

Ionizographic detector for Breast Cancer Diagnosis

Detector Ionizográfico para Diagnóstico de Câncer de Mama

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Helton Gírio Matos

ORCID: <https://orcid.org/0000-0001-6379-7027>
Universidade Vale do Paraíba, Brazil
E-mail: helton_matos@yahoo.com.br

Marco Antonio Ramirez Ramos

ORCID: <https://orcid.org/0000-0002-9667-5533>
Universidade Vale do Paraíba, Brazil
E-mail: marco.antonio@univap.br

Lúcia Vieira

ORCID: <https://orcid.org/0000-0002-9354-6533>
Universidade Vale do Paraíba, Brazil
E-mail: lucia.vieira@univap.br

Ary Oliveira Pires

ORCID: <https://orcid.org/0000-0003-0977-3838>
Universidade Federal do Piauí, Brazil
E-mail: aryopires@yahoo.com.br

Abstract

Every day the number of cancer victims increases. In 2020 alone, 626,030 people were affected in Brazil, according to estimates by the National Cancer Institute (INCA). The only way to reduce these numbers is early diagnosis. In the present study, a invention called Ionizographic Detector is described, which performs Positron Emission Tomography (PET) producing metabolic information in breast nodules. This device enables accurate diagnosis of breast nodules regarding its malignancy. To prove its effectiveness, a comparative evaluation was made between the Ionizographic Detector and the Positron Emission Tomography/Computerized Tomography (PET-CT) for analysis of the metabolic data in breast nodules. The research is being carried out with 20 patients who have histopathologically documented breast cancer. From the results it will be possible to prove the device's efficacy. It will thus enable an accurate and low- cost malignancy diagnosis option. The Ionizographic Detector can be hybridized with some anatomical imaging technology, such as Ultrasound (US). With this, it is possible to promote greater access to accurate diagnoses, significantly increasing the possibility of early diagnoses, enabling a cure or a better prognosis for the patient.

Keywords: Cancer; Nodule; Breast; PET-CT.

Resumo

A cada dia aumenta a quantidade de vítimas do câncer. Só no ano de 2020 acometeu 626.030 pessoas no Brasil, segundo estimativas do Instituto Nacional do Câncer – INCA. A única forma para a diminuição desses números é o diagnóstico precoce. No presente estudo é caracterizado um invento chamado Detector Ionizográfico, que realiza Tomografia por Emissão de Pósitrons (PET) produzindo informações metabólicas de nódulos mamários. Possibilita diagnóstico preciso de nódulos mamários quanto a sua malignidade. Para comprovar sua efetividade, foi feita uma avaliação comparativa qualitativa entre o Detector Ionizográfico e o Tomografia por Emissão de Pósitrons/Tomografia Computadorizada (PET-CT) para análise de dados metabólicos em nódulos mamários. A pesquisa foi realizada com 3 pacientes que apresentavam nódulo mamário documentado por histopatológico. A partir dos resultados foi possível comprovar a eficiência do aparelho. Possibilitará assim, uma opção de diagnóstico de malignidade preciso e de baixo custo. Seguindo a tendência, o Detector Ionizográfico pode ser hibridizado com alguma tecnologia de imagens anatômicas, como o ultrassom. Com isso é possível promover maior acesso a diagnósticos precisos, aumentando sensivelmente a possibilidade de diagnósticos precoces, viabilizando a cura ou melhor estadia do paciente.

Palavras-chave: Câncer; Nódulo; Mama; PET-CT.

Resumen

Cada día aumenta el número de víctimas de cáncer. Solo en 2020, 626,030 personas se vieron afectadas en Brasil, según estimaciones del Instituto Nacional del Cáncer - INCA. La única forma de reducir estos números es el diagnóstico temprano. En el presente estudio se caracteriza un invento denominado Detector ionizográfico, que realiza una Tomografía por Emisión de Positrones (PET) produciendo información metabólica de los nódulos mamarios. Permite un diagnóstico preciso de los nódulos mamarios con respecto a su malignidad. Para comprobar su eficacia, se realizó una

evaluación comparativa cualitativa entre el Detector Ionizográfico y la Tomografía por Emisión de Positrones / Tomografía Computarizada (PET-CT) para el análisis de datos metabólicos en nódulos mamarios. La investigación se realizó con 3 pacientes que tenían un nódulo mamario documentado por examen histopatológico. A partir de los resultados, fue posible demostrar la eficiencia del dispositivo. De este modo, permitirá una opción de diagnóstico de malignidad precisa y de bajo costo. Siguiendo la tendencia, el detector ionizográfico se puede hibridar con alguna tecnología de imágenes anatómicas, como la ecografía. Con esto, es posible promover un mayor acceso a diagnósticos precisos, aumentando significativamente la posibilidad de diagnósticos precoces, posibilitando una cura o una mejor estancia del paciente.

Palabras clave: Cáncer; Nódulo; Seno; PET-CT.

1. Introduction

According to Pereira et al. (2010) Brazil has predominantly shown the growth of the elderly population. Consequently, there is an increase in the incidence of diseases which are characteristic of this risk group. Efforts have been applied in the prevention and diagnosis of these illnesses.

