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Proposal for the creation of Breast Health Units in low- and middle-income countries

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Abstract

More than 2 million women are diagnosed with breast cancer every year and around 700,000 die, many of them in low- and middle-income countries (LMICs), where mammographic screening and modern therapies are not widely available. In this document we propose the creation of *Breast Health Units*, each consisting of one or two briefly trained female technicians, furnished with inexpensive portable equipment for breast ultrasound, thermography, and fine-needle aspiration (FNA) cytology, supported by artificial intelligence. These units will be able to operate inside or outside hospitals, and even in rural areas. The goal is to detect breast cancer in early stages, when it is still possible to cure it.

1 The burden of breast cancer

Breast cancer is the most common type of tumor in women. According to the World Health Organization (WHO), "in 2020, there were 2.3 million women diagnosed with breast cancer and 685,000 deaths globally".[1] In high-income countries, 12.5% of women (one in every 8) develop this disease during their life and more than 4% (approximately one in every 24) die of it. The survival rate is 99% when the disease is detected early but drops to 22%—i.e., 78% of patients die—when it is found in stage 4. Early detection also saves economic resources: treating breast cancer in stage 4 is three times more expensive than in stage 0. For this reason, all countries are interested in implementing screening programs.

1.1 Breast cancer screening

Self-examination is the easiest and most widely available detection technique, but its sensitivity is only around 30% and, due to its low specificity, it results in a high rate of false positives, which cause anxiety and depression in women who practice it—see the references in [Gonzalez-Hernandez et al., 2019].

Mammography (X-ray) is the standard technique for breast cancer screening since the early 1960s, due to its relatively high sensitivity and specificity. However, dense breasts—which occur in over 40% of women, especially in those below 50 y.o.—can mask the tumors. Tomosynthesis, a form of 3D mammography, increases the sensitivity, but the equipment is even more expensive. Additionally, the radiation may induce breast cancer, and the need to compress the breast causes discomfort and pain, which makes many women refuse the test.

[1] https://www.who.int/news-room/fact-sheets/detail/breast-cancer.

Ultrasound, also called echography or sonography, has the advantages of being radiation-free, painless, and cheaper than mammography, but has lower sensitivity and specificity. In some hospitals, it is used as an adjuvant technique, or even as a replacement for mammography in young women with familiar antecedents of breast cancer, who must be examined frequently.

Magnetic resonance imaging (MRI) is much more sensitive than mammography but less specific and much more expensive. Additionally, some patients experience anxiety and claustrophobia—an examination may take 30 minutes to one hour—and the contrast agent sometimes causes allergic reactions. For these reasons, MRI is not routinely used for screening in any country.

Breast thermography was initiated in the mid-20th century [Lawson, 1956]. It was approved by the FDA as an adjunct to other screening techniques in 1982, but was not widely accepted due to its poor accuracy in those years. However, three factors have contributed to a steady increase in accuracy. First, the spatial resolution and the thermal sensitivity of infrared cameras have improved significantly, being now 50 times higher than in the first devices used for this purpose [Kandlikar et al., 2017]. Second, there are standard protocols for the acquisition of breast thermograms, which is essential for the quality of images [Kandlikar et al., 2017; Gogoi et al., 2019]. And third, digital image processing with artificial intelligence can detect thermal patterns that escape the human eye.

Unfortunately, most radiologists still look down on thermography because they are unaware of the progress made in the last 25 years and the studies conducted in the last decade. For example, a screening of 1,008 female patients in India obtained a sensitivity of 97.6% and specificity of 99.17% [Rassiwala et al., 2014]. In China, a trial involving 2,036 women with breast disease showed a sensitivity of 95.8% for ultrasound, 96.1% for mammography and 97.1% for thermography [Yao et al., 2014]. A trial in Sweden examined 1,727 women; mammography detected 7 cancers, while thermography found 6 additional cancers [Hellgren et al., 2019]. Two recent studies in India have analyzed the performance of Thermalytix, a software developed by the company Niramai. In one of them, conducted on 470 women, the sensitivity was higher for thermography (91%) than for mammography (87%); the difference was larger for dense breasts, where thermography detected non-palpable lesions smaller than 4 mm [Kakileti et al., 2020]. In the other, with 459 patients, the sensitivity was 95.24% and the specificity 88.58%, which are at least comparable with those of mammography [Bansal et al., 2023].

