

Technology For Social Innovation – Hyperespectral imaging for endometriosis diagnosis

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How would you feel if you had a heart attack every month? And how would you feel if you had to go to work while suffering from it? 10% of women are diagnosed with endometriosis, a disease that causes symptoms such as fatigue, cramps, digestive issues. Hysplant leverages hyperspectral imaging technology together with artificial intelligence to understand cell behavior inside the uterus. This technology could represent a faster and less invasive way to diagnose endometriosis. But what if we could also directly match the diagnosis to the right treatment?

The problem

Endometriosis is a disease that affects more than 10% of people with a uterus, those have been diagnosed with it (WHO). Therefore, around 5% of the planet suffers from it, it is a significant issue to society because of all the symptoms accompanying the disease, such as pelvic pain, heavy bleeding, constipation, diarrhea, bowel or urination pain, pain during or after sex. Furthermore, the main issues making endometriosis a priority problem to solve are that it takes 7.5 years on average to be diagnosed and that there is no definitive treatment (Endometriosis UK).

To diagnose endometriosis, several methods that are more or less reliable, exist. First of all, on the lower level of reliability, it can be diagnosed based on symptoms and the pain level that patients exhibit. Second of all, doctors may also diagnose it when doing a pelvic exam.

Then, the doctor can use imaging tools such as abdomen and transvaginal ultrasound that can show large clumps of tissue that are likely signs of endometriosis. The former can only identify cysts associated to endometriosis, whereas the latter can more easily identify endometriosis of the ovaries, but small pieces of tissue that may also be signs of endometriosis might still not be visible. Another imaging method can be an MRI, that gives more information about the location and size of the endometrial lesions.

Finally, today, the only close to definitive diagnosis can be done with a laparoscopy, a surgical procedure in which a camera is inserted into the pelvis through a small cut near the belly button. During a laparoscopy, some tissue samples might be collected to later be tested, corresponding to a biopsy, and the surgeon often tries to treat endometriosis during this surgery.

As previously mentioned, there is not yet a definite way to treat endometriosis, it is a chronic illness. However, there are ways to alleviate the pain, although it does not work for everyone, nor forever.

Depending on the severity of the disease, based on the 5 stages scale, and on whether the patient wants to get pregnant, different treatment options can be offered to the patient. Firstly, doctors can prescribe medication. It can often start with painkillers, then hormonal treatments such as the contraceptive or combined pill can be given to the patients who are not trying to get pregnant. To give a more permanent solution, doctors will then recommend surgery to remove endometrial lesions. If the patient tries to get pregnant, a conservative surgery could help where the uterus and ovaries are preserved. To get rid of the pain, removing the organs affected by forcing menopause with a hysterectomy and/or oophorectomy can

be done. That might still not be enough. Alternative and more natural ways also exist, such as adopting a special diet removing things like gluten, or meat that reinforce inflammation.

Interview takeaways

As part of the process, we reached out and managed to interview people suffering from endometriosis as well as doctors who have experience with this disease. In total we did 19 interviews, including 17 patients from the USA, Germany and Spain, and 3 doctors from India and Spain. We summarized our findings from the patients and the doctors' perspectives below.

Patients

Symptoms

Endometriosis symptoms started from a young age, most patients recall having pelvic pain, heavy bleeding, cramps and further symptoms already when their menstruation started. For most of them, the symptoms, especially the pain worsened over the years, to the point of making them incapacitated in their daily lives. This prevented some of them from being able to attend school or work, having heavy pain while going to the toilet, where they even fainted.

Awareness

The patients tried to consult their gynaecologist regarding some of their endometriosis related symptoms, at this point not knowing these were related to the disease. Most of them got prescribed the contraceptive pill or pain killers to treat the pain and the symptoms. Doctors as well as their social environment treated their discomfort as normal menstruation pain that every woman has. Most patients experienced that society, including the doctors, did not take them seriously and even mentioned that they were just very sensitive to the pain. Their gynaecologists never mentioned the possibility of having endometriosis or even encouraged them to pursue further diagnostic methods to find the cause of their discomfort. Most patients heard about endometriosis through awareness campaigns on social media, while talking to medical professionals from their work or from friends and colleagues, who told them the symptoms they mentioned could be related to endometriosis and encouraged them to pursue a diagnosis.