According to the World Health Organization (2012) breast cancer is the fifth leading cause of death from cancer in general and the most common among women worldwide. In Brazil, 57,120 new cases of breast cancer were estimated in 2014, which represents the leading cause of death from cancer in the Brazilian female population, with 12.10 deaths for 100,000 women (INCA, 2014). These numbers increased in 2018, totaling 59,700 new cases and corresponding to 29.5% of the total number of cancers diagnosed in women (INCA, 2018).

Unlike other diseases, there is no known way to prevent breast cancer, leaving only early diagnosis for cure or treatment, prolonging the patient's life. For this, there are several techniques for detection and evaluation of breast cancer.

Breast cancer can be defined as an exaggerated multiplication of malignant epithelial cells that line the ducts or lobes of the breast. Breast neoplasm is a clonal disease, where a single modified cell is capable of express all its malignant potential (Kasper et al., 2016). Early diagnosis is of paramount importance, because from it starts the most appropriate and effective treatment increasing the patient's life expectancy. It is also important to be aware of the disease, how it behaves, and each of its stages, from diagnostic tests to treatment.

Efforts have been applied to the development of new equipment and methods, capable of providing early diagnosis of breast cancer. There has been great advances with computer-aided detection (Computer-Aided Detection - CAD), providing an increase in image quality and consequently in diagnostic sensitivity, up to 21%. As a result, there was a decrease in false positives and false negatives in the diagnoses made (Calas, 2012).

A little over 100 years after the discovery of the first method of obtaining non-invasive images of the interior of the human body, diagnostic medicine is undergoing an equally profound and transformative revolution. There was phenomenal increase in digital, computer-based techniques that seek to treat imaging as a complex problem mathematician (Sabbatini, 1999).

The image's quality can be understood as a mammographic image with optical densities perceptible to the human eye and good visualization of relevant tissues for a safe diagnosis, influenced by breast density, radiographic technique, location of the lesion, characteristics of malignancy and fatigue of the radiologist (Villar et al., 2015).

Unfortunately, most investments have been made by the private sector. Consequently, access to a more accurate diagnosis is available for a small portion of the population. For the public health system, predominantly the use of the least expensive resources that consequently present flaws and inaccuracies in the diagnosis.

According to Alvares and Michell (2003), diagnostic imaging methods such as mammography, ultrasound and scintigraphy are essential tests in the diagnosis of breast cancer and in the follow-up after the surgical procedure, however, all of them have specific limitations.

The PET-CT (Positron Emission Tomography – Computed Tomography) is a revolutionary technique for cancer diagnosis. To perform an examination with PET-CT, a radiopharmaceutical is injected intravenously to identify changes that occur

in cell metabolism.

Of the existing technologies analyzed in this work, the device with the greatest accuracy in diagnosis is the PET-CT. For this reason, it was chosen to be compared with the diagnoses generated by the Ionizographic Detector. PET-CT overlays metabolic images generated by PET with the anatomical images generated by the tomograph, enabling identify the shape and malignancy of the tumor. However, an exam with this device costs, on average, a thousand dollars. With the use of ultrasound, a more affordable exam, it is possible to observe the anatomical images of the tumor, however without the possibility of differential diagnosis of malignancy.

As a result, it is easy to imagine the difficulty of the less favored population in having access to the necessary diagnostic tests. There is a limitation of the Health Unic System (SUS) in offering this type of examination, as well as the resistance of health care plans in authorizing the procedure for the insured.

In December 2014 the Ministry of Health published Ordinance N° 1340 incorporating PET-CT to the SUS for the following tumors: potentially resectable non-small cell lung; metastasis exclusively from colorectal cancer; and for the staging and evaluation of the response to treatment of Hodgkin's and non-Hodgkin's lymphomas. Before the publication of this ordinance, the PET-CT was carried out through judicializations.

One trend is the combination of the Ionizographic Detector with the Ultrasound device. With that we will have morphological data (Ultrasound) and metabolic data (Ionizographic Detector) enabling the study of shape and malignancy of the nodule under study with the combination of two technologies that are very affordable in terms of acquisition costs and examination with these gadgets.

As it is a relatively simple equipment, it does not need photomultipliers or robust electronics inside a “gantry” (patient positioning tunnel), as occurs with other devices being used with this goal. The Ionizographic Detector is being developed in a small size, malleable and with a low cost when compared with products that provide metabolic data.

The Ionizographic Detector makes images with “count rates per second”, it’s not necessary to wait that the entire image has a good counting statistics to finish the exam, when an ionization cell encounters a standard it stops counting at the end of the exam. Thus, enabling a whole body detection where the exam would end in a few seconds instead of several minutes as with the today’s scintigraphy.

With this advance, there is the possibility of connecting nuclear medicine with other areas of imaging such as endoscopy for example. It would also make it possible to detect the sentinel lymph node (malignant tumor) visually, allowing a more safe approach to the lymph node of the internal mammary chain by the mastologist increasing the sensitivity and detectability of breast cancer.

