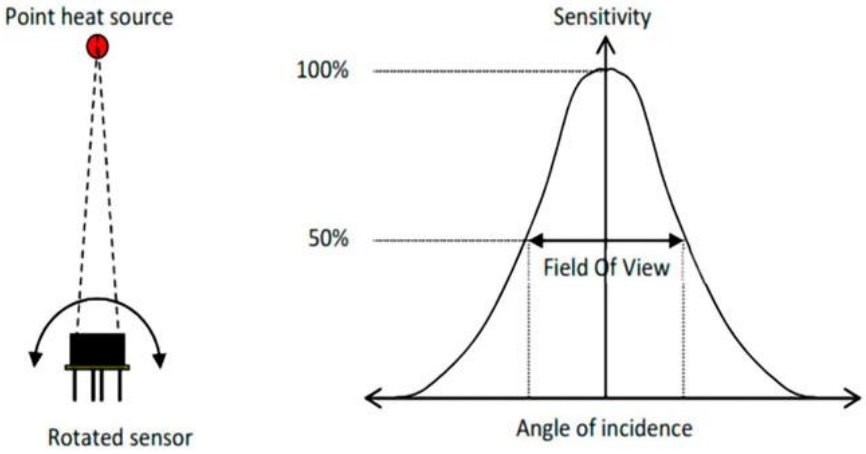

Fig. 4. Field of view measurement.

Parameter	Type xAA	Type xBA	Type xCC	Type xCF	Type xCH	Type xCI	Type xCK
Peak zone 1	0°	+25°	0°	0°	0°	0°	0°
Width zone 1	90°	70°	35°	10°	12°	5°	13°
Peak zone 2	NA	-25°	NA	NA	NA	NA	NA
Width zone 2		70°					

Fig. 5. FOV Summary Table.

a mirror, if one breast has a higher temperature than the other, a possible process of tumor angiogenesis could be taking place

To give greater certainty, the next step will be to use thermographic images to identify the area of increased temperature in the breast. For this, a thermographic camera will be used and the images will be processed through MatLab in order to perform an analysis and filtering of the images.

Infrared thermography is a technique that can be used to detect subtle changes in thesurface temperature of tissues and, in some cases, could help to identify tumor areas with active angiogenesis. The following is a block diagram illustrating the process to be followed.

3 Results

The process of analyzing the pertinent data for the integration of a clinical record thatwill help us to know the general health status of a patient, as well as the history of herfamily members, the history of cancer in her progeny will allow us to have a broad panorama that will support an early detection of infiltrating triple negative breast cancer.

In order to create a complete clinical record of a patient with triple negative breast cancer, several important data and elements must be considered. Key aspects includedin this proposal include:

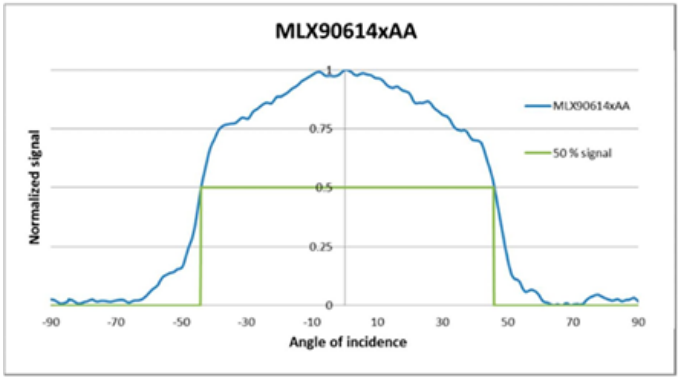

Fig. 6. Typical FOV of MLX90614xAA.

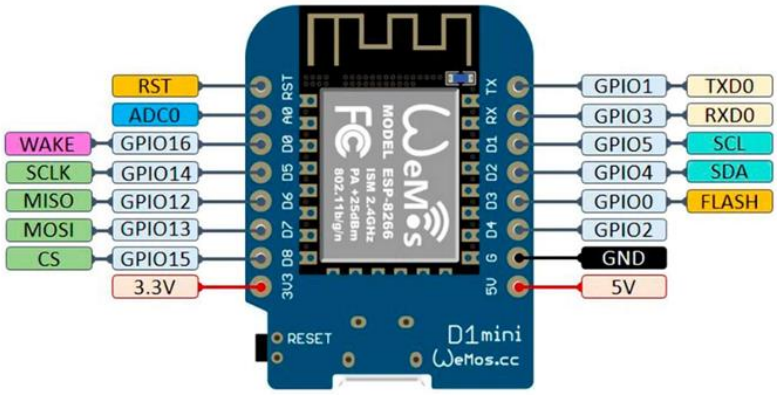

Fig. 7. ESP8266 WeMos development board.