Often, the patients consulted doctors of other disciplines for diagnosis and treatment as they were not aware of the relation to endometriosis because of the variety of symptoms. A patient for example had intestinal problems and tried to seek help from a doctor of internal medicine. She went through gastroscopy and colonoscopy without any findings for the cause. The patients received satisfactory help when they got transferred to endometriosis centres or gynaecologists specialized in endometriosis. However, getting such a transfer is hard due to the lack of initiative from the gynaecologists. One patient who asked her doctor about a transfer was told that these centres were purely profit seeking and would push her to do a surgery for that reason rather than for the diagnosis and treatment. The patients reported that it took between 4-16 years to have a definitive diagnosis to be able to look for a concrete treatment. The difficulty to find out about the disease, then to find the right doctor or centre for the diagnosis gave patients a lot of stress. Some patients mentioned that their trust in the medical system degraded over time and one patient also started having anxiety when she had to be in a medical situation such as visiting a doctor, considering surgery or having pain.

Diagnosis

Gynaecologists use ultrasound during regular check-ups, but the lesions only show when in an advanced stage of the disease, because they reach a certain size. Even when they did show, they were mistaken for cysts and no further effort was made to clarify if it could be endometriosis. The same happened with the MRI scan for a patient already diagnosed but planning a surgery, where the smaller lesions were not visible, but a big one on the intestine was. In one of the endometriosis centres a patient mentioned, laparoscopy is used mainly for treatment, their diagnosis is based on the anamnesis, ultrasound scan or pelvic exams.

Not having a definitive diagnosis of the disease, has given most of the patients a high level of self-doubt. Some patients report that they were anxious to get a positive result from their effort to check if they have endometriosis rather than ending up again with an unsatisfying answer. All the patients with a definitive diagnosis felt relief from the confirmation that they are not imagining the symptoms, and from being equipped with knowledge to plan their daily lives better.

Treatments

Some patients also reported that they sometimes preferred the endometriosis symptoms over the side effects of the hormonal treatment and thus tried to find alternative treatment solutions, that seemed to ease the pain. Osteopathy, pelvic floor physiotherapy, pain management therapy and nutritional planning were some methods mentioned. Searching for information online comes with the risk of misinformation. One patient reported that she found online a statement saying that having a baby or a hysterectomy would cure the disease.

<u>Takeaways</u>

One positive thing that patients gained from these experiences is more empathy and kindness towards the situation of people suffering from a disease, even if they do not look like they do. They also learned to trust, respect and listen more to their body. Some patients were able to meet others who were in the same situation as them, a real community was born. Talking to each other felt reassuring, especially being told that taking a break from work or other responsibilities when symptoms are bad on a day is fine and that they do not have to feel guilty about that, because they have a chronic disease.

A key point that every interviewee wishes upon is that education and awareness about endometriosis should start from an early age. This should happen already with the onset of the menstruation and the first visit to the gynaecologist, where the person gets the first information regarding the disease and what it could entail. One patient's story particularly highlights the need for diagnosing the disease early. She had visited her gynaecologist several times and did ultrasound scans. The doctor suspected she had cysts and prescribed her contraceptive pills. She did not take the pills as she had bad experiences with it. She suspects that hormones led to a rapid growth of a lesion on her intestine. By the time she had the diagnosis and did the surgery, part of her intestine had to be removed. Over the course of 5 months this lesion had grown from 8cm to 20cm in size.

The interviewees wish for further research on endometriosis. They wish to have answers to the questions such as: "What causes this disease?", "If we know the cause, is there a possibility to cure it?". They also wish that better, easily accessible and less invasive diagnosis methods can be found.

Gynaecologist and endometriosis specialists

One point mentioned by the doctor and the specialists was that the diagnosis of endometriosis is subjective. Even when doing the diagnosis with laparoscopy, because the lesion could be misidentified as non-endometriosis lesions if the surgeon does not have experience or is not specifically looking for it. One doctor hopes we could have an objective means to measure the pain patients experience. They also explained that using ultrasound would often not show the lesions if they were small. One doctor from India mentioned that the possibility to use more imaging-based diagnosis methods would be beneficial to his clinic.