The present study aims to characterize an invention called Ionizographic Detector for acquisition of metabolic data of breast nodules. To prove its effectiveness, a comparison was made between exams performed with PET-CT and the Ionizographic Detector. The Ionizographic Detector presents a significant reduction in the costs involved in the manufacture of the device, providing accessibility and efficiency, contributing to change the current scenario in breast cancer diagnosis.

Table 1 presents a summary of the analyzed technologies, with their respective advantages and disadvantages.

Table 1 – Comparative.

Technology	Advantages	Disadvantages
Mammography	Low cost. Satisfactory sensitivity most evident in breast cancer cases in initial stages.	Morphological assessment only. Difficulties in screening dense breasts, post-surgical breast changes and breast implants.
Ultrasound	Important role as a complementary exam to mammography and clinical examination.	Morphological assessment only. Difficulties in differentiating the malignant or benign characteristics as well as in identifying lesions smaller than 1cm.
Magnetic Resonance	Evaluates the size and morphological features that are characteristics of the tumor.	High cost, long exam time and its contraindications.
PET-RM and PET- CT	Metabolic images, overlay with anatomical images of cancer under analysis.	High cost.
Detector Ionizographic	Metabolic Images. Low cost.	Does not show morphological images.

Source: Authors.

2. Methodology

The research is qualitative, as it has an exploratory character, studying individual experiences. Qualitative methods are those in which the researcher's interpretation is important with their opinions on the phenomenon under study (Pereira et al., 2018).

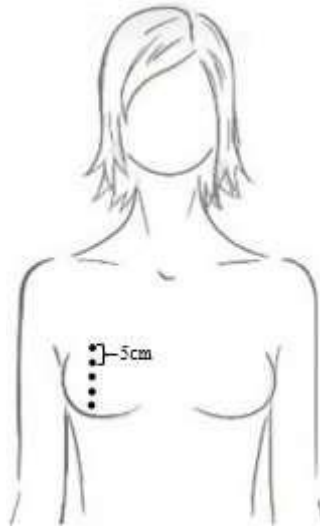
Three (3) patients who presented breast nodule(s) documented by histopathology were examined in the Ionizographic Detector. They were firstly submitted to PET-CT examination, where a radiopharmaceutical known as contrast was injected intravenously into the patient. Contrast is a radioactive material, usually the Fluorodeoxyglucose (FDG), a radioisotope of fluorine mixed with glucose. Its formula is $C_6H_{11}^{18}FO_5$.

Malignant breast nodules, unlike benign breasts, absorb a lot of glucose. In this way, it was possible identify where a greater emission of radiation occurred and the consequent diagnosis of the malignant nodule(s) was made. During the exam with the Ionizographic Detector, when there is the presence of radiation, an ionization process occurs. The injected radioactive material in the patient releases gamma rays and causes ionization in the Geiger Muller sensors. This described process is converted into energy and the detections per second are measured.

The Ionizographic Detector exam is performed with the patient taken to a room containing a Ultrasound. A gown with a front opening was provided. Then, the patient was placed in the supine position, with the upper limbs raised at a 90 degree angle.

Initially, with the ultrasound device, the nodule(s) was located and five marks were made in the patients with a brush as shown in the graphic representation in Figure 1. One central mark, where it was the morphological analysis from the Ultrasound and four other markings, two above and another two below the initial marking, spaced 5 (five) centimeters apart longitudinally. This step is justified by the need to compare radiation captures per second not only in the nodule region where there is greater emission of radiation, but also from areas with lower incidence to prove the efficiency of the device's capture.

Figure 1 - Patient markings.



Source: Authors.

The Collimator is a casing made in a 3D printer. Internally it stores 2 (two) Geiger sensors and is filled with lead. Lead is used to shield and prevent sensors from suffering spurious interference, so the capture is well targeted.

In each marking, the collimator is positioned and 20 (twenty) readings are registered in each position of the markings. The result corresponds to the average of the sum of these captures, which in turn is carried out in triplicate, enabling a most significant sample for analysis.

Related to the data collected at each collimator position, the fluorine activity present in the radiopharmaceutical decreases per unit of time, due to the release of photons and emission at random, that is, positrons are emitted in several directions, being estimated the quantity of 20 (twenty) readings to capture in each position. Fluoride activity is measured in Curie (Ci), where it represents the amount of decay per unit of time, that is, the unit in which an amount of radioactive material, 3.7×10^{10} nuclei disintegrate in every second.

Probe Detector software was used to present the received signal capture in real time. The software transforms the received signal into bars, representing each one of the sensors, it also makes the sum of the captures and totals it in a report.

With the data from the captures, an analysis was performed and a comparison with the results obtained in PET-CT. In order to compare the results, since PET-CT is a reference in the diagnosis of malignancy of breast nodules.

3. Results and Discussion

The results obtained in the comparison between PET-CT and the Ionizographic Detector are presented in the following figures. The graphs referring to the results of the exams made in the Ionizographic Detector are plotted on the X axis with the numbering from 1 (one) to 5 (five) that corresponds to each position marked on the patient. The Y axis contains the amount of captures, as described in the methodology.

