HYPER-EYE

SEE MORE, DO MORE

REACH THE INVISIBLE, DEFEAT THE ENEMY: ROBOTIC INNOVATION FOR ACCURATE AND AUTOMATED SURGERY.

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INTRODUCTION

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AIM OF THE PROJECT

CBI.ATTRACT is an International Open Innovation program designed to develop the students' entrepreneurial mindset as future innovation players while ensuring the valorization of existing innovative technologies and applying them to resolve societal needs, contributing to the United Nations Sustainable Development Goals.

In 16 weeks, 5 inter-university teams of multidisciplinary students investigate breakthrough technologies to exploit their potential and develop relevant solutions to solve society, human, and ecosystem needs.

The program methodology is a hybrid model based on the human-centred approach of Design Thinking and Tech-Driven Innovation processes to nurturing the students' ability to identify and evaluate technology opportunities with societal impact on a global and local level.

Students will connect with researchers, either with those who developed the imaging technology and with other experts, to acquire a technical understanding of the technology; with users and professionals from different fields to understand the technology's potential impact in different contexts; finally, they will develop various ideas in an iterative process and will verify with users which applications have more potential. Teams are supported by local coaches, valorizing knowledge from Attract researchers and Ideasquare professionals during scheduled design sprints.
https://attract-eu.com/projects/cbi-attract/

HYLIGHT PROJECT

Hylight project

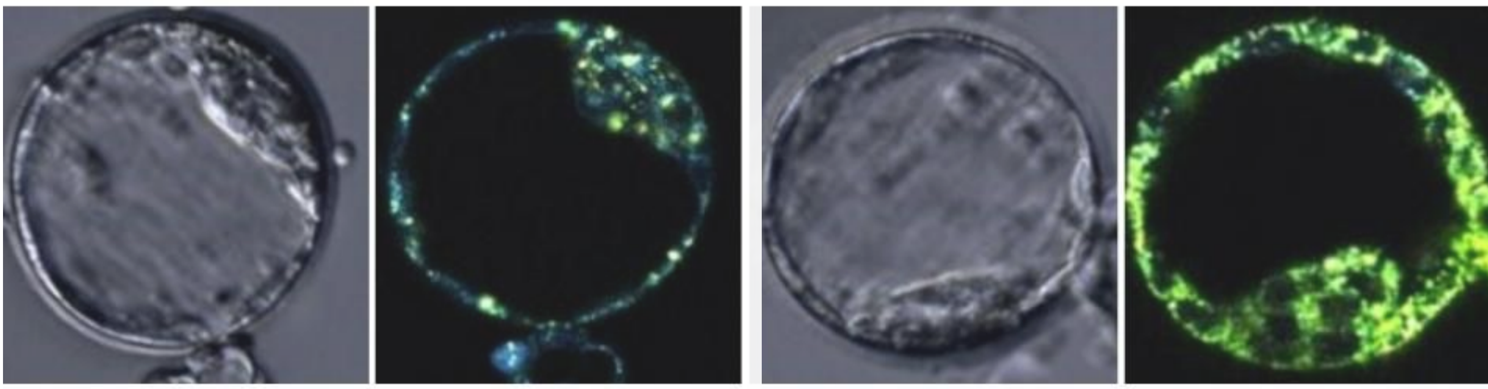
Hylight is an R&D&I project that aims to develop a diagnostic device to select embryos based on their metabolic profiles and increase the success rates of in vitro fertilization techniques.

Origin of the technology

The idea of the project is to help solve a problem affecting one out of seven couples in Europe who experience infertility problems and turn to in vitro fertilization techniques to overcome these difficulties and become parents.

Goal of the project

This project, coordinated by the Institute for Bioengineering of Catalonia (IBEC), stands for “Prototyping a light-sheet microscope for the diagnostic of embryo implantation based on hyperspectral phasor analysis”, and it’s a follow-up of the Hysplant project granted at ATTRACT phase 1, which developed a proof-of-concept device to select embryos based on their metabolic profiles.



HYLIGHT TECHNOLOGY

"HYLIGHT project will develop a robust and easy to use technology to select, non-invasively, the embryos that are competent for implantation and development, increasing the success rate and reducing the so called "time to pregnancy"".
SAMUEL OJOSNEGROS, IBEC

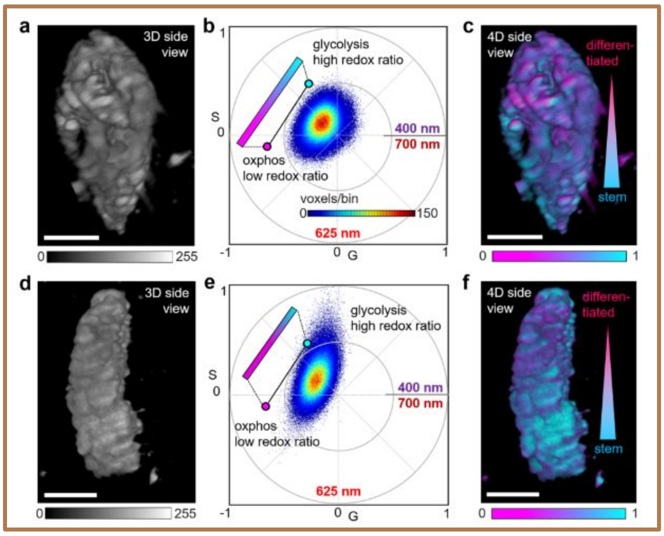
Hylight in a nutshell

A breakthrough fluorescent microscope that can take 5D images with time and spectral components with subcellular resolution. It is designed for embryo selection and for the detection of endometrial pathologies in a non-invasive way, through the application of imaging techniques and artificial intelligence classification algorithms. These images unravel features regarding the metabolic processes of the cells that can be used to classify healthy cells from pathological cells such as tumors thanks to the use of AI.

Implemented technologies

- Phasor hyperspectral analysis
- Light-sheet microscopy
- Multiphoton imaging (MPM)
- Artificial Intelligence

https://attract-eu.com/wp-content/uploads/2022/07/ATTRACT-RDI_HYLIGHT-project.pdf
https://attract-eu.com/hylight-project-developing-a-technology-to-improve-embryo-selection-for-in-vitro-fertilization-procedures/
https://attract-eu.com/projects/hylight/
https://phase1.attract-eu.com/showroom/project/metabolic-profiling-of-in-vitro-fertilization-embryos-using-hyspectral-imaging-hysplant/

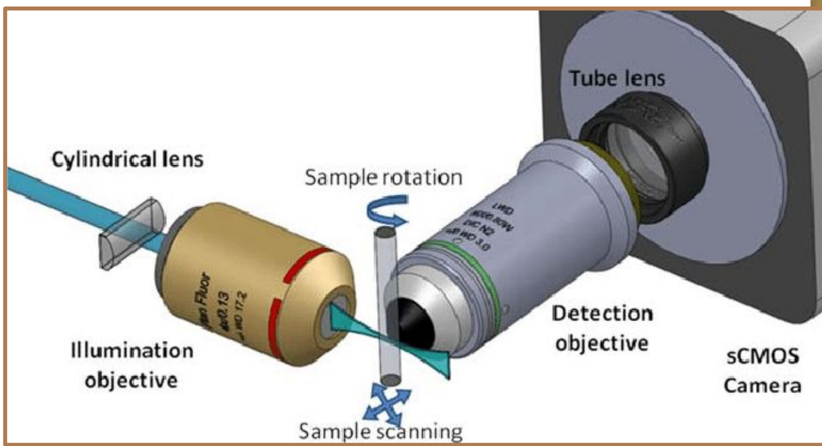


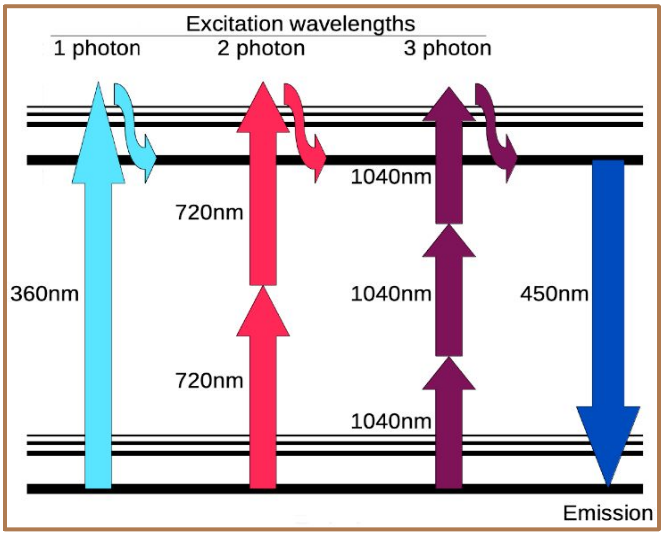
Phasor hyperspectral analysis

Imaging technique that processes hyperspectral data by representing each pixel as a phasor, capturing both amplitude and phase information. By transforming the data into phasor space, it enables exploration of complex spectral mixtures and facilitates improved classification, target detection, and material identification [2-5-6-7].

Light-sheet microscopy

Imaging method that utilizes a laser light sheet to illuminate a thin section of a specimen, while a separate objective lens captures the resulting fluorescence or scattered light. This technique enables high-resolution 3D imaging of live biological samples with minimal damage from light exposure [13].





Multiphoton imaging (MPM)

Imaging technique that provides high-resolution images and enables long-term, minimally invasive observations of dynamic processes. By using near-infrared (NIR) excitation, MPM can penetrate deeper into samples due to reduced light scattering [1-8].

DIVERGENT PHASE

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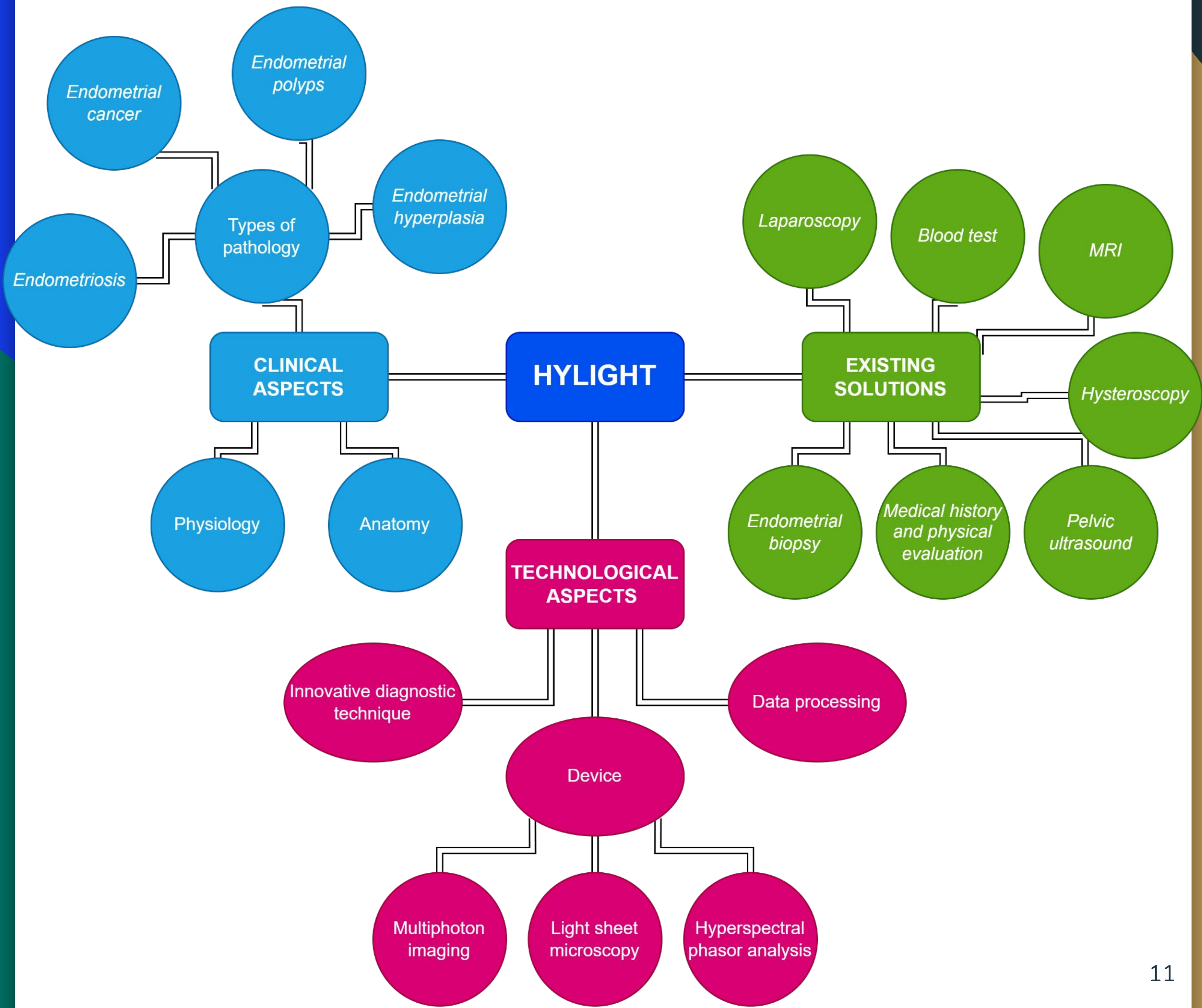
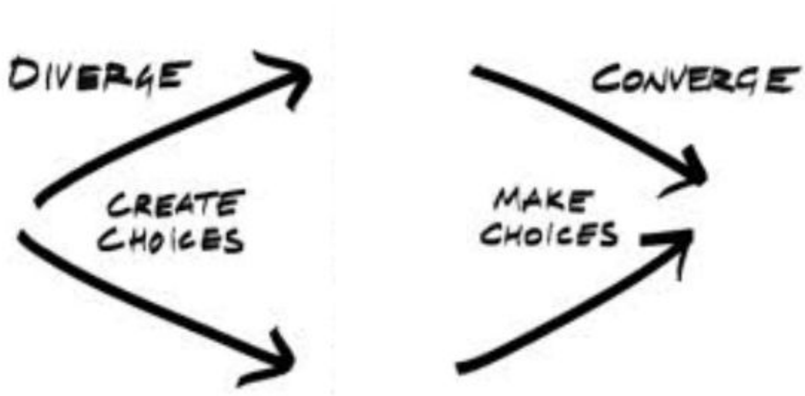
FIRST APPROACH WITH THE TECHNOLOGY