Demographic information: includes the patient's full name, date of birth, gender, address and any other relevant information to identify the patient.

Medical history: Gathers information about the patient's medical history, such as previous illnesses, surgeries, allergies, medications being taken, and any other relevantmedical conditions.

Familial diagnostic report: This should include the results of diagnostic tests, such as breast biopsy, that confirmed the diagnosis of triple negative breast cancer. It is alsohelpful to include details about the histological classification of the tumor and its grade.

The relational database structure created to manage the clinical record is composedof 16 tables:

– cardiovascular,
– datosdemograficos,
– dermatologico,
– enfermedadesinfecciosas,
– gastrointestinal,

- genitourinario,
- hematologico,
- hemograma,
- historial_familiar,
- marcadorestumorales,
- metabolico_endocrino,
- musculoesqueletico,
- neurológico,
- perfilbioquimico,
- psiquiatrico,
- pulmonario.

They store the patient's demographic data, the patient's attending physician identifier, and the patient's history with alcohol or tobacco. In the case of cardiovascular, dermatological, gastrointestinal, hematological, metabolic endocrine, musculoskeletal, neurological, psychiatric and pulmonary history, they store a check list of the diseases thatthe patient has or had in order to make an accurate differential diagnosis.

It is important to analyze the family history, as this is where the patient's risks are identified. This table stores data on the type of cancer suffered by the patient's relatives, the degree of relationship and if this cancer was studied in its tumor markers and in itsmutation in the BRCA1 and BRCA2 genes.

In addition, the results of chemical studies necessary for the differential diagnosis ofthe disease, such as a complete blood count and a biochemical profile, are stored.

In the database scheme we can see the relationship between the patient's identifier and all the patient data stored.

The second point that was addressed was the planning of the device for measuring the temperature of both breasts through the mesh of infrared temperature sensors, for this the MLX90614 sensor was used. The operating principle of this sensor is related to the movement of the molecules, these to perform this phenomenon produce infrared radiation, the higher the temperature of the body, the faster the molecules move and more infrared radiation emitted by the body, this is known as the Stefan Boltzman law.

An infrared temperature sensor is able to detect this radiation and convert it into a temperature, actually what it does is to calculate the difference between the IR radiation emitted by the object and the surrounding environment, based on this difference we calculate the temperature.

The MLX90614DAA that we will use, has an accuracy suitable for medical applications, this model has an accuracy of +-0.3oC at temperatures between 16oC and 40oC.

The field of view is a critical factor, because in our proposed solution we propose a rhomboid arrangement in which 5 sensors will be connected to allow us to map the breast in a range greater than 80% of the same to have an accurate measurement. This factor or the distance from the sensor to the object will directly affect its accuracy. Each infrared sensor has a field of view, which is nothing more than an angle of view in which all the temperatures seen by the sensor are averaged.

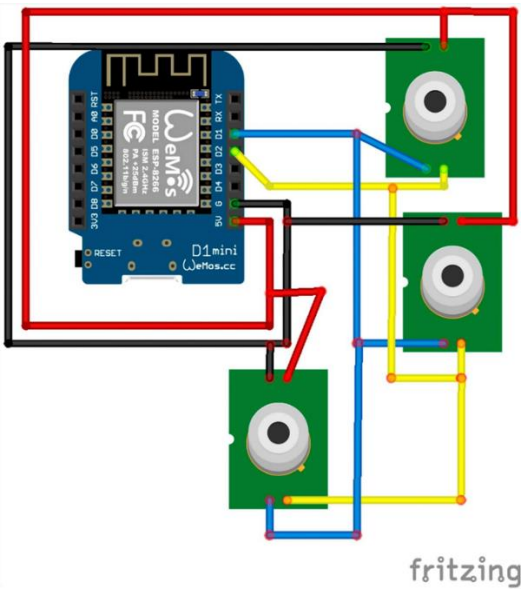

Fig. 8. Connection diagram of sensors and development board.