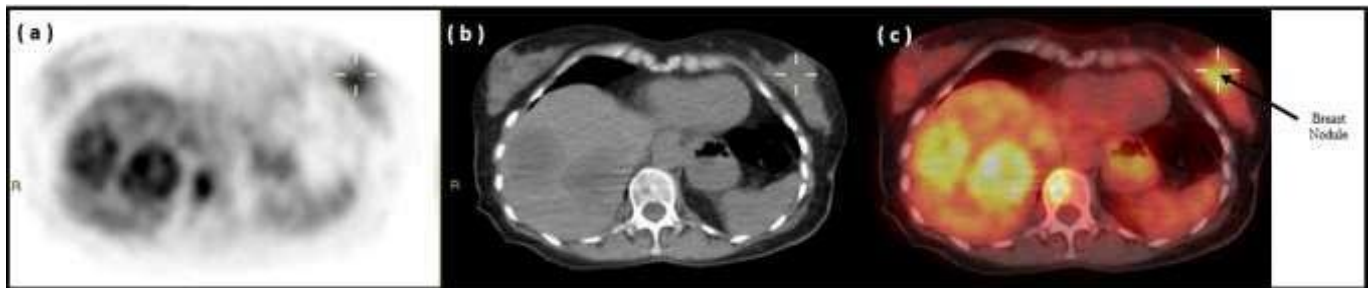
The bars in blue color indicate sensor 1 of the Ionizographic Detector, which corresponds to a possibility of variation from 0 (zero) to 250 (two hundred and fifty) captures per second. The bars in orange color correspond to sensor 2 of the Detector.

All graphs correspond to the comparative results obtained in triplicate. The triplicate was generated from 3 (three) patients undergoing examination with the Ionizographic Detector. These patients, following all the aforementioned methodology, were examined in January, February and March 2021. They were initially submitted to PET-CT and then to the Ionizographic Detector.

Figure 2 contains two images and an overlay of metabolic and morphological data obtained from the examination of the patient 1 obtained by PET-CT. The image generated by the positron emission tomography exam presents areas of greater glucose metabolism and consequently of greater radiation uptake due to the radiopharmaceutical, showing darker regions, as can be seen in Figure 2 (a). The image of the test result of computed tomography shown in Figure 2 (b) shows the shape, ie, morphological features in the nodule. The image shown in Figure 2 (c) was obtained via fusion of the above-mentioned images from the PET-CT exam.

Patient 1, when undergoing PET-CT examination, presented a nodule in the left breast, as indicated in Figure 2(c). In the image overlay, dots with more intense color can be seen, representing areas of glycolytic hypermetabolism in multiple cervical vertebral bodies.

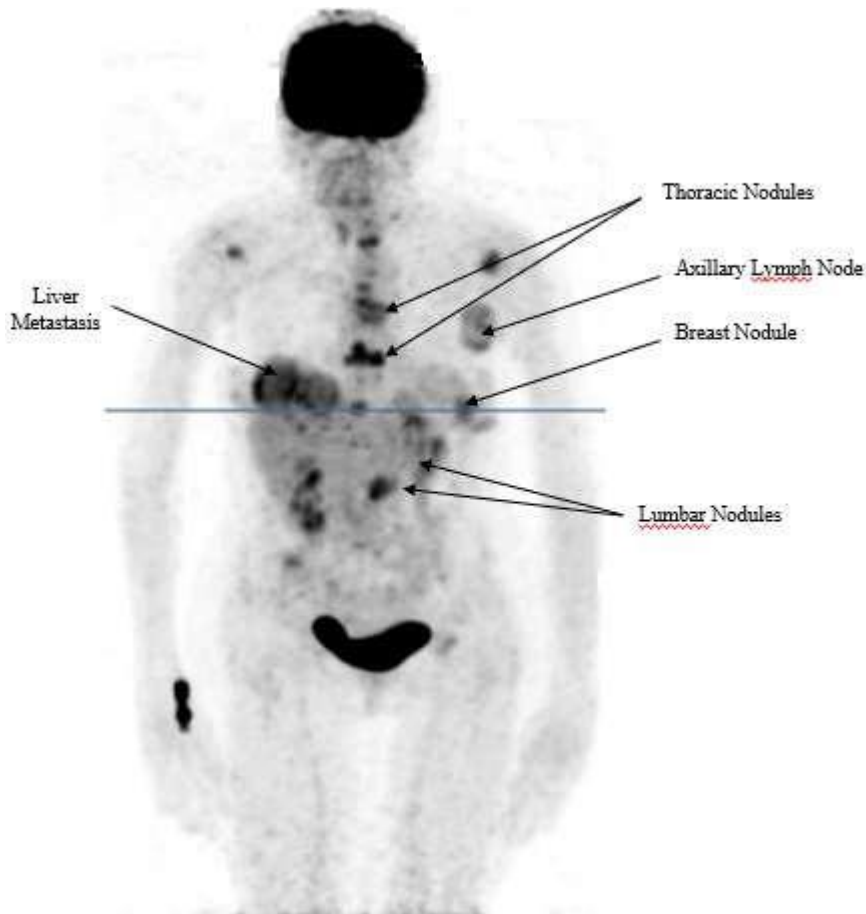
Figure 2 – Patient 1 (a) Positron emission tomography (b) Computed tomography (c) Overlay of (a) + (b) data metabolic and morphological.



