CHALLENGE BASED INNOVATION

Final Report

An in-depth study on lung cancer

Team 5 – Galilei

By Alexandre Olivé, Gianela Melero, Mbakamma Ngozichukwu, Francisco del Campo, Xavier Barriga

December 22, 2022

An in-depth study on lung cancer

Final Report

Team 5 – Galilei

By Alexandre Olivé, Gianela Melero, Mbakamma Ngozichukwu, Francisco del Campo, Xavier Barriga

Report created for the Challenge Based Innovation, program by Attract EU.

www.attract-eu.com

Table of Contents

1. Research Report

1.1 Introduction

As part of the Challenge Based Innovation (CBI), an annual program carried out between three academic institutions (i.e., Universitat Politècnica de Catalunya, Instituto Europeo di Design, and ESADE Business School), and leading research organizations such as CERN, and coordinated by the ATTRACT EU program, we started with a multidisciplinary team of 5 students from these 3 academic institutions. The team was self-named 'Team Galilei,' and from September until December 2022 we've been working in solving a huge societal problem.

Given the challenge of tackling the United Nations Sustainable Development Goal No. 3, which focuses on "Good Health and Well-being" (United Nations, 2022), and after being introduced to four technologies from the Attract EU, Phase 2, we developed *Breathe In Breathe Out*, an innovative device that allows us to detect early stages of lung cancer integrating MicroQuad[1] technology.

As lung cancer is an illness that spreads around the world and generally involves different actors in the healthcare system, we've been focused on addressing the issue one geographical region (i.e., Spain). After months of understanding the problem, and planning, we have developed a proposal that is technically and economically feasible, as we'd be describing in detail up next.

1.2 Lung cancer

According to Sociedad Española de Oncología Médica, every year in Spain 30.000 people is diagnosed with lung cancer. After 5 years, only 25% of them are still alive. For that reason, lung cancer is the cancer with highest death rate in Spain. Furthermore, the number of new lung cancer patients has been increasing during the last years and it is expected to keep this trend in the future.

Patients can be diagnosed of two different kinds of lung cancer depending on the size of the cells found in the tumour:

- Small cell lung cancer (SCLC): It usually grows and spreads fast to other parts of the body. It is almost always associated with cigarette smoking.
- Non-small cell lung cancer (NSCLC): It makes up about 80 percent of lung cancer cases. It grows and spreads more slowly than the SCLC.

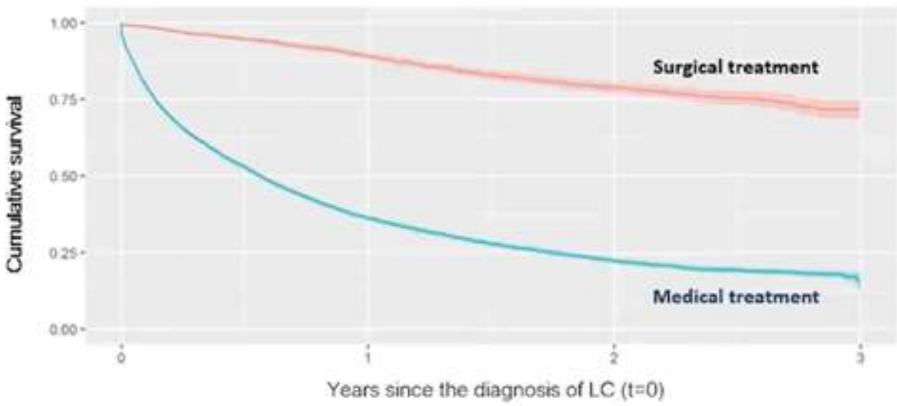
Once they are diagnosed, their cancer may be in four different stages. A lung cancer at stage 1 is diagnosed when the tumour is small and well located. Nevertheless, when the cancer has expanded to the other lung or to other parts of the body, it is considered that the lung cancer is at stage 4, at an advanced stage.

[1] MicroQuad is a technology part of Attract Phase 2.

1.2.1 Silent disease

As mentioned before, lung cancer is the cancer with highest death rate in Spain. This happens because most of them are not diagnosed until they are at an advanced stage. This is due to the fact that they don't develop symptoms until that moment so during the first scenarios of the tumour, they don't feel any kind of pain. In statistics, according to Sociedad Española de Neumología y Cirdugía Torácica (SEPAR), in Spain, the number of patients that are not diagnosed until their cancer is at an advanced stage is higher than 70%.

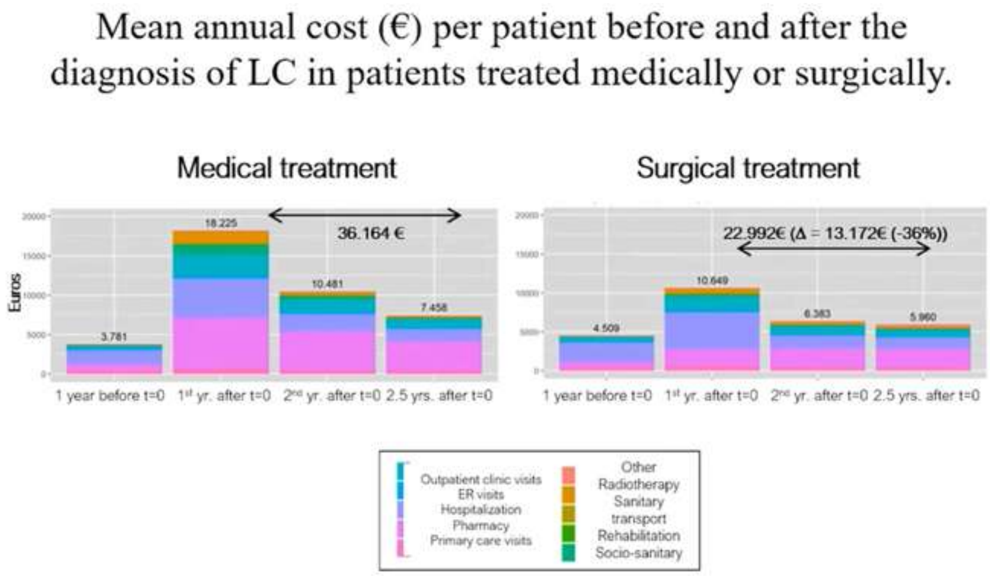
The main problem of being diagnosed at an advanced stage is that the tumour will be too big so it won't be possible extracting it by surgery. It is also probably that the cancer expands towards other parts of the body, for instance, the brain. Surgery is the most effective treatment, and it is only used when the tumour is located and small enough to extract it. The following graphic shows the results of a study done by Hospital Clinic and CatSalut based on patients from Catalonia between 2014 and 2016. There can be seen that, 3 years after their diagnosis, 75% of the patients who received a surgical treatment were still alive. Nevertheless, only 20% of the patients treated with medical treatment (chemotherapy, radiotherapy…) survived.