The first step in the innovation process was to thoroughly understand the technology, specifically exploring its functionality in terms of clinical and technological aspects, and then proceeding to understand existing solutions that address the problem that the technology subjects. In doing this, it has been crucial to retrace the evolution of Hylight, developing a map covering its main aspects.



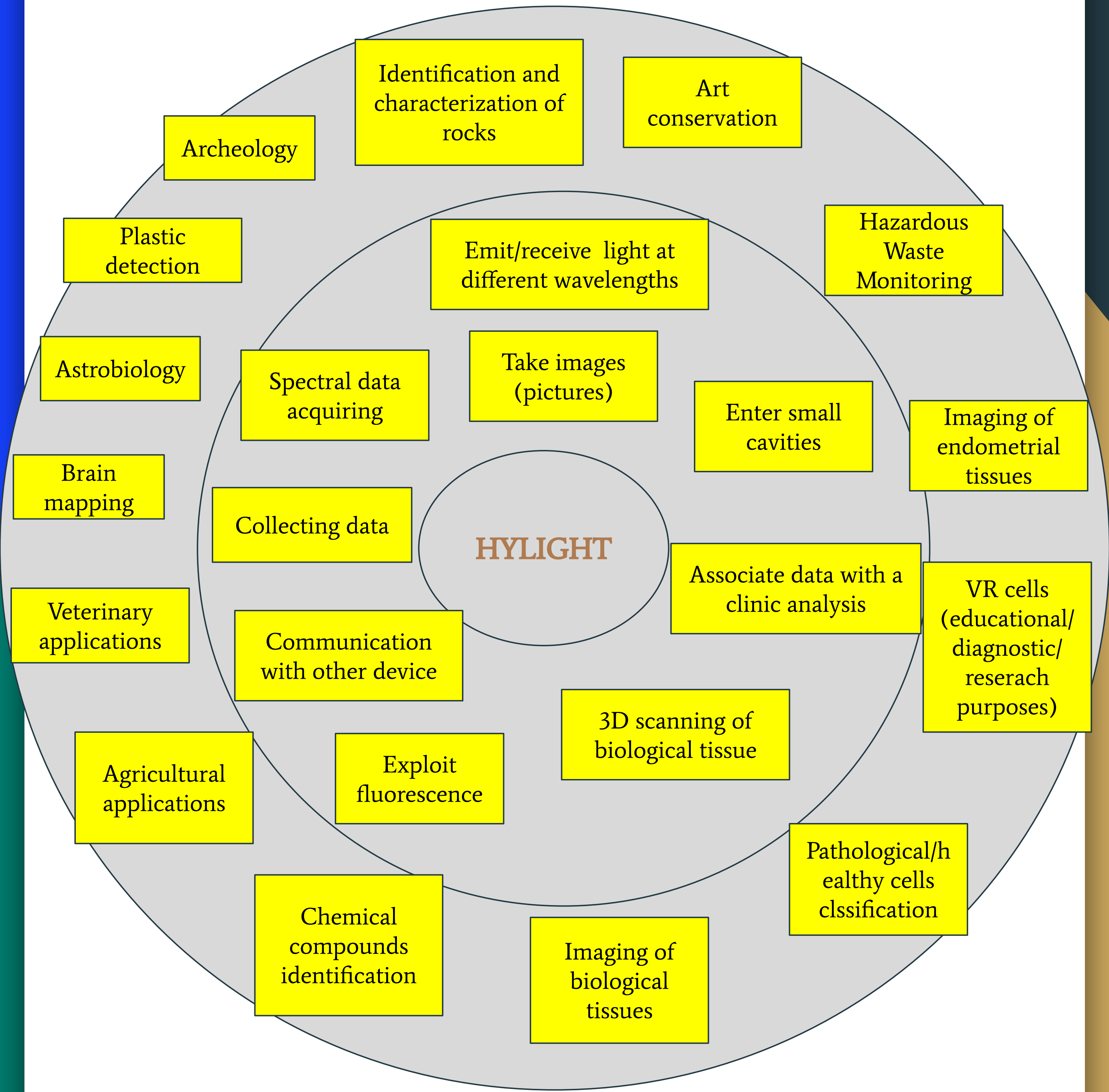
DIVERGENT PHASE

The goal of this phase was to create a divergence map that took into consideration the needs that could be met by the technology under study and the possibilities of the technology itself.



Starting from the deep understanding of the functions of technology, several divergence factors were sought to help identify the kind of needs that could benefit from these functions. The map created was concentric and included 3 levels of divergence, placing technology in the center, then identified needs, and technology solutions in the outer sector. Additional divergence maps were also created for the individual technologies that make up the device.

DIVERGENT MAP
HYLIGHT



DIVERGENT MAP
PHASOR HYPERSPECTRAL ANALYSIS

DIVERGENT MAP
MULTIPHOTON IMAGING

DIVERGENT MAP
LIGHT SHEET MICROSCOPY

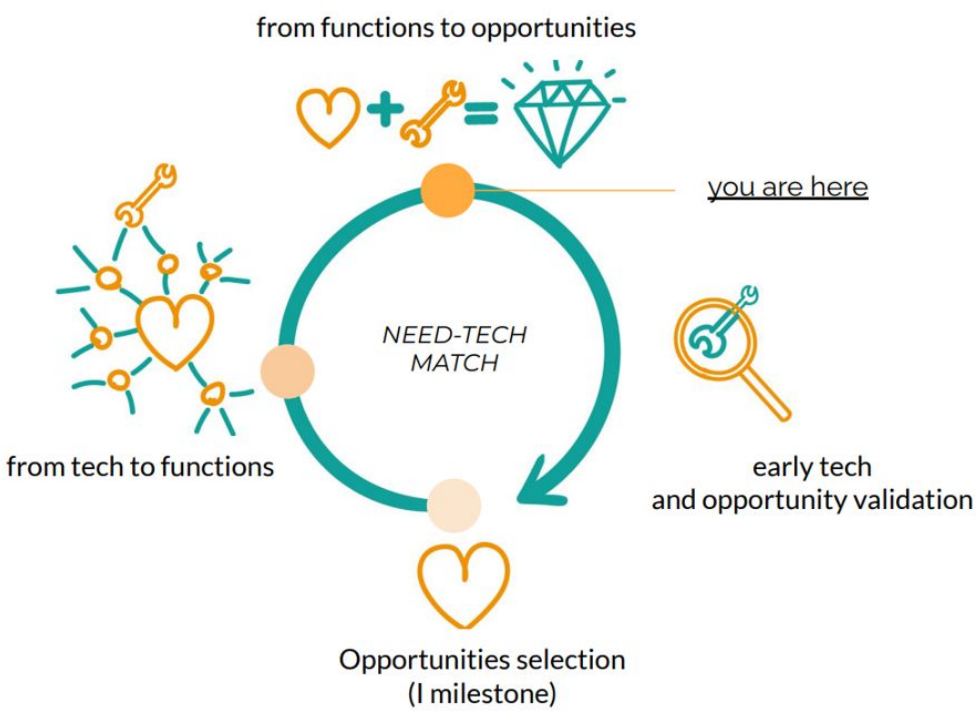
INNOVATION AT IDEASQUARE

The trip to IdeaSquare was designed to give the opportunity to meet researchers and professors, discussing with them and understanding the unexpressed potential of the technology.

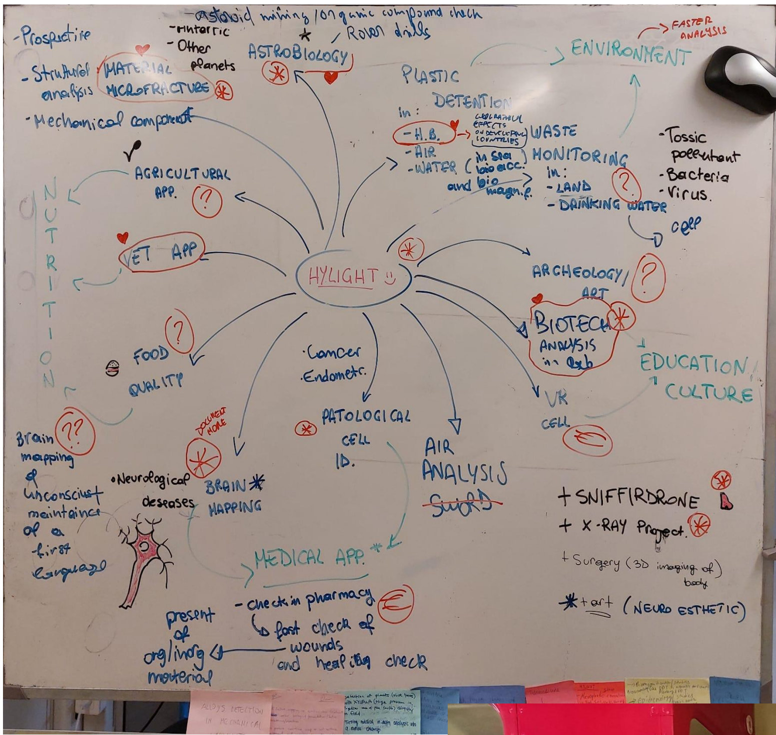
The experience included theoretical lectures, practical activities, and group works, with the aim to provide useful insight and hints to further expand the divergent thinking.

Both the interviews conducted and the information collected made possible to define a new divergent map, expanding the possible field of application of the technology.

This phase has been the prelude to the convergent one, which required to select the five most promising opportunities.



ACTIVITIES AT IDEASQUARE



During the week spent at IdeaSquare, the divergence map shown in the figure was developed and many other group activities were carried out.

INTERVIEWS AT IDEASQUARE

The several interviews conducted at CERN has revealed of fundamental importance for the development of the divergent thinking.