Source: Authors.

Figure 3 contains an image generated in the Maximum Intensity Projection (MPI) format obtained via PET. One hypermetabolic lymph node enlargement in the left axilla can be seen in this figure. A hypermetabolic nodule in the left breast compatible with a primary referred tumor. Thoracic and lumbar nodules can also be seen.

Figure 3 - Image - Maximum Intensity Projection (MPI).



Source: Authors.

Figure 4 refers to the image obtained from the ultrasound exam where it is possible to verify the nodule's shape. This is the starting point for the marking procedure made on the patient.

Figure 4 - Patient 1 – Ultrasound Image.



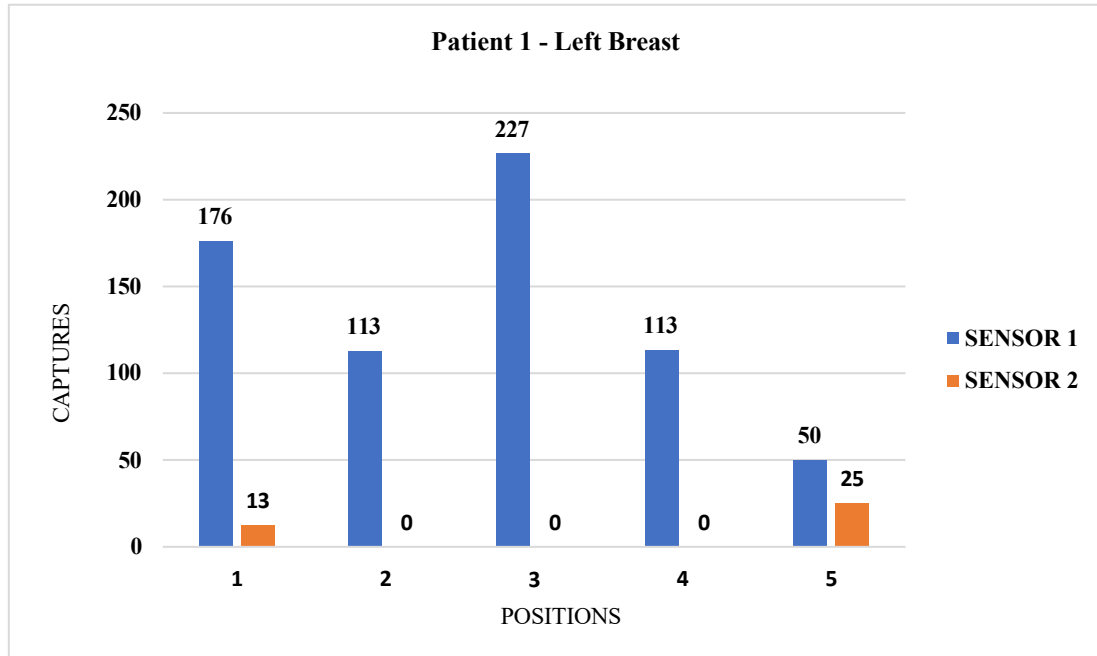
Source: Authors.

Figure 5 contains a graph with results from patient 1 regarding the examination in the Ionizographic Detector in the left breast. On the X axis, the five collimator positions on the patient are shown, with the indication of the first bar referring to sensor 1 and the second one referring to sensor 2. On the Y-axis, the possible variations of captures are presented.

The first reading demonstrated 176 captures per second on sensor 1 and 13 on sensor 2. This is explained by the presence of an axillary lymph node confirmed by the PET-CT examination. The second position shows a drop in captures, 113 captures were recorded in sensor 1 and no capture in sensor 2. In the third position, where the nodule was marked from the analysis with the ultrasound device, was detected an increase of more than 100% in the capture of sensor 1, sensor 2 remained without

recordings. In the fourth position the reading corresponds to the second position. In the fifth reading, there were 50 captures per second on sensor 1 and 25 on sensor 2.