Patients who receive a surgical treatment are those who have been diagnosed at an early stage. Nowadays, the only way of being diagnosed at an early stage is thanks to tests done for other reasons that are not related with lung cancer.

Going deeper into the treatment, it is common that the treatment that patients receive is a combination of different ones. For example, one of the most used combinations is surgery plus chemotherapy. In this case, chemotherapy is used in order to kill the possible small amounts of cancerous cells that haven't been extracted in the surgery. This kind of combination is considered as a "Surgical treatment" in the study mentioned before since the main part of the treatment is the surgery. Another typical combination is chemotherapy plus radiotherapy. This is commonly used when the tumour has expanded to the brain.

In the study mentioned before, they also evaluated the costs of the different treatments. In the following representation, it is seen that a surgical treatment is, in average, 13.000€ cheaper than medical treatment.



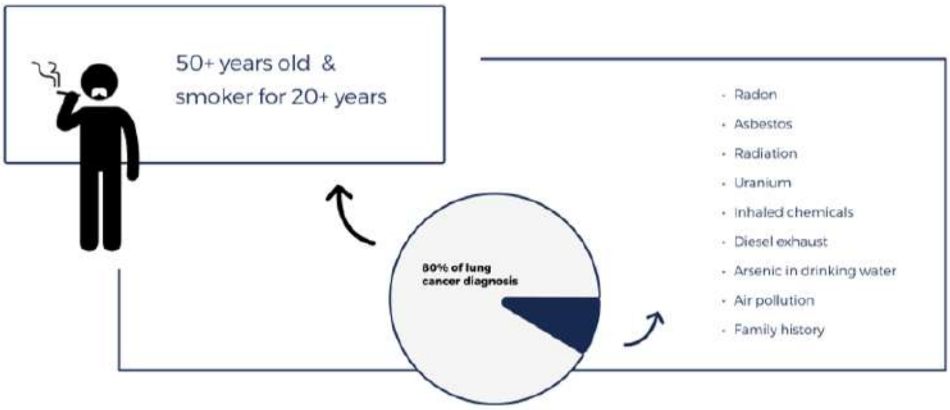
Analysing the results of the study, the following conclusion can be obtained:

Diagnosed stage of the LC	Most common treatment offered	Survival rate 3 years after the diagnosis	Average cost of the treatment
Early stage	Surgical treatment	75%	23.000€
Advanced stage	Medical treatment	20%	36.000€

This data can be extrapolated to Spain's situation in 2022. In this case, after 5 years, the survival rate of people diagnosed at an advanced stage is 20% whereas it is an 80% for patients diagnosed at an early stage.

1.2.2 Risk population

The most common lung cancer profile is that person who is more than 50 years old and who has been smoking during more than 20 years. Nevertheless, according to American Cancer Society, there are other people who can also develop lung cancer. For example, for genetic reasons or for exposure to radon, asbestos, or second-hand smoke.



It is important to highlight that any person can develop lung cancer without accomplishing any of the characteristics mentioned before. Even though they are a small minority, they exist. The main problem that they suffer during the process of diagnosis is that, as they are not considered as part of the risk population and lung cancer symptoms are shared with other illnesses, they are prompt to receive a false diagnosis.

1.2.3 Spain's context

As mentioned before, nowadays, in Spain, the only method of being diagnosed of lung cancer at an early stage is thanks to tests done for reasons which are not related with lung cancer. There isn't any kind of screening program.

In October of 2022, Europe's Beating Cancer Plan urged the countries of the European Union to implement a screening program of Lung Cancer in a stepped way as of 2025. This decision was based on the improvements and scientific evidence of several international studies which show that a Lung Cancer's screening program can detect this illness and reduce the number of deaths that it causes.

As there isn't any screening program nowadays, the path that would follow a person to be diagnosed of lung cancer would start with a patient who is already developing symptoms (i.e., is at an advanced stage of the cancer).

The patient will visit his doctor in a Primary Care Centre or a Private Insurance. If the doctor considers that the patient is part of the lung cancer profile, he will be addressed to take a test in the hospital. Nevertheless, if the patient is not considered a lung cancer profile, he will receive a false diagnosis. Therefore, he will need to visit again the doctor and probably the tumour will have grown. The firsts tests used nowadays to diagnose Lung Cancer are CT scans. These are found in the hospitals. Once the patient has been diagnosed of lung cancer in the hospital, he will be submitted to other tests in order to obtain more information about the cancer and, after that, the treatment would start.

1.3 Biomarkers

To do the early diagnosis, what we wanted to detect has been adjusting thanks to the feedback from the coaches and interviews of the experts but mainly after some scientific research (Puglisi et al., 2021), we decided to look for biomarkers.

A biomarker is something we can detect and measure, normally a molecule, protein or any particles that are in the body. Biomarkers give us the information of how the body is functioning or the current state of a disease (White, 2022).

We started figuring out the best method to detect biomarkers using samples to analyse whether there's lung cancer or not. We decided to use a non-invasive method so only saliva, urine, breath and similar could be used. Initially, saliva was our choice because the recent scientific research pointed out that in that direction there was a similar detection technique for oral and throat cancer. Then, after an interview with a biomarker's expert, we got some papers (Seijo et al., 2019) and information that the breath biomarkers had a promising future in the detection of lung cancer so we finally choose the breath as the sample. Now, there was the problem of which biomarkers to detect because there are proteins, volatile particles, DNA, mRNA or other small-sized particles.

Finally, we got to determine the particles that we detect: VOCs. VOCs are Volatile Organic Compounds consisting of any kind of chemical product that can be easily converted to vapor or gas. Recent studies show that the lung tumour growth is accompanied by the emission of specific VOCs that are present in the breath. They change their values when the lung cancer manifests and so we can detect this small change using a new and specific technology provided by CERN. Following the research from Jia et al., (2018), and Saffie et al., (2022), we have some potential biomarkers to look for, but we are waiting for more studies that can validate the use of these biomarkers for the lung cancer early diagnose.

1.4 Problem Statement

Based on the previous discussion, the main problem is both the disease and the system around it. Lung cancer is the deadliest cancer in Spain because of the low survival rate when diagnosed at an advanced stage. The last stage involves chemotherapy and radiotherapy, a lot of money in medical resources, and several visits to the hospital.

Aside from the late diagnosis, there is a problem with the risk population. There are people who does not fit with the lung cancer profile (heavy smokers, lung cancer history, exposure to asbestos and other factors) that will receive a false diagnosis. As a consequence, the tumour will keep growing without receiving the correct treatment since it will be a treatment for a different illness not related with lung cancer.