One point the endometriosis specialists agreed upon is the lack of awareness among the gynaecologists, and the lack of training for radiologists, ultrasound specialists and gynaecologists to successfully detect endometriosis. In one of the Indian endometriosis specialist's clinic, the patients come due to infertility issues and later in the process find out that they have endometriosis. At another specialist's clinic in India, the patients already have a diagnosis when they visit. The patients most often have a binary diagnosis but no knowledge on the stage and spread of the disease. These patients also consult this specialist after trying different treatments and failing to find a solution.

The specialist mentioned his first choice for treatment would be doing an excision surgery, as this has the most impact on reliving the pain. He uses the hormonal treatments to slow down and supress the disease following up to the excision surgery. There is still a chance for the lesions to grow back after the surgery and for the patients to keep having pain. The hormonal treatment for a longer term is only possible for patients who do not have the wish to bear a child. He mentioned that an IVF might be needed to have a child as 40-50% of the endometriosis patients become infertile.

One very important factor, especially in India, is the cost for diagnosis. A specialist noted that in India the insurances are motivated to focus on solving problems with infertility rather than focusing on endometriosis. There is a lack of affordability to pursue a diagnosis as well as the treatment of endometriosis.

Awareness survey

Throughout the interviews, we realised how big of a problem the lack of awareness of endometriosis was, in society in general, but also amongst medical professionals. That is why we decided to create and share a survey (See Appendix 1) to measure awareness of endometriosis and its symptoms. We asked different questions to respondents based on whether they had a regular period or not.

This survey gathered 90 respondents, coming from 21 countries between the ages of 19 and 61 years old. We know that it is only a small sample of people from our direct, secondary or third circle, and that it does not represent the entire society, especially since the age distribution is concentrated around early twenties, and most are from developed countries, with 53.4% coming from Spain, Austria or France, in

which access to education and information is easier than in developing countries. Nevertheless, we obtained 12 responses from India.

The results showed us that the younger generation seems to be more aware of endometriosis, especially thanks to social media (38.5% of all respondents who knew about endometriosis), more and more bloggers, youtubers or influencers who have endometriosis share their story online and raise awareness in this way. We also found that 29% of all respondents knew someone who had endometriosis directly, either themselves, a friend, family member or partner. This supports the finding that this disease is very common. Regarding period symptoms that could be a sign of endometriosis, we saw that there was a difference in the perception of what the most common ones were between men and women. Even amongst women, we saw that not all consulted a professional because of strong period symptoms. Therefore, there is still a lot of improvement to be made to promote awareness in the whole society.

Solution

Ideal user journey

For understanding better what is happening when you are a woman who may suffer from endometriosis, we have designed her journey from having a first period until having a treatment for mitigating the effects of endometriosis.

All this information is based on the process that most of the women we have interviewed have felt and suffer. With this journey, we would like to see which are the key points where our solution could have a big impact.

The following image shows schematically how is the process of a woman from her first period to her treatment.



From this journey we can extract some opportunities that we must highlight. By the first step, having the period, there is the opportunity of learning how to aware girls on going to gynaecologist and get tested. This is super important for our solution, because it can be our solution the one that tests those womans and help us to get more data. This is also the opportunity for our second step, start feeling pain.

Secondly, when the patient arrives to the doctor, the big opportunity is to make an impact helping doctors on be surer of diagnosing fine the disease of a patient.

Last but not least, for detecting endometriosis and linking this diagnose with the treatment we have different opportunities, but specially the one explained on the section below.

Value proposition

On the following image, we can see the value proposition of our problem and for our solution:



The key point of this solution are our gains that directly relate to our goals, make an impact on woman with endometriosis daily life. All that we win with our solution related to these gains is being able to diagnose that a woman has endometriosis, find the right treatment for every woman and help doctors to understand better endometriosis.

Even though, we have a big pain for our solution, the price of those machines. It should be as cheap as possible but, mainly, has to be enough worth it, the way to link it to treatment must have over 90% of effectiveness to be enough for justifying its price. Also, there is another problem about how aware people in our society of this disease are, if people don't get the point of going to get test, our solution means nothing.