In addition, thermography has several advantages over mammography, especially for LMICs: it is safe (because it does not use ionizing radiation), painless (because it does not compress the breast), fast (results are immediate), inexpensive (it does not require highly trained technicians to acquire images, and infrared cameras are much cheaper than mammography equipment), and portable.

When a patient presents with symptoms suggesting breast cancer (such as pain, lumps, nipple discharge…) or when screening detects suspicious lesions, it is necessary to diagnose whether those findings are benign or malignant and, in case of cancer, to determine its characteristics in order to select the most appropriate treatment. Two techniques are available:

Fine-needle aspiration (FNA), sometimes called FNA cytology (FNAC) or FNA biopsy (FNAB), consists in taking a small amount of breast tissue or fluid from a suspicious area with a very thin needle on a syringe. The procedure is usually guided by ultrasound. The sample is then placed on a glass slide, stained to highlight the nuclei of the cells, and examined under a microscope by a pathologist.

Core-needle biopsy and **surgical biopsy** are performed when there is a high suspicion of cancer. These techniques provide much more information, but require much more sophisticated equipment and highly trained personnel, and cause more inconveniencies to patients.

1.2 Breast cancer in low- and middle-income countries (LMICs)

In LMICs the burden of breast cancer is even harder for several reasons. First, **screening** is not widely available. Mammography is not affordable in many health systems due to the cost of equipment, the impossibility of extending it to rural areas, and the lack of trained radiologists. Ultrasound has been proposed as a cost-effective alternative because nowadays there are portable sonographs at affordable prices [Omidiji et al., 2017; Sood et al., 2019; Martei et al., 2022]. However, in some countries the main barrier to this technique is not the cost of the devices, but the lack of trained personnel. As a consequence, patients are diagnosed when tumors are bigger and at later stages—see, for example, [Islami et al., 2015].

Second, in many regions very few women can afford modern **treatments**, such as efficient chemotherapy and reconstructive surgery, which are very expensive or even unavailable; other patients can only receive outdated drugs, which are less effective and have more side effects; for many women, the only available treatment is mastectomy, which in addition to its strong psychological impact, only cures cancer when detected early, before it has caused metastasis.

Third, there are **ethnic factors**. In particular, Hispanic and Black women tend to suffer from this disease at younger ages. According to CancerConnect, "the median age of Mexican women at the time of breast cancer diagnosis is 51, compared with a median age of 63 in the U.S. Furthermore, 45.5% of breast cancer cases in Mexico occur in women below the age of 50, whereas only 25% of breast cancer cases in the U.S. occur in women under 50." Similarly, Beaumont points out that in the U.S., 23% of breast cancers in Black women are diagnosed before age 50 compared to 16% of all breast cancers in white women; BRCA genetic mutations are more common in Black women than in white women (although less frequent than in those of Ashkenazi Jewish ancestry); and triple-negative breast cancer, which is more aggressive and more resistant to treatments than other types of breast cancer, is more common among them.

The combination of race and **poverty** has a significant effect. Even in the U.S., a high-income country, Afro-American women are 42% more likely to die of this disease than Anglo-Saxon women despite a 3% lower incidence rate [Rebner and Pai, 2020]. Disparities are even higher between continents. According to the American Cancer Society, "within sub-Saharan Africa overall (observed) survival of women diagnosed with breast cancer is about 50% higher in patients residing in high Human Development Index (HDI) countries than in those residing in low-HDI countries. This is in part because breast cancer patients in the low-HDI countries are more likely to be diagnosed at a later stage and less likely to receive the appropriate treatment."[2]