On a second hand, currently in Spain, the only way to get an effective lung cancer diagnosis, the patient has to through a CT scan with a previous doctor's authorization and booking in the hospital.

So, based on these two previous criteria, if we manage to detect lung cancer before it develops (at an early stage), then we will increase the survival ratio for lung cancer patients.

This diagnosis has to be available for all, easy to access, and economically viable so the person can get tested on a yearly basis when is feeling well (before the symptoms are developed).

2. Conceptual Development

2.1 Research approach & overview

The research went on from September until December 2022; it came together as:

- +30 scientific papers read
- 3 structured interviews with patients and family members
- 3 webinars attended to AECAP (Asociación Española de Afectados de Cancer de Pulmón), ASEICA (Centro Español de Investigación del Cancer) and ICAPEM (Asociación para la investigación del cáncer de pulmón de mujeres)
- 8 interviews with doctors across United States, Colombia, Peru, Nigeria, Spain, Germany in the different fields of Thoracic Surgeon, Pulmonologist, General Doctor, Senior Physician Clinic for Pneumology, Occupational Therapist and Medical Oncologist.
- 2 interviews with experts in Biomarkers
- 2 interviews with Spanish NGOs for lung cancer affected people
- 2 contacts with on-going innovative solutions for lung cancer early diagnosis

This research started with a non-structured interview with a doctor in a developing country. During this conversation, there were many subjects such as lack of medication, shortcuts on power during certain hours of the day, covid cases related to pneumonia, and an interesting debate that this doctor was having with other colleagues in the hospital: all lung cancer patients are diagnosed at an advanced stage.

This particular subject was investigated furthermore only to find out that it is not only a problem in developing countries but in the whole world.

During the first stage of the research, the team looked out for doctors in Spain, Nigeria, Peru, Ecuador, and United States to have the same conversation about the lung cancer diagnosis. Through structured interviews, we found out that the main problem is that patients only go to the doctor when they are feeling unwell (with symptoms that are not common to a standard cold). This is an issue because the symptoms happen when the tumour already spread out due to a metastatic advanced stage. Concluding the first stage of research, we successfully validated the first hypothesis related to a global issue which is screening for lung cancer.

The second stage of research is characterized by the solution approach.

This stage goes deeper into the technical part of lung cancer and what solutions are currently existing in the world. For this part, we aimed to look for existing solutions in the tech world in Europe, the United States, and Japan. Based on their current praxis, it looked like the best option was to aim at a blood sample to test it in the hospitals.

This solution was discarded because it had several complications due to the target user that we later foun out through interviews with patients and forum reading of lung cancer survivors.

From this research we concluded on three principal learnings:

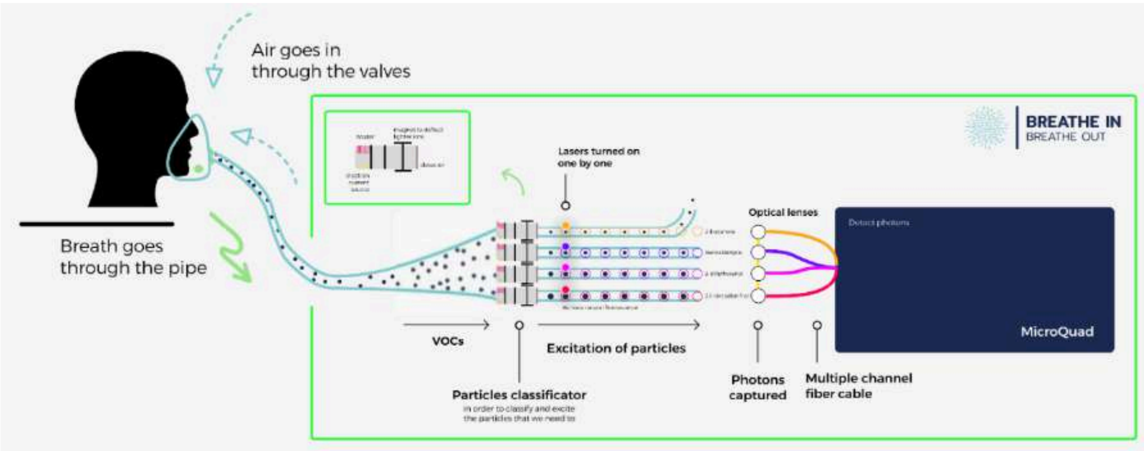
1. There's a lung cancer stigma that generates an ethical debate in the government. This goes by a simple statement: if smoking is a chosen lifestyle, why should the government pay for its consequences? This has a negative impact because, when the time comes to choose where to derivate funds to different medical initiatives, lung cancer often it's a problem.
2. Biomarkers are the right approach. Currently the investigations in UK and USA target towards different types of biomarkers such as proteins and RNA. We aim to use VOCs.
3. Medicine is a social science. Meaning that the patient is a human being and it is at the centre of everything. Patients go through this process experimenting different emotions at the same time, in addition to economic worries and physical restrictions. It's a tough journey and we should do everything to make it easier.

These learnings helped us understand better the side of the patients and conclude in a solution that will take into consideration both financial problems, accessibility restrictions and safety feelings towards a new medical process.

3. Final Solution

3.1 The solution: Breathe In Breathe Out (BIBO)

The model we are proposing consists in a device that can analyse the breath in search of biomarkers that can help in the diagnosis of lung cancer. It will be implemented in Primary Healthcare Centers where they can be used during the yearly medical check-ups or as another tool to discard the possibility of lung cancer. It will help the doctor to correctly diagnose lung cancer, and the patients to have access to the CT scan or further tests to check whether they are developing cancer.



The *Breathe In Breathe Out* device uses a peek plastic mask that secures the hygienic aspect part. The patient breathes through two valves to provide a clear way to inhale air while preventing the breath coming out. The breath will travel through the flexible tube inside the device and pass through a mass analyser sorting mechanism (similar to the one we can find in the mass spectrometers) so that the particles suspended in the air can be selected. This mechanism will separate the air particles by mass, and we will be able to select only the VOCs that we want to analyse.

Each type of VOC we are interested in will pass through a different pipe and each tube will have a laser in order to excite energetically the VOCs. The laser will be the one that makes the VOC that we want to detect natural fluorescent. This will lead to having fluorescent particles that will pass through an optical lens. As a result, we have a multiple-channel fibber cable plugged into the MicroQuad. It is important to highlight that lasers will be turned on one by one so there will only be photons emitting from one particular VOC at the same time. So, when we are detecting photons with MicroQuad, we will always know where the photons come from. Then, MicroQuad detects the photons emitted and finally, the results can be sent to be analysed and represented live in the doctor's screen.