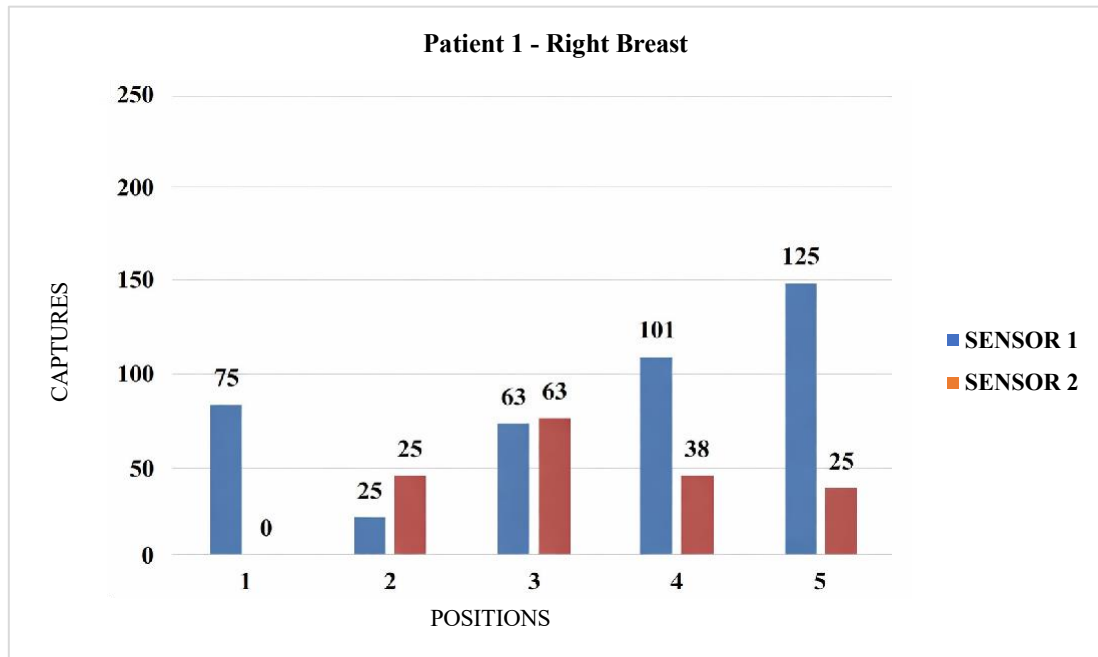
Figure 5 - Patient 1 - Captures per Second (ME).



Source: Authors.

Figure 6 contains the results of the exam performed with the Ionizographic Detector in the right breast. 75 captures per second were identified by sensor 1 and no capture by sensor 2 in the recording taken in the first position. There was a drop in the uptake of sensor 1 and an increase in the uptake of sensor 2 in the second position. On the third position, the two sensors showed an increase and recorded 63 captures per second. On the fourth reading, sensor one increased its capture to 101 and sensor 2 had a drop in captures to 38. And in the last position there was an increase to 125 captures per second in sensor 1 and drop in sensor 2 to 25 captures. This increase in uptake by sensor 1 is justified by the fact that the patient has a nodule in the liver, as seen in the PET-CT exam. In this way, as the positions move closer to the liver, uptakes increase.

Figure 6 - Patient 1 - Captures per Second (MD).

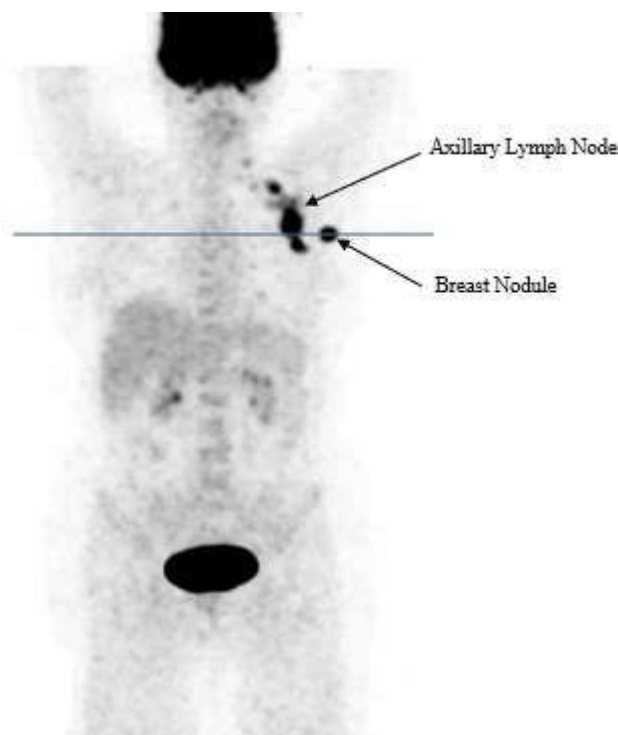


Source: Authors.

Figure 7 contains a Maximum Intensity Projection (MIP) image obtained from patient 2 via PET-CT scan. A nodule in the left breast can be seen in this figure, with an active primary tumor in addition to axillary and left subpectoral lymph node enlargement compatible with active secondary implants. No other areas of abnormal accumulation of the radiopharmaceutical by the patient's body were found.

PET-CT performed with a specific protocol for breast assessment showed good sensitivity and presented association with important histological/immunohistochemical factors related to aggressiveness and prognosis of breast carcinomas (Bitencourt et. al., 2014).