Technical requirements

The main goal of our solution is to build it up following the big constraints from our previous research, surveys and specially the technology used and provided by Hysplant. Our general requirements are:

- The solution should bring and improvement on the life of women who suffer from endometriosis.
- The solution must use as input the hyperspectral endometrial cells images.
- The way to take out samples must be less invasive than the actual solutions on the market and clinics.
- The solution should suppose an advantage for the following research on finding a new treatment for endometriosis.

Once we have those general requirements, we can detail more considering the following constraints:

- There is a lack of awareness on what symptoms can be recognised as endometriosis or which ones to any other symptomatology.
 - The solution must be accessible and relatively cheap to be used even if there is not a big chance for being endometriosis.
 - The solution must be quick to diagnose and start the process.
- There is a lack of knowledge on the illness as not enough recognised data on the topic, even if there are a lot of cases.
 - The solution must archive the data following the GDPR rules.
 - \circ The solution must learn from the new data and update the system itself.
 - The solution must be accessible for healthcare researchers to find new techniques and solutions that help the understanding of similar illness and also endometriosis.
- The main problem for gynaecologist is to guide the patient through the optimal treatment for her situation.
 - The solution must be able to guide the cells bad behaviour of the patient to the most optimal treatment from the ones nowadays listed.
 - The solution must be able to test how efficient could a new treatment be.
 - $\circ~$ The solution must learn from new strategies to mitigate or treat the effects of endometriosis on patients.

From these requirements we are going to divide our tasks into two main groups. First, the tasks related to screening and obtaining images itself. The second one, relate all these data with the right treatment, as from the section XXXX we know that the main goal here is to relate types of endometrioses with their most indicated treatments.

1. Screening as a service

One of the main constraints of the whole system is the hyperspectral camera for detection price. As it is too high for being available on ever gynaecologist clinic, our main goal is to centralize all the imaging stage and all the processing stage on one specialized centre, where most of the screenings must be carried out.

In terms of stages, the General Practitioner or the gynaecologist must send the patient to its service whenever they feel the suspect it can surely be endometriosis. Whenever the patient goes to the screening services, she would receive the visit of an imaging expert who will explore the endometrium of the patient with a hysteroscope.

The hysteroscope is operated by inserting a special rod through the vagina, tackling the cervical canal, and entering into the endometrial cavity. The aim is to provide a panoramic view of the upper genital tract through an eyepiece, which in modern apparatus is attached to a camera, and images can be displayed on a screen.

Nevertheless, here, the hysteroscope sensor will be where the hyperspectral camera work. Using all this information for being analysed by all the algorithms and techniques offered by Hysplant.

In general terms, this procedure will be similar as the radiology and X-ray procedures used nowadays for example in traumatology. The experts and the machines are mostly on big hospitals and for big cities in

some other specialized centres, where imaging is carried out for sending the results to the specialist who has ordered the screen.

This procedure will take as an output a binary classification between positive or negative with its confidence level on the detection and the hyperspectral images itself to be also analysed.

With all this, we will be able to take decisions based on the deep analysis of endometrial cells hyperspectral images. But, not only this; with these images we can also extract important features from each image, which can be useful for many reasons. As an example, we relate some of the most important in the following section.

1.1. Drug testing

All those features will be a bit different from each image, but between them, they will have common values, guiding our solution to a new classification problem, where the main goal is to distinguish between different bad endometrial cells, receiving as an output not just if it is a positive problematic cell, also it tells us how this cell could behave based on other knowledge.

The knowledge of how a cell could behave is a very interesting feature for many reasons. Applying to all the same classified cells new treatments can make us distinguish between effectiveness and specific test of new drugs for curing endometriosis or mitigate their symptoms.

Also, this classification is powerful for the information it gives to the pharmaceutic researchers on how those cells behave and why, having different values according to how they look.

1.2. Jointly learning features of bad endometrial cells for different diseases

The part designed for learning endometriosis from the images can be also applied, fine tuning its parameters and re-designing for this specific problem, to other diseases such as endometrium cancer.

As our process consists on screening through the endometrium and analysing those hyperspectral images, what is analysed is up to design phase, so this same solution, with the same testing conditions, specialized centres screening as a service, can improve the diagnose of other diseases such as endometrial cancer, that nowadays is still using invasive techniques for being diagnosed and less accurate than the help of a third-party machine learning algorithm.