It is also important to comment that in order to let the air get out of the device, once the test has finished, it will be possible to connect a propeller at the end of the tubes right before the lenses.

3.1.1 ATTRACT Technology

Our model, BIBO, uses MicroQuad. It is a high-tech detector of single photons. The key feature of the technology is its high sensitivity that is enabling us to detect biomarkers using a natural fluorescence method. And due to the low concentration of these particles, we'll be using MicroQuad technology to detect VOCs from the breath of the patient with less amount of exhaled air than other technologies currently used, while providing high precision that might be useful when the concentrations of biomarkers are really low.

MicroQuad offers the ability to detect single photons that perfectly fits our need of detecting small number of particles as they emit fluorescent photons. There's also another important point of reducing the testing time with the current technologies due to the high sensitivity of the device.

There is also a relevant point when we are using a fluorescence method. Many different biomarkers have different wavelengths of emission, but this is also covered with the broad spectrum of MicroQuad as it ranges until near IR.

This can be seen in the example of ethanol, as the promising biomarkers mentioned in Jia et al., (2018), and Saffie et al., (2022) are yet to be studied on their natural fluorescence wavelength. Ethanol has an incidence wavelength of 240 nm (Liu et al. 2005), so that means we will have to apply a laser of this wavelength to generate the natural fluorescence. Hence, the emitted wavelength of the photons we want to detect will be 150 nm red-shifted in the spectrum, they will tend to go to the infrared (IR). So, the important feature is that MicroQuad can detect these emitted photons and for that reason, having a broad spectrum that covers all the visible, UV and near IR might be necessary depending on the used biomarkers.

3.1.2 Prototype in CERN

We created a functional prototype in order to simulate how *Breathe In Breathe Out* would work. The prototype's goal was simulating the interface that the doctor would work and finding a way of differentiating when the patient is healthy and when it is developing lung cancer. Finally, depending on what is detected, a report would be generated mentioning if the patient is developing lung cancer or not. Furthermore, the process of excitation of the different pipes should also be simulated.

To simulate the detection of 4 different biomarkers, 3 different air sensors were used. They were connected to an Arduino UNO board. Each of the sensors could detect different things so they were perfect to simulate the detection of the different biomarkers:

- MQ135: It detected the CO2 (ppm). It needed to be calibrated. It wasn't well calibrated in order to obtain a different representation since T6713 detected the same.

- IAQ CORE C: Two different measurements were obtained from it. On the one hand, the CO2 equivalent (ppm) and, on the other hand, TVOC equivalent (ppm).

- T6713: It detected the CO2 (ppm). In this case it was well calibrated. It was the sensor used in order to distinguish a lung cancer patient from a healthy patient.

In order to differentiate a healthy patient from a lung cancer patient, a CO2 supplier was used. When using the normal breath of a person, the T6713 detected a determinate maximum value of CO2 (ppm). Nevertheless, when the CO2 supplier was applied, the maximum value of CO2 (ppm) increased a lot until reaching maximum values unachievable by the human’s normal breath.

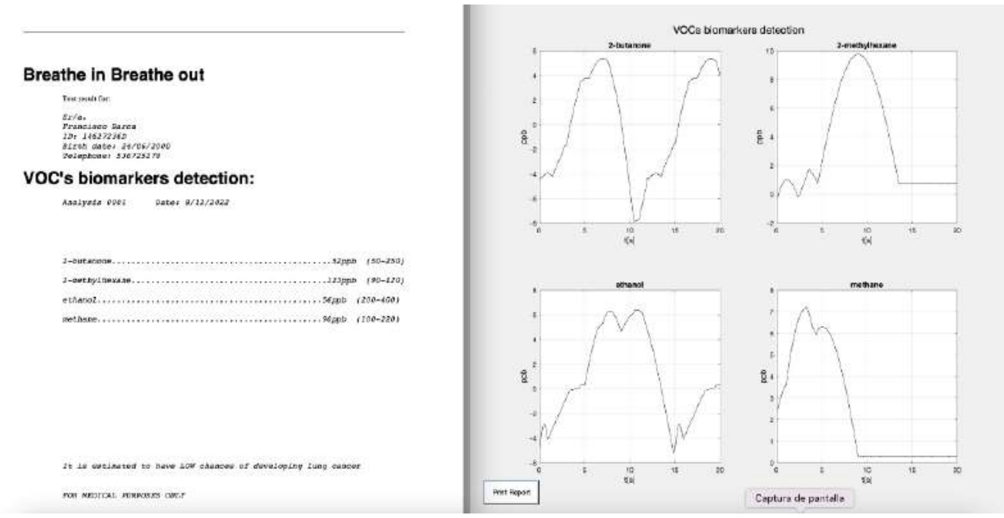
Apart from the different chemical sensors, NeoPixels were used in order to simulate the excitation of the different pipes.

In addition to this, a fan was used in order to try to force the circulation of the air from the opening of the pipe used to breath to the sensors.

The final prototype was the following one:

The first black box that is connected with the big pipe simulates the mass classifier. In order to make our solution work, we put the 3 chemical sensors and the Arduino UNO inside this box. There can be seen 4 pipes that go out of this first black box. Each of these pipes represent that would only contain the biomarker that we want to detect. In each pipe there is a NeoPixel which simulates the excitation. The output of each tube connects with a multi-channel fibber optic which connects the 4 pipes with only one pipe that will go towards the second black box which simulates MicroQuad, were the photon detector would happen.

The MATLAB interface looked like this:



On the right of the image in can be seen the different plots obtained from the values that the chemical sensors send. On the left, the report that will be generated once the test is finished.

The Arduino and MATLAB code used to make the prototype work can be found in the following folder:

Link: https://github.com/alexolpe/Breathe-In-Breathe-Out

Apart from the functional prototype, a face mask was also designed and printed. This was the result:

A valve to allow the entrance of external air inside the mask here can be found in both sides of the mask. The hole where there would be the connection between the mask and the big tube also contains a valve that allows the pass of the air to the mass classifier but not the comeback of it.

3.1.3 User Journey

BIBO is not a product, but a new screening program for people over 50 years old that aims to be part of a yearly check-up routine in the local primary care centers (all 13,000 of them in Spain).

The journey begins when the person goes to their local care center to perform a yearly general medical check-up. During the different exams that the person has to go through, at one moment they will be seated in a chair with the mask breathing through BIBO for about 10 minutes.

At the end of the test, the doctor will read the results in the printed paper and will decide wether this person needs to go to the hospital and perform a CT scan.

If the end results of the scan are negative news to the patient, then, we will be achieving our main goal: diagnose early lung cancer so the patience will have a highest survival rate.

This new screening program resolves the problem of accessibility (because we will partner with primary care centres from the public health sector), financial restrictions (it will be free to the patience), and to increase the lung cancer screening without collapsing the Spanish health system.