Unfortunately, disparities in cancer mortality, instead of diminishing, are increasing alarmingly. According again with the American Cancer Society, "in 2020, out of nearly 10 million cancer-related deaths worldwide, 70% were in low-and-middle-income countries. […] Cancer incidence in sub-Saharan Africa is projected to increase more than 92% between 2020 and 2040".[3] For example, breast cancers have doubled in Zimbabwe and South Africa over the last 15 years.[4] In Mexico, mortality rates have doubled in the past 10 years.[5]

It is, therefore, necessary to find solutions to palliate this problem without consuming more economic resources than these countries can afford.

[2] https://canceratlas.cancer.org/the-burden/cancer-survival.

[3] https://www.cancer.org/about-us/our-global-health-work/global-cancer-burden.html.

[4] https://canceratlas.cancer.org/the-burden/sub-saharan-africa.

[5] https://news.cancerconnect.com/breast-cancer/mexican-women-develop-breast-cancer-earlier-than-other-populations.

2 Proposal: Breast Health Units

In this context, we propose the creation of *Breast Health Units* (BHUs) able to perform breast cancer screening in LMICs with briefly trained personnel and affordable medical devices. They would function as follows.

Each BHU will be equipped with an ultrasound probe, an infrared camera, a microscope, and disposable materials for fine-needle aspiration (FNA): slides, needles, syringes, etc. A patient who arrives at the unit—either because she is symptomatic or because she meets the criteria of the screening program—will be examined with thermography and echography. (Thermography must be done first because ultrasound examination alters the thermal pattern of the breast.) An artificial intelligence program will analyze the images in real time and, considering all the available information (age, symptoms, births, breastfeeding, personal and familiar antecedents, risk factors, etc.), will compute the probability of breast cancer for that patient. If the probability exceeds a threshold, determined with cost-effectiveness criteria, the program will recommend doing FNA. In case of a positive result, the patient should be referred to a hospital.

2.1 Human resources for a BHU

Every BHU must have technicians able to do thermography, ultrasound, and FNA cytology. The size of each unit will depend on the volume of patients to be examined. In many cases, one technician will suffice, but in others, two technicians may be required, so that one performs the thermographies while the other does ultrasound scans and FNAs.

After a training period, these technicians should have the following competencies:

- basic knowledge of **health care**, to interview the patient about symptoms, personal and familiar antecedents, medications taken, etc.;
- **communication** skills, including empathy and fluency in the patients' language or dialects;
- **informatics**, including basic use of an operating system (such as Windows or Linux) and spreadsheets (Excel);
- breast **thermography**;
- breast **ultrasound**;
- breast **FNA**.

Additionally, candidates should demonstrate common sense and the ability to deal with unexpected situations, which are likely to occur in resource-poor settings.

Some of these competencies, which are not specific to breast cancer screening (for example, speaking the patients' dialect) and would need a long training period, should be established as a prerequisite for BHU candidates. In contrast, a person with basic knowledge of informatics requires almost no training to handle an infrared camera and applying the protocol for image acquisition, and positioning an ultrasound probe can be learned easily, provided that AI is used to examine the images [Love et al., 2018]. These two techniques cannot do any harm to the patient because they are non-invasive.

FNA is more complicated: in addition to minimizing patients' pain, it is essential to take the samples properly to avoid false negatives. It is also necessary to stain the samples so that the slides can be analyzed under a microscope. These skills can be learned in a few weeks under the guidance of an experienced radiologist.

Finally, the candidates selected for BHUs should be female, for at least two reasons. First, many women feel uncomfortable when disrobing in front of a male health professional; if BHUs did not guarantee that all technicians be female, some patients would be reluctant to visit these units until symptoms are severe.[6] This issue is even more serious in regions where women need the permission of their husband, father, or brother to be examined by a health professional. Therefore, ensuring that all the technicians at BCUs are female will make more women comply with screening guidelines and go for a consultation when symptoms are still mild. Second, employing women as health technicians will give them prestige and a salary, thus contributing to reducing gender inequalities.