This sensor has a relatively wide field of view, about 90o, which means that for every centimeter away froman object, the detection area increases by 2 centimeters. Once the feasibility of the use of this sensor has been determined, we proceeded to develop the electronic solution through which the mesh of these sensors for mapping the temperature of the breast can be made.

For this we will use the ESP8266 Wemos board that allows us to have Bluetooth and WIFI communication, so we can receive both in a base station such as a Raspberry Pior an application on the cell phone the processed data to store them and make comparisons and determine whether or not there is an increase in temperature.

Another of the benefits of this board is that it has the possibility of connecting several sensors through I2C communication, which is a serial communication protocol, whichdefines the data frame and physical connections to transfer bits between two digital devices. It has for this two communication channels SDA and SCL, allowing to connect up to 127 slave devices with these two lines, for our case we will connect 10.

4 Conclusions

Having a clinical history that allows us to know the possible inheritance as well as thefactors that may be preponderant to develop triple negative infiltrating breast cancer inyoung women to whom nuclear medicine exams are not recommended because of theirage, will allow us to broaden the spectrum of preventive care, together with the temperature analysis that identifies a process of tumor angiogenesis, will allow health professionals to make decisions to confirm

diagnoses and provide timely follow up and treatment to prevent or treat in its earliest stages this type of cancer that has such a highmortality rate.

The prototype is under development and it is intended that following the model establishes a process that allows early identification of those patients who may develop the disease, as future work is to test the implementation and corroborate the results, in addition to a clinical study with patients who have already been diagnosed so that the prototypes are validated in its operation and that this technique can be a support for health professionals and support both young women and people who cannot access bytheir geographical location or economic situation to third level health services.

References

1. Organización mundial de la salud (2023) https://www.who.int/es/news- room/fact-sheets/detail/breast-cancer
2. Barragan, J. A., Becerra, G. I., González, N. J., Mainero, F. E., Mijares, A., Patlán, R. M.: Guía de práctica clínica diagnóstico y tratamiento del cáncer de mama en segundo y tercer nivel de atención. México: Secretaría de salud (2009)
3. McPhee, S. J., Papadakis, M. A., Rabow, M. W.: Current medical diagnosis & treatment 2010. New York: McGraw-Hill Medical (2010)
4. Zepeda-Castilla, E. J., Recinos-Money, E., Cuéllar-Hubbe, M., Robles-Vidal, C. D., Maafs-Molina, E.: Clasificación molecular del cáncer de mama. Cirugía y Cirujanos, vol. 76, no. 1, pp. 87–93 (2008)
5. Paez-Gómez, M., Salas-González, E., Ojeda-Babilonia, J. A., Lomeli-Muñoz, J. A., Canton-Diaz, A., Ochoa-Herrera, R.: Características clínicas y epidemiológicas de pacientes con cáncer de mama e histología triple negativo. Cirujano General, vol. 36, no. 1, pp. 20–27 (2014)
6. Alvarado-Cabrero, I.: Cáncer de mama triple negativo. Patología Revista latinoamericana, vol. 48, no. 4, p. 262 (2010)
7. Foulkes, W. D., Smith, I. E., Reis-Filho, J. S.: Triple-negative breast cancer. New England journal of medicine, vol. 363, no. 20, pp. 1938–1948 (2010) doi: 10.1056/NEJMra1001389
8. Silverstein, M. J., Gierson, E. D., Waisman, J. R., Senofsky, G. M., Colburn, W. J., Gamagami, P.: Axillary lymph node dissection for T1a breast carcinoma. Is it indicated? Cancer, vol. 73, no. 3, pp. 664–667 (1994) doi: 10.1002/1097-0142(19940201)73:3<664::aid-cncr2820730326>3.0.co;2-s
9. Butler, J. A., Bretsky, S., Menendez-Botet, C., Kinne, D. W.: Estrogen receptor protein of breast cancer as a predictor of recurrence. Cancer, vol. 55, no. 6, pp. 1178–1181 (1985) doi: 10.1002/1097-0142(19850315)55:6<1178::AID-CNCR2820550606> 3.0.CO;2-U
10. Instituto Nacional del Cáncer https://www.cancer.gov/espanol