3.2 Business Model

First, our goal to drive impact with the BIBO device revolves around a significant reduction 3 key areas, in (1) the high cost of diagnosis and treatment incurred by the country, (2) the number of people testing positive to late-stage cancer, and (3) the lungs cancer death rate and improve quality of life of the people

Then based on the different conversations and interviews completed with different stakeholders around the lung cancer in Spain, a common denominator appeared to be present in those conversations. It is necessary to consider medicine and healthcare as a social science. As so, considering the statistical information collected from different sources (e.g., population from INE, smokers from Statista), not only as pure numbers, but reflecting upon them as human beings.

By having these aspects into consideration, it was imperative the articulation of a proposal that considers a platform business model to address both sides including (1) the patients which will be the final users of our solution, and (2) the hospitals which will be buyers of our device.

When it comes to the value proposition, we're focusing on providing an integrated product, which includes both hardware and software to improve early-stage lung cancer diagnosis for patients at risk in Spain. We're addressing the biggest pain points by making our solution accessible, non-invasive, and reliable; therefore, improving the results between first symptoms and diagnosis.

We have included a fully detailed version of the Impact Model Canvas in the *Annex 1.*

For Patients

For patients, we're focusing people over 50 years old, individuals with family history of lung cancer, miners and construction workers, people exposed to radon and asbestos and other chemicals. We're going to address them with a combination of multiple channel and campaigns in order to build awareness, not targeting them directly as buyers of our solution, but as an indirect person of interest. Our goal is to build a long-term relationship with them and building a community around them is crucial to share advice, insights and establish a support system throughout the patient's journey.

In the first stage of this proposal, a focus on gathering funds and partnerships from global institutions such as World Cancer Research Fund International, NIH, EIT Health, leading NGOs, and local governments will enable us the opportunity to focus on communication campaigns to increase awareness of the possibilities of getting lung cancer. This would require maintaining a website, creating engaging content and cultivating relationships with patients.

For Hospitals

When it comes to managing the other side of the platform, in this case with the hospitals and doctors, we're differentiating the Public Spanish Health Care System (i.e., CAPs), and the Private Spanish Health Care System (i.e., Mutua insurance company). Our sales channel for both segments will be owned by the company (i.e., direct sales), which will provide the benefit of a direct relationship with them. By not only being focused on a pure transactional basis, but on the long term, a symbiotic relationship that will benefit both parties, including third parties such as external researchers and doctors will provide the unique opportunity of creating a database to solve this global challenge.

In order to provide the hospital with the BIBO device, we're considering two important parts:

- For the mask: A contract-based system, as no major R&D will be involved. Design IP will need to be considered.
- For the device with the MicroQuad: A licensing-based business model with a manufacturing partner that best fits the market environment and regulation. This means a partial ownership model to license the IP of BIBO's design to only one company for manufacture of the vehicle, except for MicroQuad, which will be bought from another manufacturer.
- For the data analysis and interpretation: In-house development of the online platform to show results.

A key assumption for this project is that, due to the scope of our solution, the R&D for VOC biomarker detection will give us the result of which VOC biomarkers to use. This will be developed by leading scientists, hospitals, and universities around the world.

3.2.1 Expected impact

We're structuring the organization as a B Corporation, which means that we'll be looking for a financial return, but with a purpose that goes beyond just pure financial returns. Before launch, surpassing a clinical trial phase will have to be achieved in order to comply with the Spanish regulation and its later deployment in the EU market.

Our long-term goal is clear, we want to make detection of lung cancer in early stages widely accessible not only to those who are able to afford it. And to make this a reality, we're envisioning a 5-step strategy towards market domination.

We have included a fully detailed version of the Business Model Changes and Brand Extension over time in the *Annex 2.*

In the short term

When it comes to the go to market strategy, our short-term strategy consists of a dual product with 2 value propositions offering:

- **Public Health Care:** As our goal relies on focusing on having an affordable device in every CAP and private hospital in Spain, we're going to be deploying our solution at first in the 11 autonomous communities in Spain with the biggest population and percentage of smokers. We're expecting to address over 100.000 people who have the lung cancer profile in this area.

- **High End Device with a 1+1 Model:** A premium product for private hospitals in Spain and the EU with a bespoke fabrication. In this segment, we'd be promoting a 1+1 Model that considers a social component to the service. We'd be using the revenues from this premium offering to financing our expansion into Phase 3 (i.e., remote areas with no public health care system nearby).

  Due to the scope of our project, we're initially focused only in the Spanish market, so we're not going to be able to provide accurate projections for the demand and impact in the EU.

- **Integration:** Creating a cost-competitive hub to service the EU market and the international expansion via (1) an exclusive licensing agreement for manufacture our device (the one that includes MicroQuad), and (2) creating a proprietary connecting port between the mask, the tube and the device that integrates MicroQuad.

  In this way, we'd be able to extend the reach of our solution globally by allowing licencing agreement with OEM via a certified *Made for BIBO* program and extinguish competitors' chance of expansion.

In the long-term

- **Partnership for Scale:** When it comes scaling globally, we'll be considering scaling partnerships to provide local knowledge and leverage on the experience on doing business locally.

- **Direct to Consumer (Phase 3):** Once the technology improves in both size reduction and energy efficiency, we'll be moving forward with a direct low-cost testing to patients in remote and inaccessible location by relying on transportation (e.g., Vans or Mobile Hospitals).

Our goal is to push the limits on 3 fronts. On the business and societal side by becoming a healthcare start-up that puts purpose over profit. On the societal side by addressing a common illness and creating massive awareness campaigns. On the societal side by exploring the limits of what's possible when it comes to portable tech to go reduce the size of the BIBO device, and its energy requirements.

Data driven impact

With the understanding that a new set of 30,000 lung cancer patients are diagnosed yearly who usher in about 600 million euros that would be spent during the 5-year duration of their lives, our impact goal would be aiming at a reduction of:

- The high cost of diagnosis and treatment by 80%
- The number of people testing positive to late-stage cancer
- Lung cancer death rate and improve the general quality of life of the people

A summary of Our Target to Impact Treatment Cost for lungs cancer treatment (€)

Summary of Our Target to Impact Treatment Cost for lungs cancer treatment (€)	
Average current cost of diagnosis per patient	5,000
Average current cost of treatment per patient	15,000
# new lungs cancer cases in Spain (annual)	30,000
Total treatment & diagnosis cost per patient in 5 years life expectancy	20,000
Total treatment & diagnosis cost per 30k new cases across 5 years	600,000,000
Cost spread across 5-year life expectancy	120,000,000
Impact to reduce total treatment cost by 80%	24,000,000
Impact to reduce average diagnosis cost by 80%	1,000