2.2 Cost of equipping and running BCUs

Equipping a BCU is relatively inexpensive, especially when compared with mammography and with the cost of other hospital units and treatments.

Ultrasound can be performed with handheld probes connected to standard tablets. The only consumable required is a gel, of negligible cost. We purchased a linear Philips Lumify probe for €4,000 and a Samsung Galaxy tablet for around €225 (cf. Figure 1, left). According with the local technician who tested them in Makeni, Sierra Leone, in July 2022, they are sufficient to detecting breast cancer; see also the experience of Dr. Felicia Tan.

Figure 1. A handheld probe for breast ultrasound (left) and a thermal camera (right).

Thermography does not require any consumables. In our research, we are using three FLIR A700 infrared cameras (cf. Figure 1, right) in different hospitals, with an average cost of around €14,000, connected to standard laptops. There are much cheaper cameras that will likely suffice for breast thermography; we intend to prove it empirically. In the future, thermal cameras connected to smartphones, currently available for a few hundred dollars, will have enough accuracy for breast cancer detection.

FNA requires some disposable material (slides, needles, syringes…), which is inexpensive, as well as a microscope to analyze the images. It is possible to use either a digital microscope, which sends the image to a computer, or a smartphone that captures the image from a conventional microscope. The second option is affordable in all countries.

Furthermore, the cost of electronic devices goes down every year—except for transient crises, such as the one caused by COVID—and in low-income countries medical devices can usually be obtained with significant discounts.

There are also the costs of personnel, which would not be very high because BHUs do not need highly trained staff. Additionally, the money spent in this chapter remains in the country

[6] According to [Gyedu et al., 2018], "delayed breast cancer presentation is common in LMICs, where women may have been aware of changes in their breast for many months, or even years, before seeking medical help. [Several studies have shown that] Muslim women are frequently diagnosed with breast cancer in later stages and have a higher mortality rate than their non-Muslim counterparts" because of modesty and other cultural motives.

(unlike other medical expenditures) and it will contribute to reducing gender inequalities by employing women as technicians.

Finally, using portable equipment has two key advantages. First, the personnel and the equipment of a BHU can easily travel in a private car, which will allow these units to operate in remote rural areas, even those that do not have electricity. Second, if a component fails, it can be taken in a suitcase to a country where it can be repaired, something which is not possible, for instance, with a mammography device.

2.3 Implantation of BHU programs in LMICs

The implantation of BHUs in a low- or middle-income country should be done gradually, beginning with the groups for which it is more cost-effective: first, women with breast cancer symptoms; then, women with high risk for personal and familiar antecedents; and finally, the general population, progressively decreasing the starting age and increasing the ending age as budget permits, until reaching the limits of cost-effectiveness.

3 Development of the AI programs

As mentioned above, BHUs will need AI programs for the analysis of images of thermal, ultrasound, and FNA cytology. In the project we are conducting at UNED, funded by the Spanish Ministry of Science, we are developing such software, as explained below.

3.1 Current progress

Since October 2021 we are examining patients at two health centers. One of them is a public hospital carrying out a screening program of the Regional Government of Madrid, called DEPRECAM, which performs mammography every two years for women between 50 and 69 y.o. The other is a private hospital where patients undergo mammography and ultrasound every one or two years, at their own demand. Some of the women who attend these two centers program are invited to be additionally examined with thermography. Ane Goñi, a researcher of our group, has already examined around 600 volunteers in the first hospital and more than 150 in the second; every week she recruits between 25 and 30 more.

With the images collected so far and with others obtained from public datasets, we are training several neural networks. One diagnostic model, based on a Brazilian dataset (because we did not yet have our own data), was published in [Sánchez-Cauce et al., 2021]. Additionally, Ane Goñi has applied this model and several breast-segmentation techniques to the thermographic images she has collected.