1.3. Joint learning of diagnosis and treatment of endometriosis from hyperspectral images

Focusing on endometriosis, the big problem gynaecologist and other specialist must deal with, is not only the fast diagnose, it is also finding the right treatment for each patient. Based on this lack of research we have thought that advances in digital health and phenotyping technologies are crucial to ensuring increased access to high-quality sexual and reproductive health support services and treatment.

Hyperspectral images are a uniquely placed in this regard, no other imaging technology can have the principles and singular combination of physiological information from cells and other very specific and small physiological parts of our body. It is this complexity that means that hyperspectral resolution is a suitable marker for a range of different endometrial diseases.

However, much research exploring the links between cells from endometrium and being diagnosed of endometriosis is not as reliable for medicine as learning which treatments link to which bad endometrial

cells. Conditions such as which medicine should a patient take have not been exploited to help improve machine learning models that asses diagnosed endometrium diseases from hyperspectral cameras.

In this project will focus on developing end-to-end deep learning model to jointly learn self-learn suitable data representations of cells with endometriosis and treatments for each one directly from hyperspectral images. Further, it will focus on exploring the advantages of a range of state-of-the-art transfer learning to help to improve model performance and increase a model interpretability.

2. Linking hyperspectral images with the right treatment

Considering the interviews with doctors' hand by hand with the screening as a service as the joint learning of diagnose and treatment from section before, we propose a methodology for using this hyperspectral imaging, artificial intelligence and the expertise of Hysplant to help linking different cell's behaviour that originate endometriosis with the right treatment for any specific user.

As Hysplant is still in a low TRL, for this project we suggest Hysplant to match the screening service outcome to a treatment.

First, we will try to apply previous models and work with transfer learning techniques to use as much information from previous related Hysplant work, such as the matching embryo project, as it is possible. Somehow, new investigations on transferring learning and refining its data are being very successful for relating different domains with similar tasks, such as for Natural Language Processing, where language models are used for translating specific languages such as BERT¹ with CamemBERT².

As we have said transfer learning, it means we should fine-tune and use more information to refine the model. At this point, we propose to run a clinical trial.

As a way to test the viability of the possible hyperspectral camera device and its results, a good option can be run a clinical trial, defining two different groups:

- Experimental group: women who have already been diagnosed with endometriosis.
- Control group: women who do not appear to have endometriosis.

From the screenings of these participants, we need to extract two important things:

• Labelled data: all the "samples" taken from the clinical trial would be labelled as positive or negative, as we have chosen who they are. In this way, a possible training set for the next step will be available.

¹ [1] Devlin, J., Chang, M.-W., Lee, K. & Toutanova, K. (2018). BERT: Pre-training of Deep Bidirectional Transformers for Language Understanding (cite arxiv:1810.04805Comment: 13 pages)

² [2] Martin, L., Muller, B., Suárez, P. J. O., Dupont, Y., Romary, L., de la Clergerie, É. V., Seddah, D. & Sagot, B. (2020). CamemBERT: a Tasty French Language Model. *ACL*, .

- Feature extraction: we should apply some algorithm (CNN based or similar, decision up to researchers) to extract some data from its samples to have some features for the treatment that define:
 - First, how to distinguish between positive and negative.
 - Extra features informing us about the differences between positives and their cell's behaviour.

Now, we are ready to build a model to detect positive cases.

This model should be tested, and any classification method can be applied. Up to researchers. It will help increase the quantity of data we have and run an automatic predictor.

At this point, the question is how do we link this information with possible treatments.

From the clinical trial we will know some patients. In this sense, we will monitor the entire treatment process of these patients, including the effectiveness of different treatments, etc. We will build a new dataset that links the features that we have previously extracted and link it to new classes as it could be "Treatment by contraceptive pills" or "treatment by surgery", for example.

With this new classification, we have arrived to the point of joint learning of diagnose and treatment of endometriosis from hyperspectral images. Which has some pros and some cons that we should consider:

- Strengths:
 - Currently, the main complaint from doctors and patients is finding an efficient treatment early enough in the patient journey. The issue is they spent years not knowing what they have and then more years not knowing what treatment is right for their case.
 - Feminist movements have helped empower women to fight for their rights, and getting the right diagnosis of this disease that affects 10 % of the women around the world is also a right?
 - Even if some faster and cheaper methods arrive for diagnosing endometriosis, this solution is still useful.
- Weaknesses:
 - Ethics. As it is known, letting an algorithm make medical decisions and suggestions is not yet widely accepted in the world, but we know cooperation is needed.
 - However, a widespread awareness campaign will be needed to ensure people get tested from endometriosis to archive enough data for this model to work properly.