3.2.2 Revenue Streams

We will be exploring various revenue options to ensure a healthy runway all through the first few years of the business. These revenue options include three options.

a. Grants

At the initial phase, we will take advantage of grants and funding from public and private institutions who would fund this kind of project. For example, we have identified the following sources available:

- EIT Health
- ILC2 grant by AstraZeneca supported by the Charities Aid Foundation (CAF)
- International Lung Cancer Foundation (ILCF) [2]
- National Institute of Health (NIH) [3]
- The European Union Cancer Projects
- The Spanish National Research Council (CSIC)
- World Cancer Research Fund International

[2] ILCF provides funding opportunities each year to facilitate research advances and save lives.
[3] NIH is the largest public funder of biomedical research in the world, investing more than USD 32 billion a year to enhance life, and reduce illness and disability. NIH funded research has led to breakthroughs and new treatments, helping people live longer, healthier lives, and building the research foundation that drives discovery.

b. Series A Funding

Subsequently after the first year of launching, we intend to consider raise money from impact investors and venture capital funds. Based on our research, we have identified some firms with an investment thesis that focuses on health-tech products and sustainability driven businesses.

- Andera Partners, Private Equity/VC in France
- Asabys Partners, VC Spain
- Bewater Funds, Private Securities investment in Spain
- Cabiedes & Partners, VC in Spain
- CDTI, an Angel Group in California, US
- Innogest Capital, VC in Italy
- iSeed Ventures, VC in California, US
- JME Ventures, Venture Capital in Madrid, Spain
- Johann "Hansi" Hansmann, Angel Investor in Austria
- Kurma Partners, VC in France
- Nauta Capital, VC in London
- VI Partners, VC in Switzerland

c. Operating Cashflow

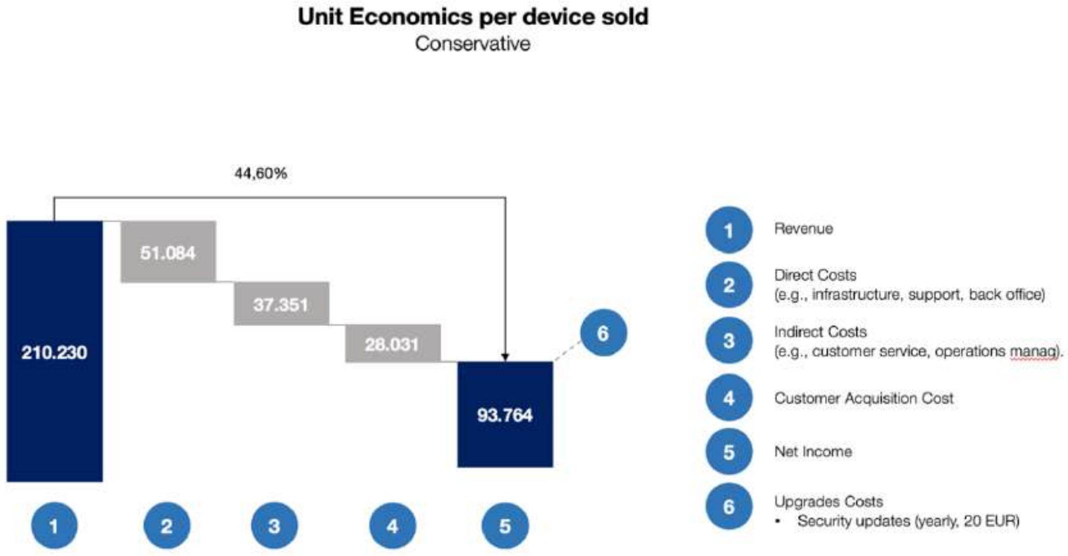
From the normal income of 6.3million generated by the business in the first year, we plan to recover the investment costs. We intend to sell 29 units of our product to 29 hospitals in Spain in the first year, with an estimated revenue of 6.3 million and profit of 2.9 million for the company.

Total Target Hospitals @Launch/ first year	Total Target Patients @Launch/ first year	Estimated Diagnosis Price Per Patient	Price Per Unit Device	Total Cost for BIBO Project	Expected Profit post initial launch
29	**26,851**	**50**	**210,230**	**3,446,409**	**2,896,150**

3.2.3 Pricing strategy

We have considered a price for a package that includes the device and 10 reusable masks that would cost EUR 210.230 and EUR 40 for every additional mask that the hospital wants to buy.

We're assuming our direct cost would amount up to EUR 51.084 while our indirect costs would be EUR 37.351, and due to the nature of this kind of business focused on sales to Governments and private hospitals, we're also considering our customer acquisition cost to be a maximum of 30% of the price of our device. A visual and detailed description of the unit economics for our BIBO solution can be found below.



On another note, we have analysed the market, which is relatively new, and seen that we have a lot of potential to secure a significant market share once we launch early. Based on some communications that took place with various potential competitors (i.e., Owlstone Medical, Breathe Diagnostic, ApoCell, Inc., Veracyte, Inc.,) they are still unable to factor their way around using biomarkers to detect cancer.

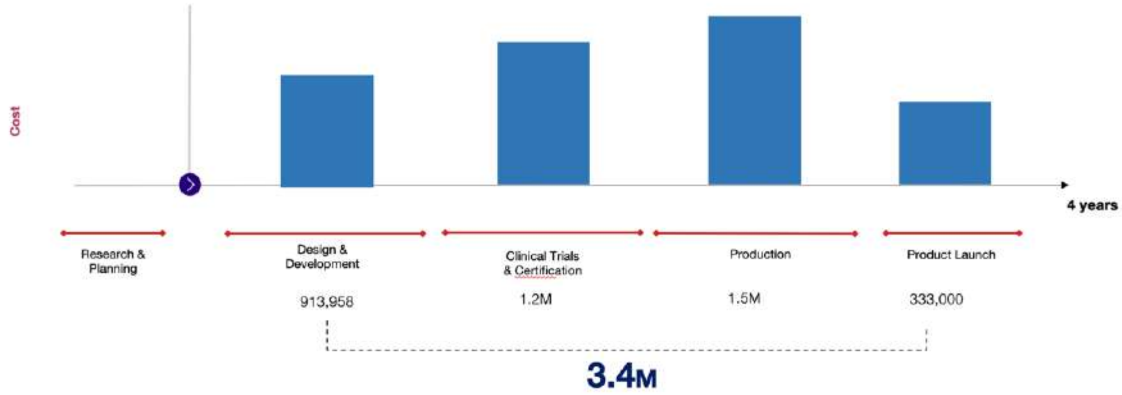
For us, this is a positive news as it reinforces our ability to gain significant market share before they can catch up.

3.2.4 Product Roadmap

We estimate a 4-year timeframe to complete the 5 different phases of this project as indicated in the diagram below.