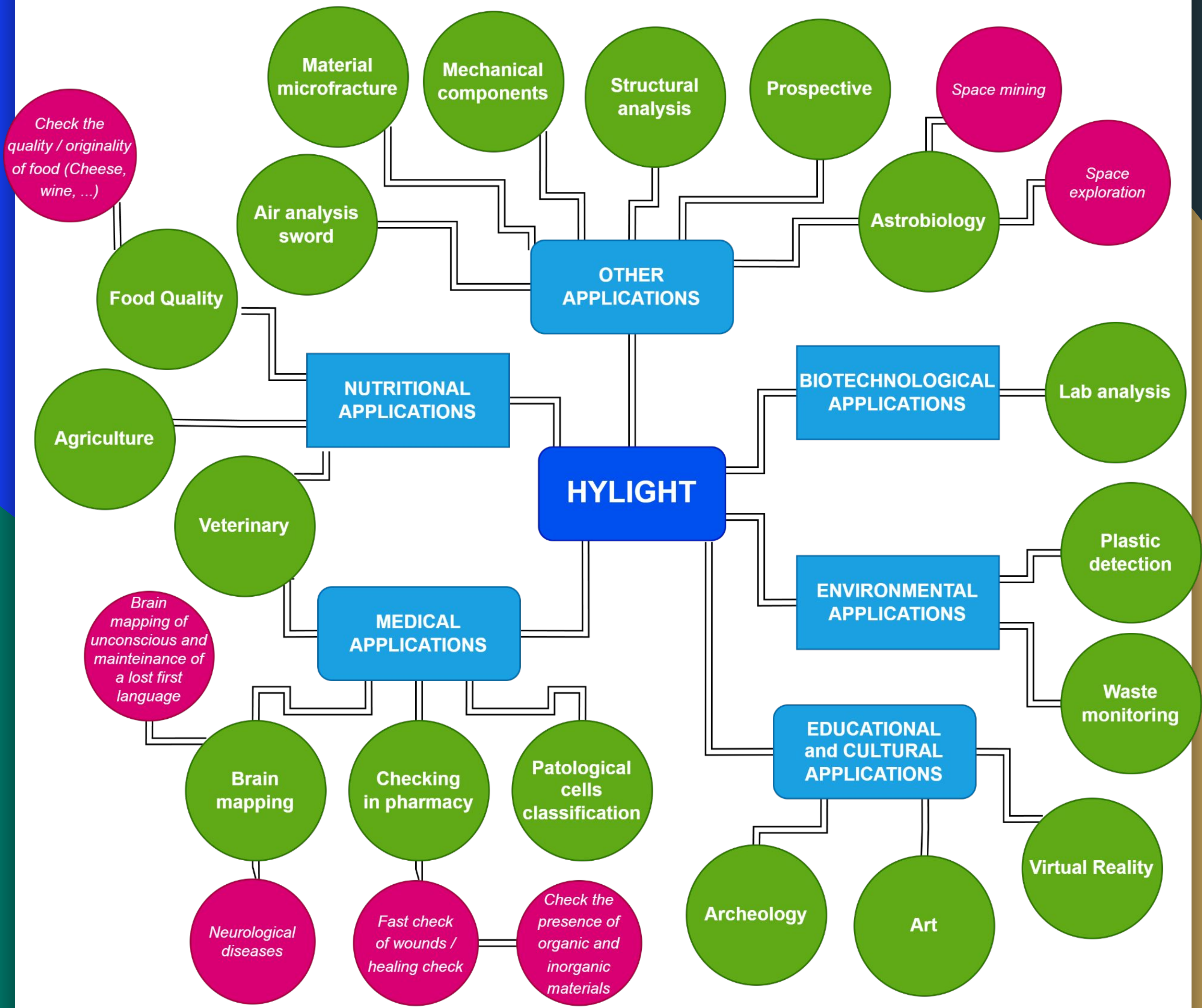
The possibility to meet and discuss with renowned experts, groundbreaking researchers, inspiring teachers and other students, such as John Wood, Marcus Nordberg, Catarina Batista, Pablo Garcia Tello, Ole Werner, Pinelopi Christodoulou, Etiennette Auffray Hillemanns, Benjamin Frisch, Rita Pinho and others, gave us a crucial help during the whole experience.

Through these interviews and conversation, it has been possible to gain a deeper understanding of the technology and to assess which of the identified applications were the most feasible, based on societal needs. The interviews were always followed by moments of group reflection, as can be seen in the photo below, in order to process within the team the information obtained and the new knowledge gained.

SDG
SUSTAINABLE DEVELOPMENT GOALS

Based on the Sustainable Development Goals (SDGs), numerous applications and uses of technology have been devised. By analyzing the SDGs, it was possible to understand what current problems exist worldwide, and the possibility of using the device under study to make consistent changes in these contexts was evaluated. For instance, Hylight's potential was considered in the areas of medical, nutritional, biotechnological, environmental, educational and cultural applications and many others. Additional, more sectoral application areas were observed for each of these classes, and the whole was reported in a concept map. An additional map was developed to identify the most important technological abilities and opportunities offered by the technology in order to better select the fields of application of the technology.

FIELDS OF APPLICATION



ABILITIES, OPPORTUNITIES AND APPLICATIONS

TECH ABILITIES

- Gather precise images
- Images have 5D - spatial, time, spectral
- Non-invasive imaging
- Probe is few mm
- Fast data transfer to external devices
- Classification algorithm for pathology detection
- Deep imaging

OPPORTUNITIES

- Assistance tool of 5D video for real-time interventions
- Probe can enter small cavities
- Replace invasive methods for imaging
- Detecting compounds in non-invasive way
- Take images of cellular structures

FIELDS OF APPLICATIONS

- Space mining Space exploration
- Thickness of nanocoathing
- Tissue diseases detection
- Material Microfracture
- Food safety / quality
- Cleaning / Sanitizing industry
- Art industry
- Surveillance for animal production
- Plastic / Metals detection in human body
- Cave exploration Mineralogy
- Brain mapping
- Surgical real-time video assistance
- Microorganisms in water / air / biological fluids
- Biotech and laboratory applications

CONVERGENT PHASE: 5 APPLICATIONS

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CONVERGENT PHASE: IDENTIFY 5 APPLICATIONS

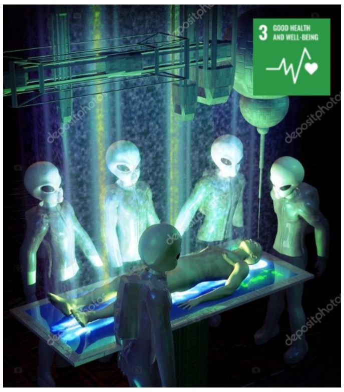
Completed the identification of various potential applications, the following step involved an analysis of each opportunity to determine which ones were worthy to focused on. The selection criteria encompassed a range of factors, including the feasibility of application, the degree of innovation it offered, its potential societal impact, and the possibility of future development. This marked a pivotal moment for the project as it transitioned from a divergent phase to a convergent one, with the primary objective shifting towards identifying and selecting five distinct opportunities. During the decision-making process, the starting point was the exploration of the technological capabilities and possibilities offered by the Hylight device. The group sought to capitalize on the unique advantages provided by the technology, leveraging them to construct the opportunities without revolutionising or altering the underlying technology. With this consideration in mind, each application was extensively discussed, analysed, and then ranked in order of suitability, from the most fitting to the least. The outcome of this rigorous selection process culminated in the creation of the first presentation that we conceived. Each identified application was also associated with specific SDGs in order to enhance its potential in terms of global need. below are the main SDGs considered by the selected 5 applications

OUTCOME OF THE FIRST PRESENTATION

The initial shape of the first presentation originated from a comprehensive understanding of Hylight and its various aspects.
The primary purpose was to effectively convey to an external audience the essence of the technology, clarifying its distinctive features, illustrating its operational mechanisms, and showing its future applications.

While the majority of the slides were dedicated to providing a detailed description and facilitating a deeper comprehension of Hylight itself, the most captivating and intriguing section was the one focusing on potential opportunities.

From the image below, it is possible to look how the first draft was like.

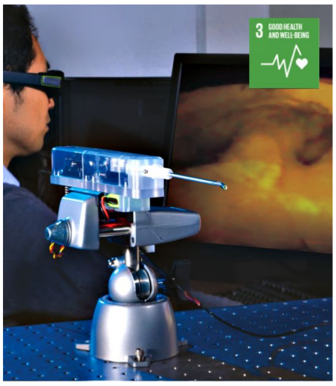


Alien compounds in human body.
The idea was to exploits Hylight capability of taking sub-cellular images in a non-invasive way to detect alien compounds in living organisms, working in the field of pollutant detection. More specifically, we wanted to help industrial workers who need health monitoring, giving them the possibility to make fast and non-invasive checks for microplastics and metals.

Food safety.
The precision and resolution of Hylight gave us the idea to apply it in the field of food safety, to detect food contaminants in a non-invasive way. The ultimate goal was to help the food control industry with a fast, flexible, and efficient method for the identification of contaminants in large amount of food.

Space exploration.
Starting from the necessity of space companies to improve vehicles' equipment to simplify space exploration, we wanted to integrate Hylight in the instrumentation to increase its capabilities, efficiency and lifetime.

Microorganisms in the environment.
Keeping in consideration a social problem affecting billions of people, the goal was to use Hylight in the field of water sanitation to help developing countries, who need constant and accessible monitoring of water, to check the drinkability.



Surgical assistance.
The possibility to hasten cells imaging and minimize damages on them gave us the idea to use Hylight in combination with to help surgeons who need fast video recording at a cellular level in order to enhance the safety and precision of the surgery.

THE VALUE OF INTERVIEWS

As the process unfolded, there emerged a growing need to explore and uncover more information about the technology itself, its components, and the potential areas where it could be applied. For this reason, interviews played a vital role in expanding our investigation and providing leads to further development: engaging in conversations with experts allowed us to access their deep understanding, comprehensive research, and up-to-date information. Their expertise empowered them to explain complex concepts, clarify misconceptions, and offer contextual insight that might have otherwise elude us: several times it happened to verify or discredit hypotheses and to change or modify the course of our inquiry based on new information that came to light. Comparing the theories presented in textbooks, articles, and papers with expert's practical application has been beneficial: their real-world experience often proved crucial in gaining different perspectives and a more accurate comprehension of the technology and its functioning. This does not undermine the importance of a theoretical approach: previous research was fundamental in understanding the subject matter and guiding fruitful discussion. However, the most valuable and precious insight mainly arose from opinions and practical examples of experts. This continuous exchange of ideas fosters critical thinking, stimulates innovation, and encourages a deeper comprehension of complex issues, enabling us to question our assumptions, reevaluate our positions, and adapt our strategies accordingly. Beyond the intellectual benefits, engaging in discussion and interviews with experts helped us in enhance the credibility and accuracy of the information. It strengthened our arguments and facilitated more effective communication of our positions and ideas. Part of the interviews that revealed vital to the continuing of our investigation are collected in the following pages.

INSIGHTS INTO LIGHT SHEET MICROSCOPY

A conversation with Peter Egelberg

Prof. Egelberg, an esteemed expert in microscopy and imaging technologies, shed light on the Hylight project and the transformative potential of light sheet microscopy in the field of bio-cells. Prof. Egelberg emphasized the groundbreaking nature of light sheet microscopy as a non-invasive method for studying bio-cells. This technology offers superior imaging capabilities, surpassing conventional modules and presenting exciting possibilities for pharmaceutical drug development and other bio-cell research. During the interview, Prof. Egelberg acknowledged certain challenges associated with light sheet microscopy. Excessive light exposure during imaging poses a risk to cell viability and can limit the ability to study the same cell over an extended period. To address this issue, researchers must analyze new cells for time-lapse imaging, leading to potential disruptions in data continuity. Additionally, the high cost of light sheet microscopes hinders widespread accessibility, primarily restricting their usage to well-funded pharmaceutical companies. Moreover, Prof. Egelberg suggested a novel application of light sheet microscopy in the early detection of bacterial growth and determining the effectiveness of antibiotics. By counting bacteria in cultures, researchers could identify the appropriate antibiotics in the early stages, potentially revolutionizing treatment approaches.

INSIGHTS INTO OPTOELECTRONIC DEVICES AND ARTIFICIAL INTELLIGENCE

A conversation with Giovanni Gibertoni

In a meeting with Giovanni Gibertoni, a PhD student working on optoelectronic devices for ocular stimulation, the discussion centered around the feasibility and practicality of combining various technologies into a single instrument. Giovanni's research in this field led him to believe that merging these technologies is a complex task. The main question posed was, what can be done practically with this technology, Giovanni stressed the need to focus on the application of each technology individually and highlighted the advantages of capturing images at different wavelengths, such as obtaining hyperspectral images with multiple layers, providing more detailed information. One of the specific applications discussed was the use of light sheet microscopy, which allows for three-dimensional imaging of embryonic cells in rats. However, the challenge arises when considering how this technology can be applied to the human body. In conclusion, the meeting with Giovanni provided valuable insights into the practical considerations and challenges involved in utilizing optoelectronic devices and AI. Understanding the capabilities and limitations of each technology are crucial steps in harnessing the full potential of these technologies.