3. Prototype

Considering section 2, to test this idea and see the reaction of different stakeholders such as the researchers, doctors, gynaecologists and patients, we have developed a video that explains this whole process that ensures the achievement of the solution with its requirements.

The video can be seen on the next LINK.

3.1. Testing the prototype

We have been unable to test this prototype with all the desired stakeholders such as doctors or patients, we have just test it with the researchers.

Their opinion about it was surprisingly affirmative. They were excited by the opportunities that this solution can open, such as different work that can be done from here.

They have given us the following feedback, remembering us that the solution should consider to work for other stakeholders, such as testing drugs effects for endometriosis.

Business considerations

Finding this conceptual and technical solution is not enough to tackle our problem, we need to make sure this solution is accessible and used by people who need it. Therefore, it needs to be brought to the right market. To do so, we conducted an analysis in order to investigate the market and who could be the potential customers.

Our initial business model canvas was the following:



Market analysis

The global endometriosis market is expected to experience market growth during the forecast period 2020 to 2027. Data Bridge Market Research analyzes that the market is growing at a healthy CAGR during the aforementioned research forecast period. Emerging markets and large investments in research and development are the factors responsible for the growth of this market.

The global endometriosis market is primarily driven by the high prevalence of endometriosis, a rich pipeline of promising drugs, a high diagnosis rate, and a vulnerable female population. Furthermore, advancements in the pharmaceutical and biotech sectors or industries and increased collaboration are some of the factors impacting the growth of the market. However, the reduced number of revenue

opportunities along with expiring patents with high processing cost are some of the main factors hindering the growth of this market.

Despite major advances in non-invasive diagnostic methods, including imaging techniques such as ultrasound, MRI or CT scans, currently only the removal of endometriotic lesions via laparoscopy under general anesthesia and their histological analysis enables the diagnosis of endometriosis with certainty. The average delay between disease onset and its effective diagnosis is estimated between 7 to 11 years. This significant delay due to the lack of a non-invasive diagnostic test, leads to frequent misdiagnosis and associated unsuitable treatments, as well as to more severe cases as the disease may progress and damage additional organs.

The general population and the majority of frontline healthcare professionals are frequently unaware that having unpleasant and life-altering pelvic pain is not typical, which causes symptoms to be normalized and stigmatized and causes a considerable delay in diagnosis. Due to primary healthcare professionals' lack of knowledge about endometriosis, patients who would benefit from pharmacological treatment of symptoms do not usually obtain it. Delays in diagnosis frequently prevent patients from receiving non-steroidal analgesics, oral contraceptives, and progestin-containing contraceptives in a timely manner. Access to specialist surgical interventions for those who require them is poor due to the constrained capacity of health systems in many nations. Additionally, and particularly in low- and middle-income nations, there is a scarcity of multidisciplinary teams with the broad range of expertise and tools required for early diagnosis and successful endometriosis therapy. There is a lack of techniques to effectively detect and forecast which patients and communities are most likely to have the condition, despite the fact that primary health care practitioners have a role to play in the basic screening and treatment of endometriosis. In addition, there are a lot of knowledge gaps, and non-invasive diagnostic techniques and therapies are required.

To answer this problem the WHO advocates for, and is compromised, with the following actions;

- Health policies that guarantee access to at least a minimum level of treatment and support for patients with endometriosis.
- Establish referral systems and care pathways consisting of well-connected primary health care centers and secondary and tertiary care **centers that have equipment for advanced imaging**, pharmacological, surgical, fertility and multidisciplinary interventions.
- Strengthen the capacity of health systems to diagnose and treat endometriosis in the early stages of the disease by improving the availability of equipment.