- **PHASE I:** The research and planning will involve several engagements and interviews with specialists, lung cancer patients, and health institutions to determine the level of the problem and the solution needed to solve it.
- **PHASE II**: Design and development Activities… prototype, preclinical research, risk management, verification & validation.
- **PHASE III:** Clinical Activities: clinical trials, medical affairs, clinical operations & safety monitoring, market access, biometrics
- **PHASE IV**: Production Activities: manufacturing, quality assurance & control, fabrication of the product, {designing a manufacturing process, scale-up, ongoing process improvements.}, 3D imaging, additive manufacturing/3D printing, and laser manufacturing.
- **PHASE V:** Product launch Activities: sales and marketing, sales support, post-market surveillance

The sum of 3.4 million euro will be needed to complete the product journey. However, as already explained in the operating cashflow above, we will recoup this cost at the final phase, which is the launch of the product.



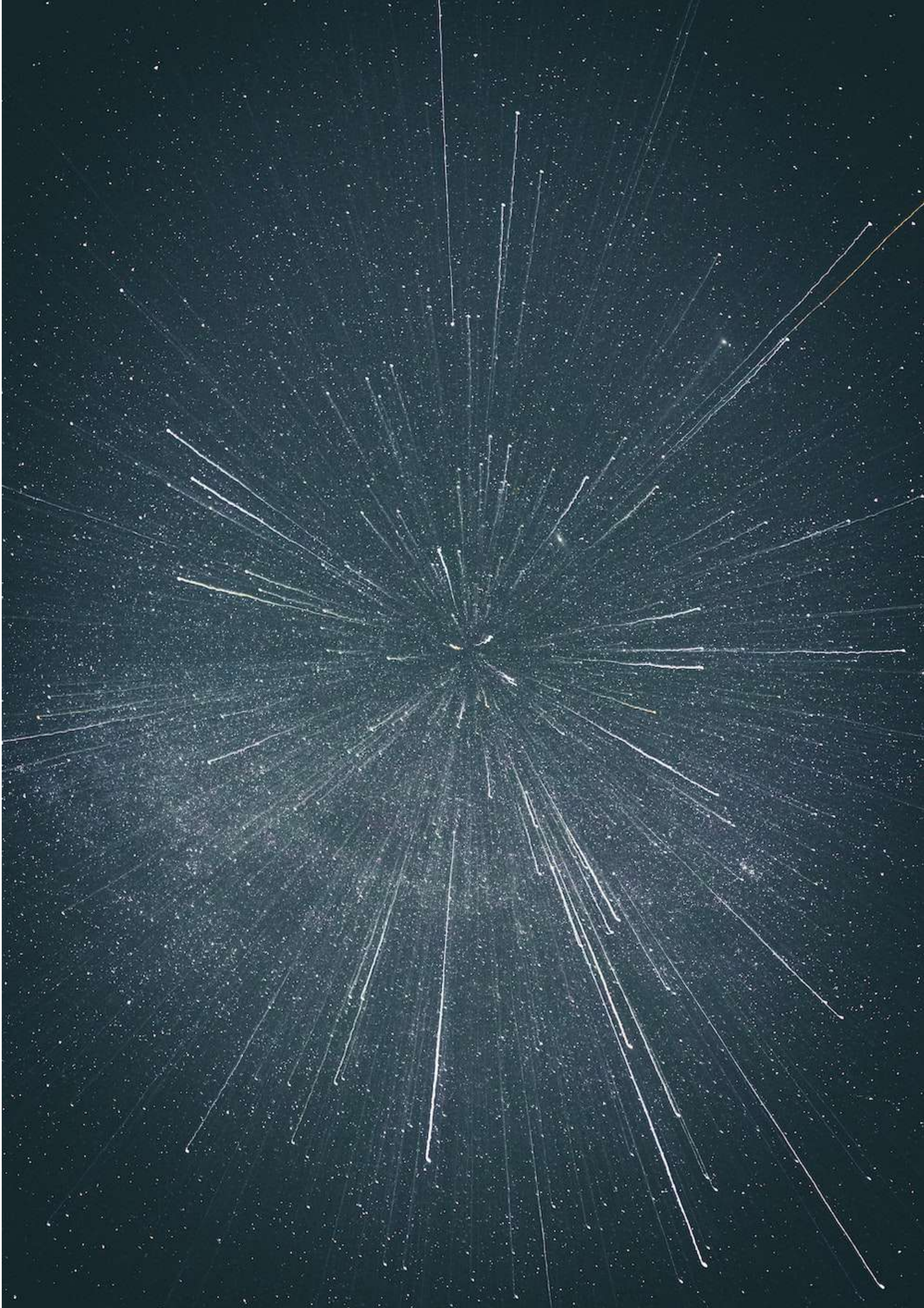
3.3 Conclusions

After 4 months of intense and hard work, both individually and as a team, the following learnings and insights could be analysed over 3 categories.

- **Systemic analysis:** When it comes to addressing societal problems, due to its own nature, these require a systemic analysis that goes beyond the boundaries most people are used to. By getting a hands-on approach, we've come to realize the different perspectives from stakeholders around the lung cancer in Spain and in sometimes heart-breaking realities from distant corners of the world.

- **Exploration and idea development:** After an initial phase of understanding the different Attract technologies, and the challenge itself, the ideation and validation phase were crucial to move forward with the prototyping experience. Without the opportunity to be wrong, and creatively explore solution was an important step for this project to move forward. In this research project, we were lucky, we did not have the need