INSIGHTS INTO FOOD QUALITY ANALYSIS

A conversation with Giampiero Pagliuca

As a professor specializing in the detection of microplastics in food, Prof. Pagliuca expressed that our research is quite distant from their area of focus. Microplastic analysis requires the identification of individual molecules, a level of precision that our current methods may not provide. He suggested that we concentrate on the traditional approach, which typically involves chromatography and mass spectrometry, commonly used in official food control analyses. During the discussion, it became evident that Prof. Pagliuca and his team faced challenges in their work on bacterial activity in fish. Despite their efforts, progress has been limited. The traditional approach using chromatography and mass spectrometry remains the gold standard in food analysis, and there is a constant demand for faster methods. However, the challenge lies in the presence of mycotoxins, which are found in most food samples. Certain substances are strictly regulated due to their dangerous nature, such as hormones and growth promoters, and are forbidden by law. Water analysis also poses limitations due to low tolerance levels. The presence of bacteria in water samples was briefly mentioned as a potential area of investigation.

In conclusion, the meeting with Prof. Pagliuca provided valuable insights into the challenges and specific requirements of food quality analysis, particularly regarding the detection of microplastics and mycotoxins. The exchange of ideas and suggestions will aid in shaping our research direction, focusing on optimizing traditional approaches and identifying unique molecules for detection.

INSIGHTS INTO ANIMAL BIOTECH

A conversation with Eleonora Iacono

In a meeting with Prof. Eleonora Iacono, a prominent figure in animal biotechnology, discussions revolved around the fascinating realms of stem cells and organic studies. Prof. Iacono elaborated on various aspects, highlighting the significance of species such as horses, dogs, and cats in this domain.

When considering potential applications, Prof. Iacono indicated that medicine companies and similar entities like Minitube could greatly benefit from Hylight technology. These companies engage in studying the development of cells and could leverage light sheet microscopy for their research purposes. While organic studies were not their primary focus, embryo development and microplastic analyses were identified as viable areas for exploration.

During the meeting, the question arose regarding other possible applications, particularly in the realm of bacteria. Prof. Iacono acknowledged the potential of using light sheet microscopy to identify bacteria without the need for laboratory processes. By directly observing samples through the microscope, it may be possible to expedite bacterial identification. Prof. Iacono cited an example of studying bacteria in the uterus by taking a swab before reproduction and waiting for a week to obtain results. Similarly, sperm analysis could benefit from light sheet microscopy, offering a potential alternative to electron microscopes, which are challenging to use and require specialized technicians.

Furthermore, the potential for expedited bacterial identification and improved sperm analysis showcases the diverse range of applications that can be explored with the Hylight project.

INSIGHTS INTO HYLIGHT PROJECT

A conversation with Anna Ferrer

In the meeting with PHD. Anna Ferrer, the contact person from the research team at IBEC (Institute for Bioengineering of Catalonia), we gained valuable insights into the Hylight project and its potential applications. Anna Ferrer shared information about the project, addressing various questions related to the technology's capabilities and limitations.

The limitations of the Hylight device were discussed, particularly regarding imaging moving targets. Anna explained that the exciting systems can be modified to overcome this limitation. Regarding flexibility, Anna emphasized the possibility of utilizing specific parts of the technology, particularly the probe, which can be flexible. In response to questions about detecting receptors, Anna clarified that while the technology enables the visualization of molecules, direct receptor detection is not its primary function.

In terms of applications, questions were raised about the range of wavelengths for the spectra and the potential use of Hylight in various fields, including brain surgery and food safety monitoring. Anna mentioned the feasibility of different wavelength ranges and shared that ongoing research is exploring the application of Hylight on tissues and embryos outside the body.

In conclusion, the ongoing research and development efforts, coupled with the flexibility and potential of Hylight, hold promising prospects for future advancements in the field of bioengineering and microscopy.

SCENARIO FORMULATION

Once the five primary applications were identified, taking in consideration experts and researchers' opinion, a comprehensive and in-depth analysis was conducted to carefully examine the benefits and risks associated with the integration of Hylight in those specific fields.
The objective was to assess the impact of the technology on each opportunity, taking into account a multitude of crucial aspects.

In order to gain a thorough understanding of the feasibility and the potential offered by each application from an end-result perspective, a series of fictitious scenarios were devised.
These scenarios were carefully constructed to encompass a wide range of factors that were deemed essential for the evaluation process.

By considering these hypothetical situations, it became possible to delve into the details of each opportunity, scrutinizing the underlying needs and problems that could be addressed, identifying the enabler behind the technology, exploring the experience it would offer to consumers, and thoroughly evaluating the value it would add to existing solutions in the respective fields.

SCENARIO FORMULATION
ALIEN COMPOUND IN HUMAN BODY

NEED / PROBLEM
Metallurgical industrial workers exposed daily to harmful compounds who need periodic health monitoring to prevent diseases.

ENABLER
Workers use Hylight to detect aliens compounds in their bodies in a non-invasive way, with high frequency.

EXPERIENCE
Workers submit to health checks in a fast and comfortable way.

VALUE
Workers discovers their health conditions and try to prevent potential diseases.

Constructed scenario:
Workers in the metallurgical sector often come into contact with dangerous substances while performing their daily tasks, which poses a serious health risk.
For this reason, there is an urgent need for routine health monitoring to maintain these workers' wellbeing and guard against dangerous infections.
Hylight would serve as the enabler for meeting this demand.
With the use of this technology, it is possible to simplify the monitoring process, so that employees can non-invasively find alien chemicals in their body, learning important details about their health problems and taking proactive steps to ward off any potential diseases.
Early detection and identification of dangerous substances give people the knowledge and awareness they need to take preventative measures and protect their health.

SCENARIO FORMULATION
SPACE EXPLORATION

NEED / PROBLEM
NASA wants to build a rover with least amount of instrumentation to increase lifetime and flexibility in the emission

ENABLER
We use Hylight to combine different technologies used in rover into a single entity.

EXPERIENCE
Simplify the analysis process and reach more difficult places thanks to the small probe and depth component in the imaging in order to collect more data from small cavities, e.g., drills and small caves.

VALUE
Easier data acquiring and data from variety of places.

Constructed scenario:
NASA faces a pressing need to develop a rover with the least amount of instrumentation possible in order to maximize its lifespan and mission flexibility. This is necessary in order to meet the demands of space exploration missions and maximize the rover's capabilities.
This need is met by a potent enabler in the shape of Hylight: thanks to it, NASA can combine the various technologies used in the rover into a single, cohesive entity.
Among the advantages, Hylight would make data collecting and analysis simpler, enabling more effective exploration and research.
Moreover, its compact probe and image depth feature would allow the rover to investigate hard-to-reach locations, including small cavities, such as drills and caves.
The application of Hylight would increases the potential for scientific discovery and would improve NASA's capacity to collect data from many sources.

SCENARIO FORMULATION
MICROORGANISMS IN THE ENVIRONMENT

NEED / PROBLEM
Charities must check water safety and drinkability before providing humanitarian medical care in developing countries

ENABLER
Hylight can detect and classify microorganisms in water in a fast way and directly in the source of water.

EXPERIENCE
Charities can assess the safety of water directly from the source, promptly reacting in case of contamination.

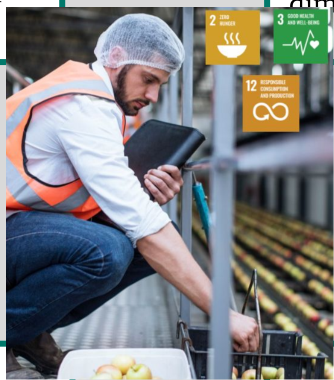
VALUE
Give to populations in need safe and drinkable water.

Constructed scenario:
In the context of providing humanitarian medical care in developing countries, charities face the critical need to ensure the safety and drinkability of water before distributing it to the population. This need arises from the importance of preventing waterborne diseases and promoting public health in vulnerable communities.
For this purpose, Hylight could be a possible solution: thanks to its capabilities, it allows a rapid detection and classification of microorganisms present in water, running the analysis directly at its source.
In this way it is possible to eliminate the need for time-consuming and costly laboratory tests, allowing for real-time assessment and decision-making.
This would contribute to improving public health outcomes and enhancing the overall effectiveness of humanitarian medical care efforts.

SCENARIO FORMULATION
FOOD SAFETY

NEED / PROBLEM
Increase safety and quality control: local laboratories are wasting food from taking samples.

ENABLER
With Hylight we don't need to take samples, or we can do it minimally invasive, exploiting the dimensions of the device.



EXPERIENCE
Fast and efficient way to check large quantity of food.

VALUE
Decrease food wasting phenomenon and reducing the probability to eat contaminated / unsafe food.

Constructed scenario:
To address the critical need for increased safety and quality control in local laboratories, an innovative enabler comes in the form of Hylight.
With this technology, the traditional practice of taking extensive samples can be eliminated or minimized, thanks to the unique dimensions and capabilities of the device.By leveraging its advanced features, the need for extensive sampling is significantly reduced, as Hylight enables minimally invasive or even non-invasive analysis. This not only saves time and resources but also minimizes food wastage, making the quality control process more sustainable.
Additionally, Hylight enables the identification and detection of potential contamination in food, thereby reducing the probability of consuming unsafe products. This enhances consumer safety and contributes to overall public health.

SCENARIO FORMULATION
SURGICAL ASSISTANCE

NEED / PROBLEM
Surgeons need a precise and fast video recording system (on cell) to assist surgical interventions (e.g. brain surgery for tumor removal).

ENABLER
Hylight can record live videos of cells while the surgeon is operating.

EXPERIENCE
The surgeon can look at the screen and monitor the specific cells he/she is working on.

VALUE
Surgery is safer and more target specific.

Constructed scenario:
A precise and quick video recording system is essential for surgeons to use during surgical interventions, especially when performing difficult procedures like brain surgery for tumor removal.
Hylight could reveal a possible answer to this need.
This innovative technology enables real-time visualization of the specific cells that the surgeon is operating on, offering a valuable tool for monitoring and guiding their actions.
Using Hylight, the surgeons can easily observe the targeted cells on a screen while performing the procedure, enhancing their ability to make precise and informed decisions in real-time.
Moreover, the possibility to review the recorded videos post-surgery allows for valuable insights, enhancing surgical training and facilitating knowledge sharing among medical professionals.

FIRST MILESTONE

The First Milestone has been the occasion to evaluate the evolution of the project from its beginning until that moment.
It consisted of a presentation in which all the information collected during the interviews and the scenarios formulation were gathered with the aim to present them to an external public.
For its creation, the team adhered to an “EPO framework”.
This approach involved a systematic investigation of each field of applications, considering the Evidence that supports the use of Hylight, addressing the Problems that hinder its implementation and outlining the Opportunities that can be realized.
In doing this, the team exploited the fictitious scenarios previously elaborated.
Subsequently, the presentation was showed to a diverse audience consisting of researchers, teachers and fellow students.
Of particular significance was the opportunity to engage in discussions with members of IBEC, the research center responsible for developing Hylight technology.
This interaction provided valuable insight that proved crucial for the progression of the project.
The following pages shows how the five applications were discussed and proposed during the First Milestone.

FIRST MILESTONE
ALIEN COMPOUND IN HUMAN BODY

DETECTION OF ALIEN COMPOUND IN HUMAN BODY

Average number of microplastic particles consumed by a single person per year → **100,000**

These substances can enter the body in three main ways:
- **ingestion**;
- **inhalation**;
- **skin contact**.

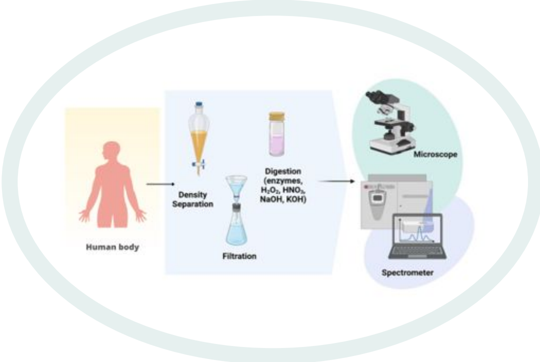
Where are these substances located?
Which path do they follow?
What is their effect on human health?