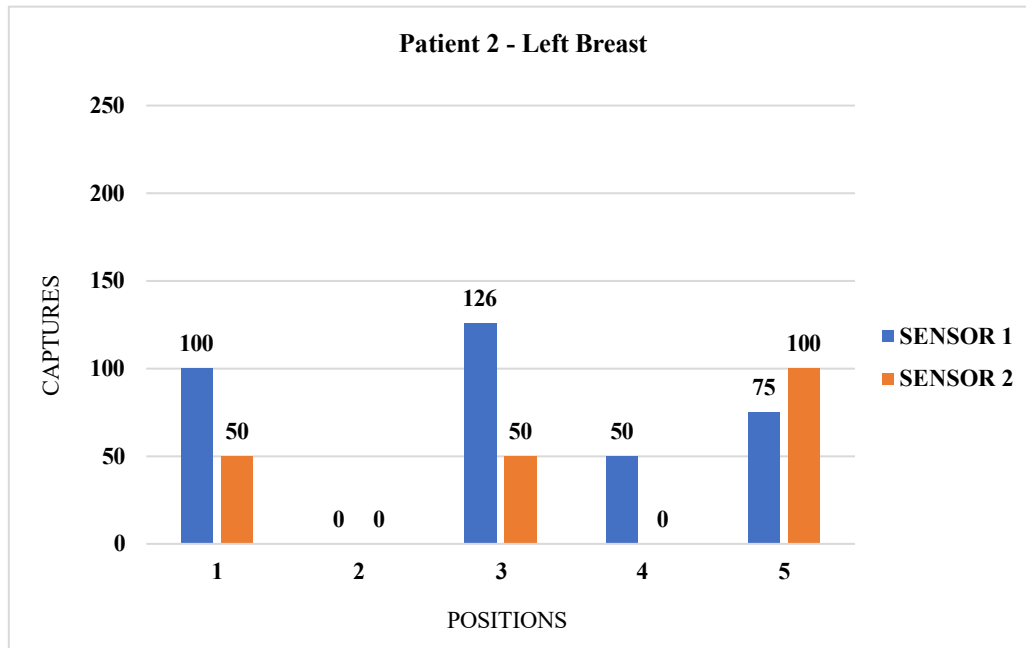
Figure 7 - Patient 2 - Maximum Intensity Projection (MPI).



Source: Authors.

The examination with the Ionizographic Detector, initially performed on the left breast of patient 2, captured a hypermetabolism at the first reading, according to the graph in the Figure 8 where sensor 1 presented 100 and sensor 2 recorded 50. In the second position, there was no record of radiation. On the third reading, there was another point of hypermetabolism, with the first sensor detecting 126 uptakes and the second 50. On the fourth reading, sensor 1 registered a recording of 50 and sensor 2 did not pick up radiation. And in the last reading, there was again a radiation capture by the sensors, 75 from sensor 1 and 100 from sensor 2.

Figure 8 - Patient 2 - Captures per Second (ME).



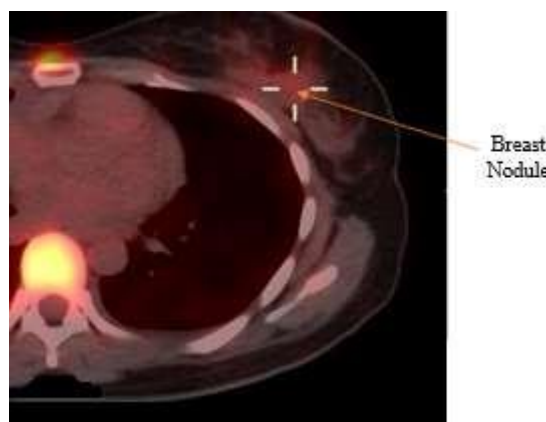
Source: Authors.

It can be seen that there are hyper-uptake regions of glucose, identified in the darkest region at the region of the thorax of the patient 2, proving the existence of an axillary lymph node enlargement as shown in Figure 6. That's the reason why the first reading showed hypermetabolism, that is, a higher consumption of glucose and, consequently, a region with greater radiation regions. In the other readings, recordings of uptake were presented, where is observed a left breast nodule.

From the data collected at the examination of the patient's right breast, there were zero or very low uptakes. Considering these small fluctuations as spurious data. Therefore, concluding that there are no malignant nodules.

The result shown in Figure 9 refers to patient 3 when undergoing the PET-CT examination, overlapping morphological and metabolic images. The staging for Cancer Antigen (Cancer Antigen – CA) was observed, that is, a discrete uptake in a left breast nodule compatible with a primary tumor was seen.

Figure 9 - Overlay of morphological and metabolic images.