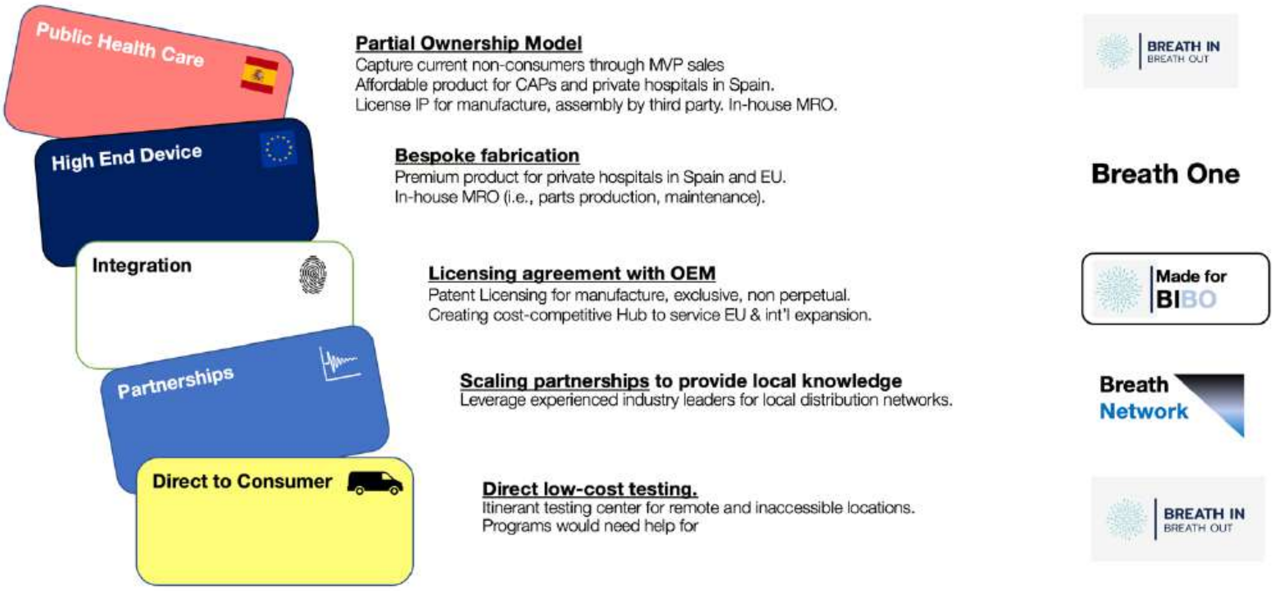
- **Problem articulation:** Being able to articulate a proposition for lung cancer patients wouldn't have been accomplished without taking ownership of the challenge itself. Any invention, even a technological one, needs to be paired with an application and knowledge of a problem for it to be applicable.



4. Annex

4.1. Impact Model Canvas

4.2 Business Model Changes and Brand Extension over time



5. References

American Lung Association. (n.d.). Types of Lung Cancer. https://www.lung.org/lung-health-diseases/lung-disease-lookup/lung-cancer/basics/lung-cancer-types

Andrade, P. (n.d.-a). The Economic Burden of Cancer in Spain: A Literature Review. https://www.iomcworld.org/open-access/the-economic-burden-of-cancer-in-spain-a-literature-review-46813.html

Biomarker Testing for Cancer Treatment. (2021a, December 14). National Cancer Institute. https://www.cancer.gov/about-cancer/treatment/types/biomarker-testing-cancer-treatment

Biomarkers. (n.d.-a). National Institute of Environmental Health Sciences. https://www.niehs.nih.gov/health/topics/science/biomarkers/index.cfm

Bloomberg - Are you a robot? (n.d.-b). https://www.bloomberg.com/tosv2.html?vid=&uuid=2f42835b-8220-11ed-b4d7-4d6652425554&url=L25ld3MvYXJ0aWNsZXMvMjAyMi0wNC0wNC9jcmlzcHItcGlvbmVlci1kb3VkbmEtc2Vlcy1nZW5lLWVkaXRlZC1iYWJpZXMtd2l0aGluLTI1LXllYXJzP3NyZWY9WU1WVVhUQ0s=

El Proyecto CASSANDRA de cribado de cáncer de pulmón arrancará en más de 20 hospitales que representan a 14 comunidades autónomas, con el apoyo de sociedades científicas, asociaciones de pacientes y fundaciones | separ. (n.d.). https://www.separ.es/node/2446

Esmo, E. (2015a, February 24). Cancer Research Grants & Funding | Foundations | Europe | EU. ESMO. https://www.esmo.org/research/research-funding-opportunities/other-research-funding-opportunities/national-research-funds

Global Breath Biopsy Market â“ Industry Reports. (n.d.-a). Market Growth Reports. Retrieved July 19, 2022, from https://www.marketgrowthreports.com/global-breath-biopsy-market-21344704

Hou, T., Deu, F. L., Shao, Y., & Tian, J. (2021a, September 15). Managing China's growing oncology burden. McKinsey & Company. https://www.mckinsey.com/industries/life-sciences/our-insights/managing-chinas-growing-oncology-burden

Jia, Z., Zhang, H., Ong, C. N., Patra, A., Lu, Y., Lim, C. T., & Venkatesan, T. (2018). Detection of Lung Cancer: Concomitant Volatile Organic Compounds and Metabolomic Profiling of Six Cancer Cell Lines of Different Histological Origins. ACS Omega, 3(5), 5131–5140. https://doi.org/10.1021/acsomega.7b02035

Liu, Y., Lan, X. F., Shen, Z. H., Lu, J., & Ni, X. W. (2005). Guang pu xue yu guang pu fen xi = Guang pu, 25(2), 242–245.

Lung Cancer: Screening. (2021a, March 9). https://www.uspreventiveservicestaskforce.org/uspstf/document/RecommendationStatementFinal/lung-cancer-screening

Puglisi, R., Bellenghi, M., Pontecorvi, G., Pallante, G., Carè, A., & Mattia, G. (2021). Biomarkers for Diagnosis, Prognosis and Response to Immunotherapy in Melanoma. Cancers, 13(12), 2875. https://doi.org/10.3390/cancers13122875

Radiological Society of North America (RSNA) and American College of Radiology (ACR). (n.d.). Tratamiento del cáncer de pulmón. Radiologyinfo.org. https://www.radiologyinfo.org/es/info/lung-cancer-therapy

Seijo, L. M., Peled, N., Ajona, D., Boeri, M., Field, J. K., Sozzi, G., Pio, R., Zulueta, J. J., Spira, A., Massion, P. P., Mazzone, P. J., & Montuenga, L. M. (2019). Biomarkers in Lung Cancer Screening: Achievements, Promises, and Challenges. Journal of Thoracic Oncology, 14(3), 343–357. https://doi.org/10.1016/j.jtho.2018.11.023

Shaffie, A., Soliman, A., Eledkawy, A., Fu, X. A., Nantz, M. H., Giridharan, G., van Berkel, V., & El-Baz, A. (2022). Lung Cancer Diagnosis System Based on Volatile Organic Compounds (VOCs) Profile Measured in Exhaled Breath. Applied Sciences, 12(14), 7165. https://doi.org/10.3390/app12147165

Sample, I. (2022a, September 11). Blood test spots multiple cancers without clear symptoms, study finds. The Guardian. https://www.theguardian.com/science/2022/sep/11/galleri-blood-test-multiple-cancers-before-clear-symptoms-study

Spain - Government Health expenditure 2020. (n.d.-a). countryeconomy.com. https://countryeconomy.com/government/expenditure/health/spain

United Nations. (2022, August 2). Sustainable development goals report. United Nations Sustainable Development. Retrieved December 20, 2022, from https://www.un.org/sustainabledevelopment/progress-report/

White, L. (2022, September 30). What is a biomarker? MS International Federation. https://www.msif.org/news/2021/04/16/what-is-a-biomarker/?lang=en