The detection of an alien compound in the human body has raised significant concerns: it has been found that the average number of microplastic particles consumed by a single person per year is around 100,000. These substances have the potential to enter the body through three main pathways: ingestion, inhalation, and skin contact.

Microplastic particles can be found in various locations within the body. They have been detected in the gastrointestinal tract, respiratory system, and even within tissues and organs. The path these substances follow depends on their mode of entry. When ingested, they may travel through the digestive system, potentially reaching the bloodstream. Inhalation allows them to enter the respiratory system and possibly reach the lungs. Skin contact can lead to absorption and distribution throughout the body.

The presence of these alien compounds in the human body raises concerns about their impact on human health. Studies have suggested potential health risks associated with microplastic exposure, including inflammation, cellular damage, and the release of harmful chemicals. However, the full extent of their effects on human health is still being researched, and further studies are necessary to understand the long-term consequences.

FIRST MILESTONE
ALIEN COMPOUND IN HUMAN BODY



DETECTION TECHNOLOGIES

- Fourier transform infrared (FTIR)
- Raman Spectroscopy

LIMITATIONS

- The analysis cannot be performed on the patient → Necessity to obtain a sample (blood, urine, feces)
- The sample can be damaged or contaminated → The analysis is time consuming

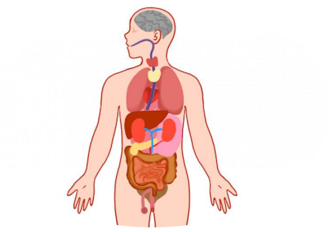
To detect these compounds, advanced technologies such as Fourier transform infrared (FTIR) and Raman Spectroscopy are employed.
These techniques analyze the molecular composition of the samples, allowing for identification and characterization of the alien compounds.

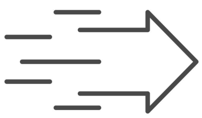
However, these detection methods have limitations.
The analysis cannot be performed directly on the patient, requiring the collection of samples such as blood, urine, or feces. This introduces the possibility of sample damage or contamination, making the analysis time-consuming and potentially less accurate.

FIRST MILESTONE
ALIEN COMPOUND IN HUMAN BODY

IMPROVEMENTS WITH HYLIGHT

Detection directly inside the human body





Faster detection

Improving scientific research

To address these limitations, several improvements are needed.
Faster detection methods could significantly reduce analysis time and enable more efficient monitoring of microplastic exposure.
Additionally, advancements in technology could allow for detection directly inside the human body, eliminating the need for invasive sample collection. This would provide real-time information and a more accurate understanding of the extent of microplastic presence.

Improving scientific research in this field is essential.
Conducting comprehensive studies to determine the health effects of microplastic exposure is crucial. This includes understanding the mechanisms of entry, distribution, and potential interactions within the human body.

Collaborative efforts between researchers, medical professionals, and policymakers can drive advancements in detection technologies and promote awareness of the risks associated with alien compounds in the human body.

FIRST MILESTONE
LABORATORY RESEARCH

LABORATORY RESEARCH

The research using in vitro cell colonies and living animals for:

- Study pathologies;
- Find news health care techniques;
- Check the safety of drugs and PPCPs

Laboratory research plays a crucial role in various aspects of scientific inquiry, particularly in the study of pathologies, the development of new healthcare techniques, and the assessment of drug and PPCP safety.

Researchers employ in vitro cell colonies and living animals to investigate these areas and advance medical knowledge.

FIRST MILESTONE
LABORATORY RESEARCH

CURRENT PROBLEMS OF RESEARCH

CURRENT TECHNOLOGIES

Immunoassay Fluorescence microscopy

- only 2D images
- Invasive
- phototoxicity
- photobleaching

TIME

The manufacturing of cell-based therapies can take up to several weeks

SCALE

Available tools are not suitable for large-scale biomanufacturing

Currently, technologies such as immunoassay and fluorescence microscopy are commonly utilized in laboratory research. However, these methods have certain limitations.

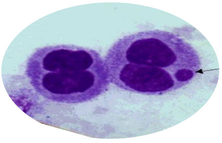
They primarily provide 2D images, which may not fully capture the complexity of cellular interactions in three-dimensional environments. Additionally, these techniques can be invasive, potentially affecting the natural behavior of cells and organisms. Phototoxicity and photobleaching, which are adverse effects caused by light exposure during imaging, further constrain the accuracy and reliability of results.

Another critical aspect that researchers face is time.
The manufacturing of cell-based therapies can be a lengthy process, often taking several weeks. This can impede the rapid development and translation of new treatments into clinical practice.

Furthermore, the scale of biomanufacturing is a challenge.
The current tools and techniques used in laboratories may not be suitable for large-scale production of cell-based therapies and other bio-manufactured products. This hinders the widespread application and accessibility of these innovative healthcare approaches.

FIRST MILESTONE
LABORATORY RESEARCH

PPCPs EFFECTS



- take sample from the culture;
- wait to see the biomarkers;
- secondary answers like growth/death rates.

PATHOLOGIES

- see how cells and tissues react to the disease process:
- directly in the body of the animals;
- in real time.

Researchers are exploring alternative approaches that offer improved capabilities and efficiency.

Instead of relying solely on 2D imaging, efforts are being made to develop techniques that enable three-dimensional visualization of cellular structures and interactions. Non-invasive imaging methods are also being explored to minimize the disruption of natural cell behavior and reduce the risk of phototoxicity and photobleaching.

In terms of time and scale, researchers are striving to optimize manufacturing processes for cell-based therapies, aiming to shorten production timelines while maintaining high-quality standards.

Thanks to these advancements, researchers will be able to take samples from cultures and obtain real-time insights into biomarkers, growth rates, and cell viability. Moreover, observing cellular and tissue responses to disease processes can be achieved directly within the body of living animals, providing a more accurate understanding of pathologies and their progression.

FIRST MILESTONE
WATER QUALITY MONITORING

WATER QUALITY MONITORING

At least **2 billion** people use a drinking water source contaminated with **faeces**

485 000 people **die from diarrhea** caused by microbially contaminated drinking water

European Environment Agency

14 LIFE BELOW WATER

6 CLEAN WATER AND SANITATION

Water quality monitoring is a critical aspect of ensuring the safety and availability of clean drinking water.
Over 2 billion people worldwide use drinking water sources contaminated with fecal matter, resulting in approximately 485,000 deaths annually from diarrhea caused by microbially contaminated water.

FIRST MILESTONE
WATER QUALITY MONITORING

CURRENT PROBLEMS OF WATER MONITORING

TIME CONSUMING

- Transportation
- Laborious
- Results are slow

LOCAL INFORMATION

- Biased
- inhomogeneity of water
- Lack of data

METHODS

- Specific contaminants
- Lack of variety

The current methods of water monitoring face several challenges.

Firstly, the process is time-consuming, involving the transportation of samples to laboratories and laborious testing procedures. Consequently, obtaining results can be slow, hindering timely interventions.

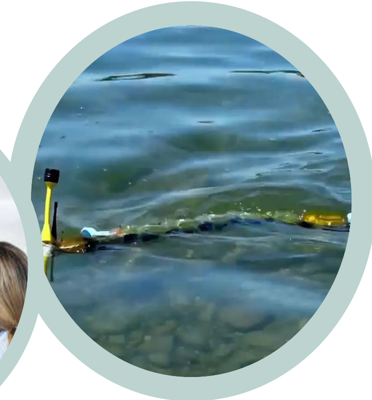
Moreover, local information about water quality tends to be biased and inconsistent due to variations in water sources and limited data availability.

Additionally, existing methods often focus on specific contaminants, lacking the variety needed to comprehensively assess water quality.

FIRST MILESTONE
WATER QUALITY MONITORING

IN SITU MONITORING AND MAPPING

Autonomous device which maps and monitors contaminants in a body of water



Improvements

- Mapping various pollutants
- Large area coverage
- Faster method
- Source of contamination
- Prevention of contamination

Who benefits:

- Water pollution prevention organizations
- Water quality monitoring organizations
- Agriculture and ocean sustainability

To address these issues, in situ monitoring and mapping techniques are being developed.

These innovations offer several improvements over traditional methods.
They enable the mapping of various pollutants, providing a comprehensive understanding of water quality over large areas.
Furthermore, these devices offer faster monitoring capabilities, allowing for prompt action and interventions when contamination is detected.
They also facilitate the identification of sources of contamination, aiding in preventing further pollution and protecting water sources.

The benefits of these advancements in water quality monitoring are far-reaching.
Water pollution prevention organizations can utilize these technologies to enhance their efforts in safeguarding water resources and preventing contamination.
Water quality monitoring organizations will benefit from the more efficient and comprehensive data collection, enabling them to make informed decisions and take timely action.
Moreover, the agricultural and ocean sustainability sectors can use this information to ensure responsible practices and mitigate potential harm to water ecosystems.

FIRST MILESTONE
FOOD SAFETY

FOOD SAFETY: MYCOTOXINS DETECTION

Why mycotoxins?

- Toxic compounds naturally produced by fungi
- Infection of crops
- Adverse health effects in humans and animals

Exposure?

- Contaminated food
- Animals fed with contaminated feed

Major threats?

- Cancer
- Liver diseases
- Immune-system suppression
- Mutagenicity
- Nervous disorders

Ensuring food safety is a fundamental concern, particularly when it comes to the detection of mycotoxins.
Mycotoxins are toxic compounds produced naturally by fungi, which can infect crops and contaminate food sources, posing adverse health effects for both humans and animals.

Exposure to mycotoxins primarily occurs through the consumption of contaminated food or the consumption of animal products derived from animals fed with contaminated feed. These toxins present significant threats to human health, including the risk of cancer, liver diseases, immune system suppression, mutagenicity, and nervous disorders.

FIRST MILESTONE
FOOD SAFETY: MYCOTOXINS

CURRENT PROBLEMS AND LIMITATIONS

- Time-consuming analyses
- Lack of accuracy
- Lack of precision

Techniques employed so far:

- Analytical techniques
- Hyperspectral imaging
- Fluorescence spectroscopy

Who is involved:

- Consumers and sellers
- Analytical laboratories
- European Organizations (EFSA, JECFA)

The current methods employed for mycotoxin detection face several challenges and limitations: the analyses involved in their detection are time-consuming, often lacking the desired level of accuracy and precision.

Existing techniques, such as analytical methods, hyperspectral imaging, and fluorescence spectroscopy, have their own limitations and may not provide the sensitivity and specificity required for robust mycotoxin detection.

Various stakeholders are involved in addressing the issue of mycotoxin detection, including consumers, sellers, analytical laboratories, and European organizations like the European Food Safety Authority (EFSA) and the Joint FAO/WHO Expert Committee on Food Additives (JECFA). Their primary objective is to control and detect mycotoxins in food, ensuring the safety and quality of food products.

FIRST MILESTONE
FOOD SAFETY: MYCOTOXINS

PRIMARY NEED: CONTROL AND DETECTION OF MYCOTOXINS IN FOOD

Improvements offered by Hylight:

sensitivity and accuracy

- Detection of low levels of mycotoxins
- High specificity for different types of mycotoxins

speed

- Quicker identification
- Removal of contaminated products

cost

- Cost-effective
- Savings in laboratory tests and analysis

Hylight could offer significant improvements in mycotoxin detection.
First of all, it addresses the limitations of current methods by providing enhanced sensitivity and accuracy, detecting low levels of mycotoxins and demonstrating high specificity for different types of mycotoxins. This ensures a more comprehensive and reliable analysis [9-10].

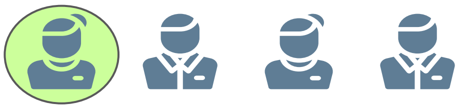
In addition to accuracy, Hylight also offers speed in identification, enabling quicker detection and prompt removal of contaminated products from the market. This contributes to a more efficient response in preventing the consumption of mycotoxin-contaminated food, safeguarding public health.