Recently, the study of the molecular bases underlying the disease, as well as its pathology, has allowed a more targeted current approach, in the same way that it allows the potential development of new and better drugs against the disease. Although its definitive diagnosis continues to be surgical, the clinical picture suggestive complemented with advances in imaging studies allows a presumption of reliable diagnosis and in most cases is considered sufficient to initiate treatment, although our interviews suggest that these treatments these treatments might not always be the right choice for the patients. The medical management of the disease, despite not being definitive, is very varied, and offers relief symptomatic to most patients with few or minimal side effects. Laparoscopy In addition to its diagnostic utility, it is curative in many cases and provides benefits in the management of infertility. Ovarian induction and

intrauterine insemination are an effective option in the treatment of infertility related to endometriosis, as well as in vitro fertilization, which is the approach which provides the best fertilization rates.

It is safe to assume that the endometriosis industry will have healthy expansion due to a boost in patient and physician awareness. The development of novel non-hormonal medications, diagnostic tools, and surgical methods together with significant financial support for research have all contributed to the market's continued expansion. Therefore, the unmet needs in the market for endometriosis curative treatments will boost it's growth in the near future. According to a study conducted by Proficient Market Insights, growing Asian nations would be the main drivers of the worldwide endometriosis market expansion as nearly 15% of the region's female population suffers from the condition in this region.

Competitor analysis

The endometriosis market has been guided by the drugs industry for a long time, underestimating the potential for early diagnosis with the means of improving patient outcomes to treatments. There seems to be a direct correlation between the negligence caused by pharmaceutical enterprises to provide specific solutions and the boost in profits they have experienced while doing so.

The major players in relation with drugs used for endiometrosis treatment are TerSera Therapeutics LLC, AstraZeneca, Sun Pharmaceutical Industries Ltd, Novartis AG, Teva Pharmaceutical Industries Ltd, Pfizer Inc, AbbVie Inc, Bayer AG, Neurocrine Biosciences, Inc, Meditrina Pharmaceuticals Inc, among others.

As the demand for early diagnoses has proven to be vital, new startups emerge with the objective of solving the complex problems that before were overlooked. The most promising startups regarding early diagnoses are Endodiag and NextGen Jane, which are using a set of innovative tools to transform and tackle this problem.

EndoDTect is a blood test based on the analysis of a combination of biomarkers. Changes in their expression levels indicate if a subject has endometriosis or not. Combining high sensitivity and specificity, EndoDTect has the potential to dramatically reduce diagnosis delays. Endodiag is currently conducting validation studies to confirm the predictive value of EndoDTect for disease detection. Endodiag has partnerships with prestigious medical, academic and industrial teams around the world. They believe that such collaborations are key enablers to achieve their vision and change the lives of millions of women.

Moreover, NextGen Jane offers insight into women's reproductive health through its Smart Tampon System - a device that can help track biological changes in a woman's body and enables them to manage their healthcare more autonomously.

NextGen Jane was founded in 2014 with this IP as its core patent technology, and its headquarters are located in Oakland, California, United States. Initially, the company had nothing to do with tampons. It was about fertility and empowering women to manage their own reproductive health by themselves. Later on, the tampon aspect was added to help women manage their reproductive healthcare much better.

By understanding that there are disruptive competitors in the market, we acknowledge that it is imperative for our enterprise to offer a value proposition that is attractive enough to succeed and thrive.

The risk associated with these competitors implies a lower-cost offering plus chain disruption since patients will be able to get diagnosed without having to visit a gynecologist or an endometriosis centre.

Business proposal

We propose a business model where the main customer are dedicated endometriosis centres around the globe, which acquire the required hardware to run the diagnostic tests and are in direct contact with the ultimate beneficiary, the patient. With this business approach, our main customers the endometriosis centres, will have the opportunity to generate an extra source of revenue by providing the service. Our research concludes that these centers are strongly focused on providing awareness to the affected women, and this added product is a suited complementary tool to achieve that. Our ultimate business goal is to provide a SaS subscription model where this extra revenue is shared among us and them.

To reduce product-related costs, since it won't be our main source of income, we suggest to form a collaboration with a hyperspectral camera manufacturer.

- Propose partnership with major hyperspectral camara manufacturer.
- Create a ready to use camera for customers.
- Increase adoption of the required hardware.

The effectiveness of the machine learning model will be key in assessing the success of our service, therefore there must be a streamline of fresh data constantly flowing though it.