Similarly, two master students are analyzing several public datasets of breast ultrasound images with deep learning: Iñaki García developed a new neural architecture for segmenting tumors, while Mikel Carrilero has built a neural network that categorizes the nodes and describes them in natural language using BI-RADS terms; his work was presented at the Annual Scientific Meeting of the European Society of Breast Cancer Imaging, EUSOBI (Malmö, Sweden, 2022).

The main problem is that our sample of patients, virtually all asymptomatic, contains very few positive cases, which makes it difficult to train neural networks. We are trying to include more symptomatic patients in our study, but for several reasons, it is proving to be more difficult than expected.

More recently, we have contacted a hospital in Madrid that has a large collection of FNA cytology samples. We intend to digitalize them and build a deep neural network for detecting malignancy.

3.2 Possibilities of implantation in different countries

In January and July 2022, we traveled to Sierra Leone with a NGO that runs several health programs in that country, including cervical cancer and breast cancer screening. A radiologist visiting from Spain used ultrasound to examine women with suspicion of breast cancer and, when appropriate, performed an FNA. Images of the samples were sent by telemedicine to Madrid, where a pathologist made the diagnosis. When cancer was detected, the team of surgeons performed a mastectomy, the only treatment available there. The campaign in January examined 34 women and found 9 cases of cancer, with an average age of 33 years. In July, 39 patients were examined, in this case also with thermography.

We would like to implement similar programs in other countries. In particular, we are collaborating on a European Union project that aims to transfer biomedical technology and medical artificial intelligence from North America and Europe to sub-Saharan countries. In a meeting of this project held in the Canary Islands in March 2022, the participants from Mauritania and Senegal showed great interest in the idea of combining ultrasound and thermography for breast cancer detection, because, as mentioned above, the incidence of breast cancer is increasing alarmingly in their countries, but they cannot afford mammographic screening nor expensive treatments. (In fact, our idea of creating BHUs arose after meeting the African partners in this project.)

Similarly, in a conference about health economics we attended in Washington DC in May 2022, we met a Colombian researcher, general manager of a health care foundation in his country, interested in screening with ultrasound and thermography. Even though this is an upper-middle-income country according to the World Bank, many women are never screened and in 33% of cases, the diagnosis of breast cancer was made in advanced stages, stage III or higher [Duarte et al., 2021].

3.3 Financial support for further developments

So far, this research has been supported by a grant from the Spanish Ministry of Science and Innovation, which amounts to only €67.300 (plus overheads), with additional support from other sources to employ a Ph.D. candidate and a master's student. The main reason for the slow progress of the research is that the health professionals who collaborate on this project do not receive any financial compensation for their work (nor do the university professors), so we cannot ask them to devote more time than they do. Offering them some incentives for working out of hours and involving more radiologists would certainly accelerate the pace of development.

It would also be necessary to hire more computer scientists and engineers with expertise in deep learning applied to medical imaging, as well as Python programmers that make the AI programs ready to be used in LMICs.

Furthermore, conducting pilot studies and implanting screening programs in the above-mentioned countries requires the acquisition of medical equipment, mainly for ultrasound, thermography, and cytology, as well as financial support for traveling.

For these reasons, we are looking for donors interested in supporting this project.

4 Conclusion

Breast cancer takes the lives of a large number of women every year, many of them in LMICs, where they do not have access to early detection and modern therapies. In this document, we have proposed the creation of *Breast Health Units* that, using inexpensive portable equipment and briefly trained health personnel supported by artificial intelligence, will aim to detect breast cancer in early stages, when it is still possible to cure it.

With a relatively small research grant and the collaboration of teachers, students, and a few health professionals, our research group has made slow but significant progress in the creation of the AI programs required by BHUs. However, completing these programs and making them ready to be used in LMICs requires additional funds, which will be employed in:

- electronic equipment, such as infrared cameras, ultrasound probes, laptops, and tablets,
- greater involvement of health professionals,
- hiring computer scientists and engineers, and
- traveling expenditures.

The more funds we raise, the faster the development of the project and the more people will benefit from it.