Moreover, Hylight brings cost-effectiveness to mycotoxin detection.
By offering a more efficient and reliable method, it helps save costs associated with extensive laboratory tests and analysis, streamlining the detection process while maintaining accuracy.

FIRST MILESTONE
NEUROSURGERY

NEUROSURGERY: BRAIN TUMOR REMOVAL

Survival rate after brain surgery: 1 out of 4 people survives surgery within 5 years



PRIMARY NEED: Pathological cells visualisation and identification in order to remove as much tumoral cells as possible without killing healthy cells

otherwise

- Damage to surrounding brain tissue may lead to motor, cognitive and speech impairments
- Tumoral cells residual may lead to an extension of the disease, to cerebral hemorrhage and coma

Neurosurgery plays a crucial role in brain tumor removal, with the survival rate after brain surgery currently standing at 1 out of 4 people surviving surgery within 5 years.

The primary need in this field is to visualize and identify pathological cells accurately, allowing for the removal of as many tumor cells as possible without harming healthy cells.

Failure to accurately remove tumor cells can result in damage to surrounding brain tissue, leading to motor, cognitive, and speech impairments. Additionally, residual tumor cells can contribute to disease progression, cerebral hemorrhage, and even coma.

FIRST MILESTONE
NEUROSURGERY

CURRENT PROBLEMS AND LIMITATIONS

CURRENT CLINICAL PRACTISE

- Intra-operative MRI
- 3D exoscopes
- Exogenous contrast agents fluorescence methods

LIMITATIONS

- Extreme cost
- Special operating room set-up
- Low efficacy
- Administration of potentially toxic dyes

NEW METHODS

- Endogenous fluorescence methods

LIMITATIONS

- Slow data acquisition
- Post-operative data processing

IS HYLIGHT THE SOLUTION?

Current clinical methods utilized in neurosurgery include intra-operative MRI, 3D exoscopes, and exogenous contrast agents fluorescence methods.
Their main limitations are related to the fact that they are costly, requiring special operating room setups, and that they have shown low efficacy. Moreover, the administration of potentially toxic dyes adds another layer of concern.

New methods, such as endogenous fluorescence methods, have emerged as potential alternatives. However, they also have some limitations, including slow data acquisition and post-operative data processing.

Could Hylight be the solution?

FIRST MILESTONE
NEUROSURGERY

POTENTIAL HYLIGHT USAGE IN SURGICAL SETTINGS

Imaging device able to assist surgeons by recording live videos of the cerebral tissue and by automatically identifying pathological cells

Speed

Live video recordings

Depth

Deep cells and deep vascular structures identified

Resolution

Images at a cellular level and big amount of data recorded

Live AI application

Live classification of cells

Hylight presents promising potential as a solution in surgical settings.

This imaging device can assist surgeons by recording live videos of cerebral tissue and automatically identifying pathological cells. The speed of live video recordings allows for real-time monitoring and decision-making during surgery.

Hylight has the capability to identify deep cells and deep vascular structures, providing valuable insights into intricate areas. Furthermore, the device offers high-resolution imaging at a cellular level, capturing a substantial amount of data.

In addition, Hylight could be implemented with live artificial intelligence (AI) algorithms, to allow the live classification of cells, assisting surgeons in identifying and differentiating between healthy and pathological cells during surgery.

CONVERGENT PHASE: 2 APPLICATIONS

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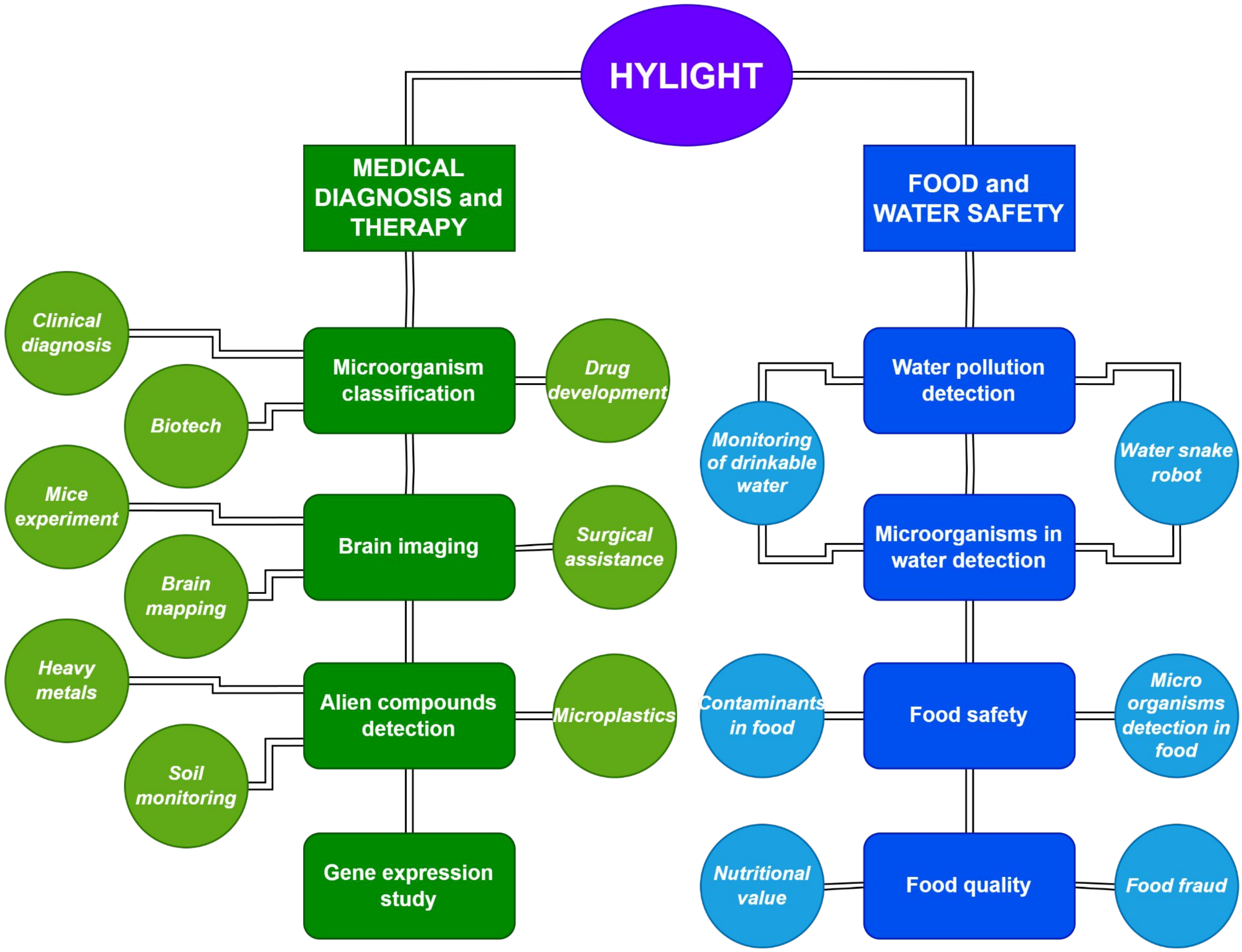
CONVERGENT PHASE: IDENTIFY 2 APPLICATIONS

The first milestone presentation marked the conclusion of the technology understanding phase and signalled the beginning of the critical prototypes one.
Following a convergent approach, the team faced the crucial choice of selecting which field of application to prioritize and which ones to discard.

To facilitate this decision-making process, the opportunities were categorized into two main groups: applications related to the medical sphere and those pertaining to safety and control. This categorization helped the team gain insights into whether multiple applications addressed similar problems but from different perspectives.

The medical category encompassed the classification of microorganisms, brain imaging, detection of alien compounds, and the study of gene expression. On the other hand, the safety category consisted of detecting contaminants and microorganisms in water, as well as ensuring food safety and quality.

The final decision was reached through a series of group meetings characterized by extensive discussions. These sessions allowed for comprehensive exploration of the strengths, weaknesses, and potential impacts of each application.
The objective was to achieve a unanimous choice by fostering an environment of open dialogue among team members.



After careful consideration, the team decided to focus on laboratory research and neurosurgery.
The selection process involved evaluating the level of innovation, the capacity to effectively meet diverse needs, and the feasibility of future development.
Moreover, also the team's prior knowledge and experience in these domains played a crucial role in the evaluation of the best pick.
Finally, both laboratory research and neurosurgery hold significant scientific and medical importance, providing an opportunity for the team to make a tangible impact by advancing drug analysis and improving surgical procedures.

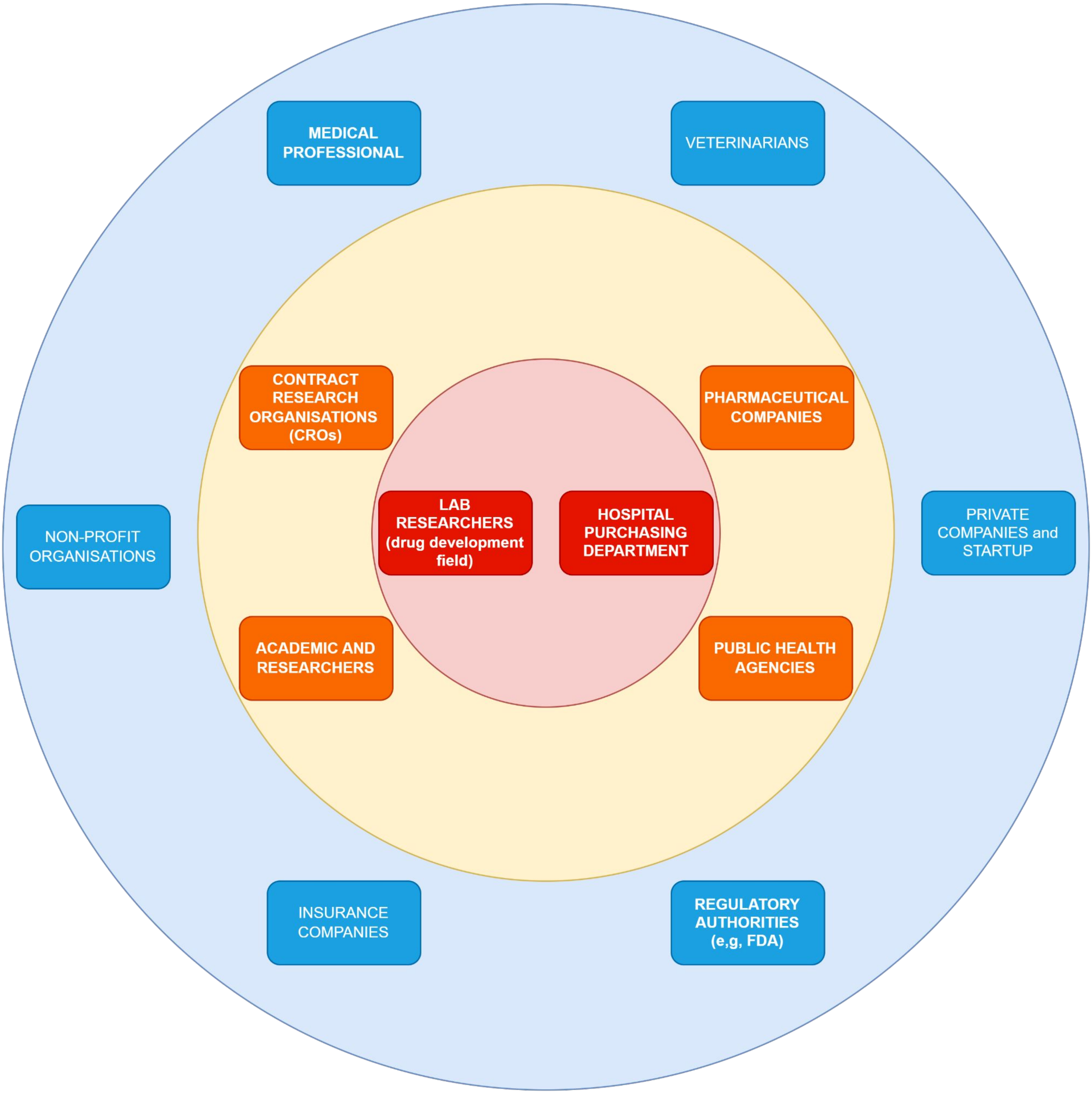
To validate this decision, the team thoroughly analyzed various factors.
A fundamental passage was the outline of the primary subjects involved in the implementation of Hylight in the selected field.
To this end were created stakeholders and users map for both the applications.
Once identified, the team began engaging with them to gather further insights on the project's viability.