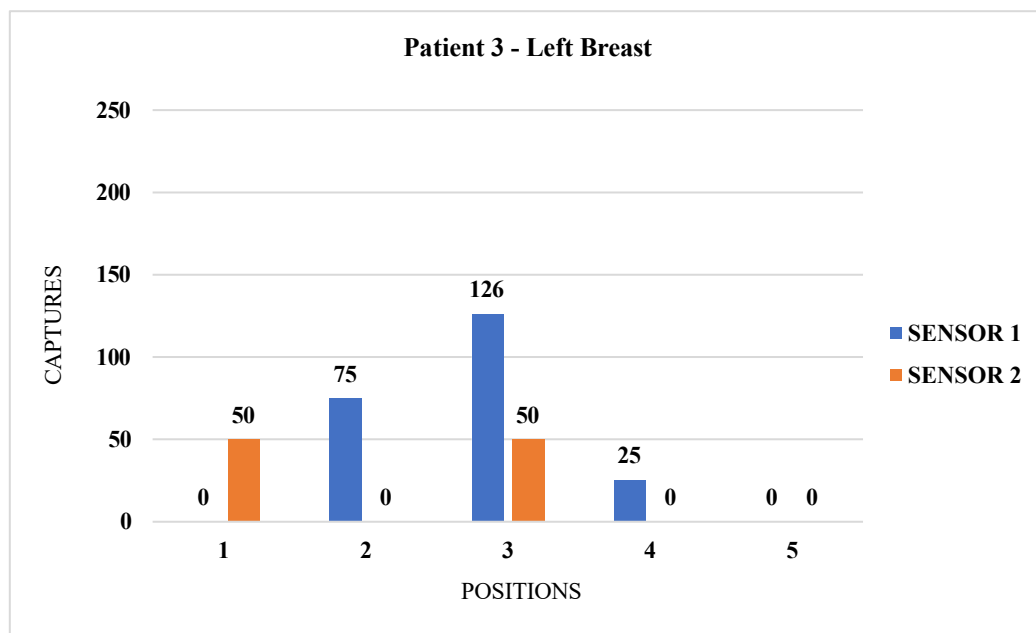
Source: Authors.

The patient reported that she had undergone two sessions of chemotherapy. That's the reason for, although already with a malignant nodules diagnosis, have presented this result.

The result shown in figure 10 contains a graph of the test results carried out with the Detector Ionizography on the left breast of the patient 3 where it can be seen that a subtle uptake occurred in the third point marked as the location of the nodule. The captures started with zero on sensor 1 and 50 on sensor 2. Right on the second reading there was a capture of 75 in sensor 1 and none in sensor 2. In the third position, a recording with the highest capture was noted, which was 126 by sensor 1 and 50 by sensor 2. In the fourth reading, a decrease was presented, that is, the sensor 1 recorded 25 captures and sensor 2 none. And finally, in the fifth position, no capture was registered.

It can be seen that it is compatible with that presented by the PET-CT exam in the left breast, as shown in Figure 8 where there is an over-uptake in the third reading, that is, point identified with the Ultrasound being from the nodule. The result presented by the Ionizographic Detector in the patient's right breast was satisfactory. With very low uptakes or none recorded in the positions marked on the patient. Corresponding to the diagnosis presented by the PET-CT exam.

Figure 10 - Patient 3 - Captures per Second (ME).



Source: Authors.

4. Conclusion

After analyzing the results, it is possible to conclude the reduction in the number of markings depending on the point of interest caused it was already visualized on ultrasound. The other readings are merely for checking the equipment's calibration. For the other exams, three marking procedures will be made instead of five. The equipment will be parameterized to no longer take 20 readings at each marking (position), 40 will be made, with the intention of obtaining a larger sample of captures, consequently, more representative recording, since the emission of positrons is random.

With the analysis of the experiment, we can conclude that the record of 50 captures in a given position previously marked in the patient, may be disregarded, as they represent a base average of the circulating radiopharmaceutical in the patient. Taking into account higher recording, according to the graphs presented in the survey, associated with the diagnoses generated with the PET-CT exams.

From the results obtained through the performance of the three exams described in this publication, it is possible to observe the correspondence in 100% of the diagnoses of the exams performed in PET-CT and in the Ionizographic Detector. All hypermetabolic uptakes recorded outside the region marked by the breast nodule, were justified by the existence of other capturing elements in the patient's body. As for example what happened in patient 2, where the Detector Ionizography captured the metabolic information of the left breast nodule, as well as the high metabolism corresponding to the presence of a lymph node enlargement in the left axilla and liver lesions.

In the analysis of the most relevant technologies for detecting breast nodules, we concluded that the methodologies available when they present satisfactory results, are expensive and inaccessible for the majority of the population. The most accessible are less accurate in such detection. The Ionizographic Detector has advantages in terms of metabolic information accuracy as efficient as PET scans, with a very affordable cost when compared to other technologies. But as a disadvantage, it does not capture morphological information, as does PET.

With the proof of the effectiveness of the Ionizographic Detector, a natural consequence, as happened with the PET-CT and PET-RM, is the hybridization of the technologies, already mentioned above. Enabling to associate metabolic with morphological data. Accurate diagnosis of breast nodules will be more accessible, enabling early diagnosis or even a better staging for the patient affected by this disease. As an inevitable consequence, which occurred with all equipment analyzed in this publication, an evolution of the device so that it can increasingly keep up with advances and needs of this specialty of medicine.

As a suggestion for future work, further experiments with the Ionizographic Detector should be carried out. Not only in breast examination, but in analyzing thyroid nodules and assessing kidney function. This makes it possible to prove not only the effectiveness in diagnosing the invention, but also its diversity of applications.

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