- Perform transfer learning with the current Hysplant model.
- Run a trial to finetune the model and get it approved.
- Work alongside regulators to get licensed approved.

Marketing is the third pilar of this organization. A proper sales team will be needed to expand and grow business operations worldwide.

- Create a webpage to showcase and promote the organization.
- Hire a minimal sales team to start with.
- Build customer trust by conducting free trials.

In order to make some projections for the first year of commercialising this technology, we made the following assumptions and estimates. The focus will be on countries in Europe with important endometriosis centers or hospital units, such the reproductive Institute Bernabeu or the endometriosis unit in Hospital Clinic in Barcelona. Indeed, hyperspectral imaging technology is expensive, currently around 200,000 euros, thus, a market with sufficient means to pay for this is the priority for now. In reproductive centers particularly, budgets are higher as patients will be willing to pay more for high end technology. Eventually, just like other medical technologies have shown in history, the cost of the technology is expected to decrease and become more accessible but being a first mover and gaining world

recognition early on is crucial. After a few years, medical centres such as the CAP in Catalunya, and private gynecologists would become the market of interest, in order to further spread the use of the hyperspectral imaging diagnostic.

For this first year, the expenses would include sourcing the hyperspectral cameras (200k per client), salespeople, marketing efforts (paid ads, 2 medical tradeshows, email automation tool, CRM), patent application, UX/UI professional, software developers and medical research consultant to develop the desktop and laptop platform that will display the results needed of the test, the outcome and probability, but also treatment information. Therefore, some initial funding will be needed to start commercializing this technology. We would expect to make at least 15 sales in the first year. However, we will also expect to be conducting the clinical trial to gather data between diagnosis and treatment.

Patent price	6,000	Software subscription	225,000
		fees	
Employees (1 UX/UI, 2	275,000		
software developers, 5			
salespeople)			
External expert	10,000		
consultant			
Marketing	10,000		
Total expenses	301,000	Total revenue	225,000

Reflection on student learning

This project was a great opportunity to develop soft skills working in a multi-disciplinary team with students from engineering, design and business, where we got to learn from one another, thanks to our different knowledge, experience, and way of thinking. Specifically, the skills we most improved are teamwork, intercultural awareness, communication. After careful research and dedication, we have found that endometriosis pathology is complex and there is still a long way to go to get to the level where demand meets the appropriate solution for the patients, but with the help of this and other relevant upcoming ventures, the market seems to be pointing in the right direction. The thrive and emotion we have gathered during the conducted interviews will forever live within us, and it's safe to assume that we will all keep looking for promising innovative solutions within the sector until all women are able to receive the appropriate treatment at the right time.

Conclusion

The purpose of this project was to identify effective strategies for applying hyperspectral imaging to the social problem that endometriosis represents. Based on the analysis conveyed, it can be concluded that there is a social need for early diagnosis and furthermore for choosing the right treatment for each patient as early as possible in their journey. Future exploration into fine tuning the Hysplant model could be useful to finding further therapy techniques. The amount this could improve the lives of women with endometriosis is worth exploring.

References

WHO https://www.who.int/es/news-room/fact-sheets/detail/endometriosis

Instituto Bernabeu <u>https://www.institutobernabeu.com/es/unidad-de-endometriosis-del-instituto-bernabeu/</u>

EPO https://www.epo.org/service-support/faq/own-file.html

SCIELO https://www.scielo.sa.cr/pdf/mlcr/v35n1/1409-0015-mlcr-35-01-23.pdf

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Endometriosis UK https://www.endometriosis-uk.org/getting-diagnosed-endometriosis

Appendix

Appendix 1: Awareness Survey answers

https://docs.google.com/forms/d/1Zxz0PGX0-0Lc82Liw7H-Bh4d0cgkFoAcUbxF01d6nQs/edit







What is your biological sex? 90 responses







Select the symptoms that you experience during your period ³⁸ responses



Have you ever taken any contraceptive pill? 38 responses



Have you ever asked your gynecologist about the pain you experience during your period? ^{38 responses}



Do you know any woman who suffers from painful period? 52 responses



Which symptoms do you think that they could have? 52 responses





If you know what endometriosis is, how did you discover it? 67 responses



Do you know anyone who suffers from endometriosis? ⁶⁷ responses



Who?