STAKEHOLDERS - USERS MAP

NEUROSURGERY

STAKEHOLDERS - USERS MAP

LAB RESEARCH



VISIT AT THE RESEARCH CENTER

In the first day, the Hylight team and the research team at IBEC convened to discuss the feasibility, applications, and challenges associated with the Hylight project. The meeting focused on neurosurgery and research lab applications. In neurosurgery, the feasibility of implementing Hylight technology was explored, particularly in scanning biological tissue in vivo. While the answer to its feasibility remained uncertain, advancements in skin imaging for melanoma were noted.

Integrating Hylight with endoscopes or robotic arms posed challenges due to size reduction requirements. Requirements for utilizing Hylight technology were discussed, emphasizing the need for a dark environment around the sample. Solutions such as synchronizing room lighting or implementing filters were considered. The meeting also addressed scanning speed and resolution, with adjustments available for higher resolution at slower processing. In research labs, the application of Hylight for identifying organoids and similar samples was explored. Sample sensitivity and compatibility with different applications were crucial considerations. Defining specific biomarkers of interest, such as in cirrhosis research with liver cells, was highlighted as an initial step. Concerns regarding photobleaching and sample damage were addressed, with ongoing experiments aiming to minimize harm by controlling illumination power and duration. The integration of AI algorithms for predicting outputs and saving time was discussed as a potential avenue for development.

The first day meeting provided valuable insights into the feasibility, potential applications, and challenges of the project. While the feasibility of implementing Hylight in neurosurgery and research labs remained uncertain, the benefits of fast hyperspectral imaging and sample preservation offered exciting possibilities for future advancements.

During the second day, the challenges associated with separating biomarkers and the potential applications of Hylight in neurosurgery were discussed. The team explored the idea of using specific wavelengths of light to detect and quantify biomarkers in a sample. However, separating the signals from different biomarkers proved to be difficult, and the use of filters was suggested to address this challenge. It was noted that if a tumor has a significant amount of a specific biomarker, it may exhibit a distinct peak in the signal, aiding in separation. The need for minimizing imaging time and ensuring unique emission profiles for accurate analysis was emphasized.

Regarding tumor cell destruction, the meeting touched on the use of lasers. While the Hylight device aims to minimize harm, the specific method of laser application for cell destruction was not known. Different approaches, such as long exposure of longer wavelengths or short exposure of UV, were mentioned, but their limitations and compatibility with Hylight were unclear. The resolution of the device and its potential for real-time adjustment were discussed, with the ability to change resolution during imaging confirmed.

The meeting also touched on the application of Hylight in organoid research. The advantages of non-invasive imaging and the analysis of metabolic activity were highlighted. The limitations in terms of imaging time, sample characteristics, and comparison with other techniques were considered. The issue of maintaining a consistent distance between the device and the sample during imaging was raised, with suggestions such as using distance sensors or ultrasound to address it. The importance of a dark environment and the use of filters in the imaging process were also mentioned.

In conclusion, the meeting provided insights into the challenges of separating biomarkers, the potential applications of Hylight in neurosurgery, and the perspectives on organoid research. And the meeting identified the need for further research and development to address the technical limitations and optimize the performance of the Hylight device in various applications.

INSIGHTS INTO SURGICAL IMAGING TECHNIQUE

A conversation with Prof. Alba Scerrati

In an interview with Prof. Alba Scerrati, a renowned neurosurgeon, the discussion revolved around surgical imaging techniques and the existing methods for real-time imaging during tumor surgeries. Prof. Scerrati highlighted the use of fluorescent markers for tumor detection, emphasizing that the marker selectively targets the tumor while sparing the normal brain tissue. By integrating this marker into the surgical microscope and employing specific filters, surgeons can visualize the areas with fluorescence and distinguish them from non-fluorescent regions.

When questioned about potential improvements in the current technology, Prof. Scerrati acknowledged the availability of various tools such as navigation systems, ultrasounds, and fluorescence for tumor recognition. However, she expressed skepticism regarding significant advancements that could revolutionize the field. Nonetheless, Prof. Scerrati suggested focusing on finding a fluorescent marker to identify nerves during any surgery to prevent damage.

Regarding micro CT tools for cellular imaging, Prof. Scerrati acknowledged their existence but highlighted their limited impact on surgical practice. While these tools provide microscans of the brain's surface to detect tumors, their high cost and availability mainly in major cities like Rome or Milan restrict their widespread usage. Prof. Scerrati emphasized that these tools do not necessarily improve patient survival rates or the success of skilled surgeons, suggesting that the focus should shift towards preserving nerves during surgery rather than removing them.

In conclusion, the interview with Prof. Scerrati shed light on the current state of surgical imaging techniques and the challenges of introducing significant advancements. The integration of fluorescent markers and the use of specific filters in surgical microscopes have provided valuable insights during tumor surgeries. While improvements and automated tools may emerge in the future, the preservation of nerves and surgical expertise remain essential factors in achieving successful outcomes.

HYLIGHT FOR ORGANOID DEVELOPMENT AND TUMOR ANALYSIS

A conversation with Monica Baiula

In the interview with Prof. Monica Baiula, an update on the Hylight project was discussed. Prof. Baiula highlighted the potential of light sheet microscopy in evaluating the effects of drugs on both healthy and tumor cells. Understanding the response of healthy cells to drug effects is crucial in drug development. The technology can be applied to 2D and 3D cultures, allowing researchers to study cell colonies for primary analysis and more complex organoids for assessing drug penetration.

The interview delved into the challenges faced in organoid studies, which typically involve fixation, slicing, and analysis of different sections. However, the use of multiphoton microscopes that can directly analyze thicker tissue pieces offers an alternative approach. Monica Baiula also discussed the advantages of multi-content analysis technologies.

The conversation shifted to the application of light sheet microscopy in neurosurgery and tumor analysis. The possibility of using fluorescence microscopy to detect and classify biomarkers in tumor cells was explored.

In conclusion,the discussions shed light on the advancements, challenges, and potential solutions in utilizing this technology for lab research, neurosurgery, and tumor analysis. Continued research and innovation in this field will pave the way for further advancements and the realization of its full potential in various scientific and medical disciplines.

HYLIGHT IN NEUROSURGERY AND BEYOND

A conversation with Daniele Cartelli

In the meeting with Prof. Cartelli Daniele. the Hylight team explored the potential of light sheet microscopy in the field of neurosurgery. Prof. Daniele raised important doubts and suggested discussions with engineers and physicists to ensure the feasibility of implementing the magic angle required for light sheet illumination.

One of the challenges discussed was the need for markers in cell imaging. Prof. Daniele emphasized the potential advantage of developing a method that can discriminate between tumor and healthy cells without the need for staining. He mentioned existing techniques that show promise in literature but stressed the lack of human applications. The value of light sheet microscopy in neurosurgery lies in its potential for high lateral resolution, which can aid in precise surgical procedures by minimizing damage to healthy tissue.

During the interview, the Hylight team also explored the possibilities of light sheet microscopy in organoid studies. Prof. Daniele suggested that the system could easily be applied to organoids due to their self-contained nature. However, he noted that more research has been conducted on confocal microscopy in organoid studies, highlighting the need to determine the unique advantages that light sheet microscopy can bring to this field.

The potential application of light sheet microscopy in discriminating different types of cells was also discussed. Prof. Daniele mentioned the use of hyperspectral analysis and techniques like second, third, and fourth harmonic generation to distinguish between different components of tissues based on their fluorescence and signal properties. This innovative approach could contribute to advancements in tissue analysis and discrimination, particularly in neurosurgery.

SECOND MILESTONE

The project's Second Milestone is connected to the research group of Hylight. It examines two possibilities and their potential effects on user personas, user journeys, relevant evidence and learnings, and value statements.

After the interviews with expretises, the team selected two surgical and laboratory research possibilities. It improves surgical precision, reduces complications, and advances surgical procedures, improving patient safety and surgeon empowerment. Hylight accelerates drug development, improves discovery, and helps generate precision medication in lab research, advancing science and improving treatment efficacy.

Hylight's 5D imaging and endometrial disease and embryo selection applications are relevant evidence and learnings. Light-sheet microscopy, multi-photon imaging, phasor hyperspectral analysis, and AI can use Hylight . The technology can improve surgical precision, reduce complications, advance surgical procedures, accelerate drug development, improve discovery processes, and generate precise medicine.

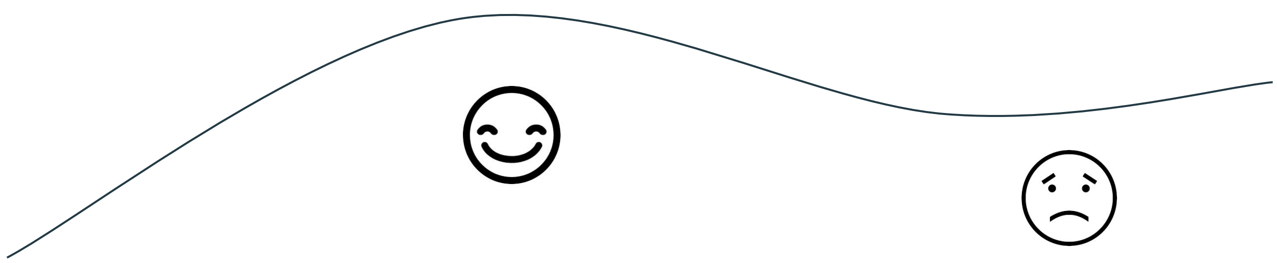
The value statements for Hylight technology emphasise the need of pursuing this route to boost drug development, accelerate discovery procedures, and generate precise medicine to advance science and improve treatment efficacy. Improved surgical precision, reduced complications, and advanced surgical procedures ensure patient safety and empower doctors. In laboratory research, this direction accelerates drug development, improves discovery procedures, and develops precision medicine, advancing science and improving treatment efficacy.

USER PERSONA AND USER JOURNEY

A user persona is a fictional representation of a specific target user group, created to better understand their characteristics, preferences, behaviors, and goals in order to tailor products and services to their needs.

In the human-centered design of the device Hylight, user personas are instrumental in identifying the potential audience for our technology. The team employs personas as a communication tool to engage with and understand the needs of potential users of our device.

A user journey refers to the entire process that a user undergoes while engaging with a product or service, starting from their initial interaction until they achieve their desired outcome. It encompasses all the stages and touchpoints within the user's experience.



The user's journey can be likened to a roller coaster, with its ups and downs representing the emotional fluctuations experienced by users. Each step along the journey can elicit positive or negative experiences. When mapping the user journey, we gather valuable information in the form of user actions, emotions, and relevant data. By combining these elements, we obtain the necessary data for analysis.

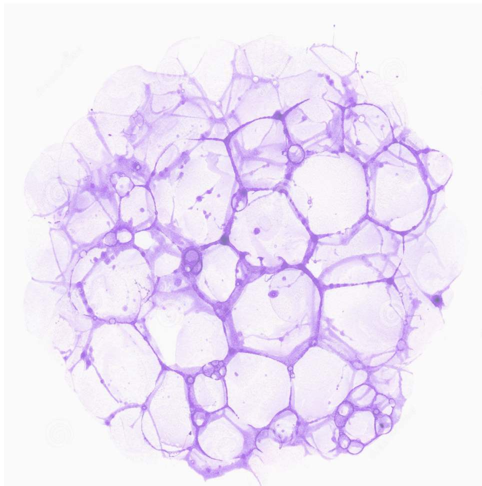
USER PERSONA
LABORATORY RESEARCH

Name: Dr. Emily Rodriguez
Occupation: Drug Development Researcher

"Frustrations arise when traditional methods fail to capture the intricate metabolic process es and subtle changes within organoids, hindering our ability to fully understand the drug's impact."

Profile:

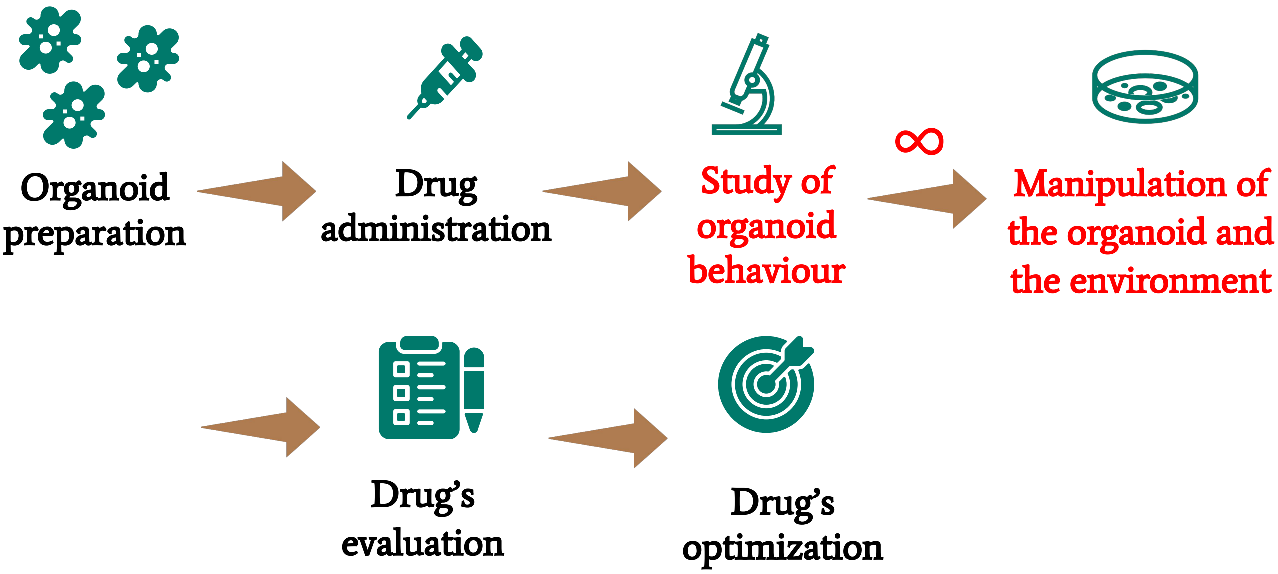
- researcher in the field of organoid-based drug testing
- needs of ACCURATE and EFFICIENT analysis



Dr. Emily Rodriguez, this character was simulated as a representative of the user, is an accomplished drug development researcher specializing in organoid models, seeks innovative solutions to study cellular metabolism. With a Ph.D. in Pharmacology, she analyzes the effects of drugs on organoids to enhance drug discovery. Driven by curiosity, she thrives on solving complex problems and collaborates to push scientific boundaries.

Introducing Hylight, a revolutionary product for studying cellular metabolism in organoids. It offers high-precision detection and real-time monitoring of metabolic processes. Dr. Rodriguez values collaboration and requires user-friendly interfaces, seamless integration, and robust validation to adopt new tools. She currently uses imaging techniques and manual data processing but aims for optimized workflows and more reliable data.

USER JOURNEY
LABORATORY RESEARCH



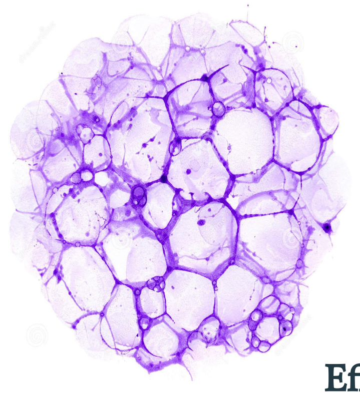
Throughout their user journey in drug development and lab research, the process involves specific steps. Firstly, the researcher prepares a specific organoid to test the drug on. Once the drug is chosen, it is injected into the organoid. Using Hylight, the researcher captures time-lapse images with a spectral component, enabling fast output without cell damage. By exploiting the fluorescent characteristics of the cells, the researcher visualizes different cell types and their reaction to the drug over time.[8]

With the help of AI intelligence, the researcher predicts the organoid's future behavior, such as its evolution or potential cell death. These predictions inform the manipulation of the organoid or its environment, allowing the researcher to modify inputs and conduct multiple experiments simultaneously, saving time and resources. Analyzing the experiment's outputs, the researcher draws conclusions about the drug's response inside the organoid.

EVIDENCE AND LEARNING
LABORATORY RESEARCH

Organoid Analysis and Imaging: MORPHOLOGY, VIABILITY, AND FUNCTIONALITY

Monitoring Cellular Environment: pH levels, the presence of SPECIFIC MOLECULES and other compounds



In Vitro Scanning: allow for CONTINUOUS MONITORING

AI Integration: AI algorithms allows to PREDICT CELL BEHAVIOUR AND OPTIMIZING THE PROCESSES

Efficiency and Reliability: RELIABLE RESULTS

Hylight has its advantages in the field of drug development research due to its potential for analyzing cellular processes. It offers advanced imaging and analysis techniques specifically designed for characterizing complex cell models known as organoids. Researchers can take advantage of Hylight's unique feature of repeated in vitro scanning, allowing them to continuously monitor and observe changes in the cellular environment over time [3-11].

Moreover, the integration of AI algorithms enhances Hylight's functionality by predicting cell behavior and optimizing drug-related processes. With its emphasis on efficiency, reliability, and real-time monitoring, Hylight provides researchers with valuable insights into the metabolic and morphological changes occurring within cell cultures. By empowering researchers in their drug development endeavors, Hylight proves to be a valuable tool in advancing scientific knowledge and accelerating the discovery of new therapeutic solutions.

VALUE STATEMENT
LABORATORY RESEARCH

Pursuing this direction is important to:

Improve Drug Development

Accelerated Discovery

Develop Precise Medicine

Impact:

Scientific Advancements

Improved Treatment Efficacy

The utilization of Hylight in drug development research holds great importance due to its advanced imaging capabilities. By leveraging Hylight, researchers can gain deeper insights into cellular behavior, leading to more effective drug development and optimization. This accelerates the research process, enabling efficient drug delivery, cell colony preparation, and evaluation of cellular responses. Furthermore, Hylight's ability to classify healthy and pathological cells opens doors for personalized medicine approaches. By tailoring treatments based on individual cell characteristics, Hylight contributes to the development of targeted and effective therapies.

USER PERSONA
SURGICAL FIELD

Name: Dr. Michael Roberts
Occupation: Expert in neurosurgery

"Currently, I heavily rely on pre-operative imaging scans and my expertise to identify and remove brain tumors."

Profile:

- work shifts of more than 10 hours
- intense concentration and high responsibility

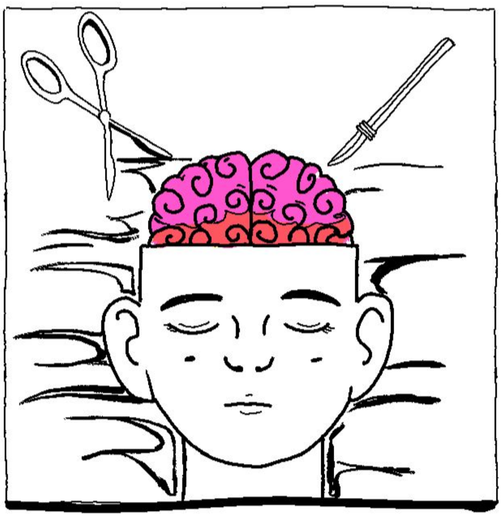
Challenges, Frustrations, and Fears:

- difficulty of achieving complete tumor resection while preserving critical brain functions
- lack of real-time feedback
- emotional and physical toll

As a virtual representative, Dr. Michael Roberts, he is a highly experienced neurosurgeon specializing in brain tumor removal.. He faces the challenge of achieving complete tumor resection while preserving critical brain functions. Dr. Roberts collaborates with scientists and engineers to explore innovative techniques and devices that can improve tumor detection and removal for his patients. In his evaluation of products, he values reliable and real-time information about tumor location, extent, and margins during surgery, as well as seamless integration into his current surgical workflow. Rather than focusing on the price, Dr. Roberts prioritizes the effectiveness and reliability of the new product.

USER JOURNEY
SURGICAL FIELD

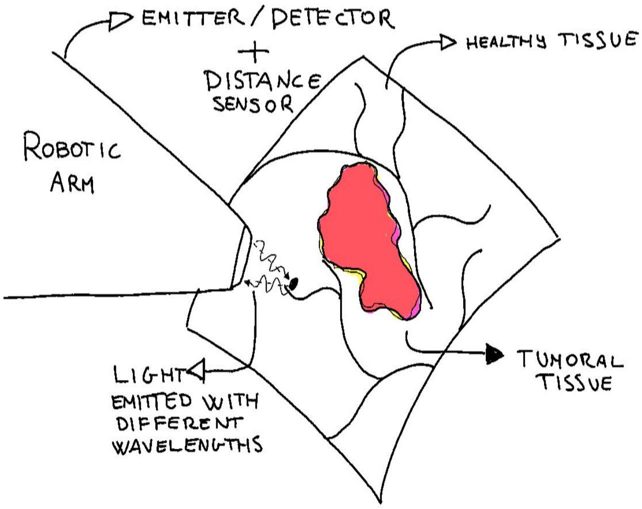
Prior set up



The first step in Dr. Michael Robert’s journey is the prior set-up, which involves conducting initial analyses such as MRI or CT scanning. These tests are performed to assess the patient's condition, including the presence of tumors and their extent. The purpose of these procedures is to provide the surgeon with a clear understanding of the specific situation they will encounter. Once this set-up is completed and the necessary information is gathered, the surgeon can proceed with the craniotomy.

USER JOURNEY
SURGICAL FIELD

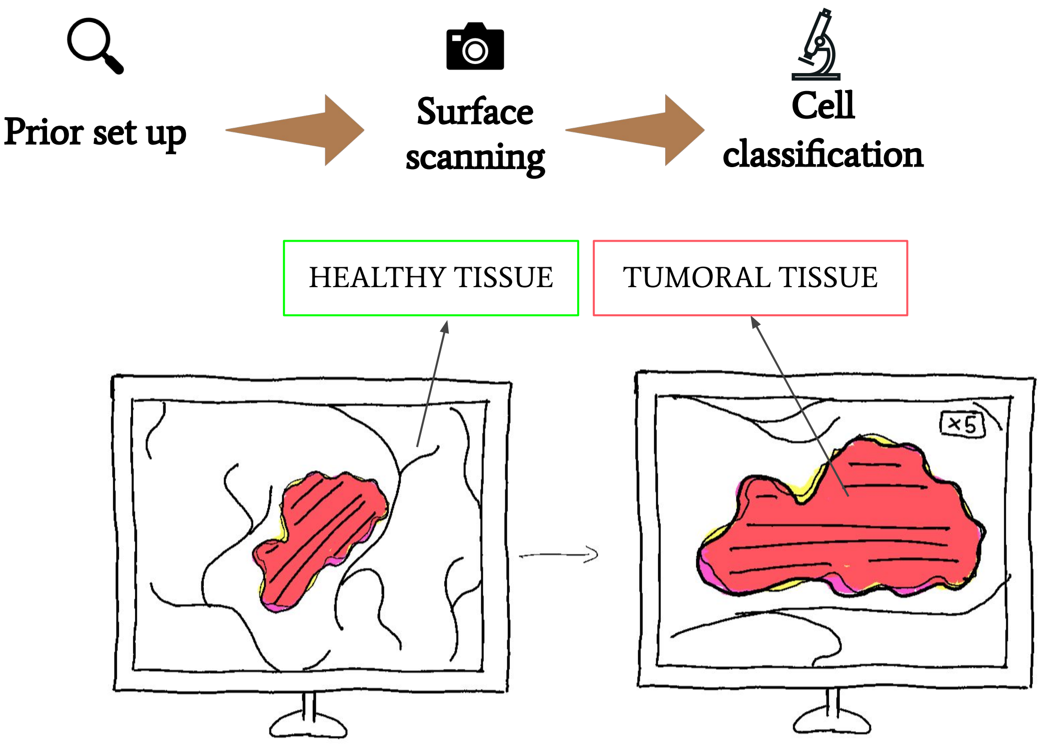
Prior set up → **Surface scanning**



After the cranium has been opened, the next step involves utilizing Hylight to perform surface scanning of the brain, capturing three-dimensional images with a spectral component.

However, it is important to address a specific problem during this process. Hylight requires either a dark environment or a controlled lighting setting that does not interfere with the specific wavelengths used for the analysis. This consideration ensures accurate and reliable data acquisition without any external light interference.

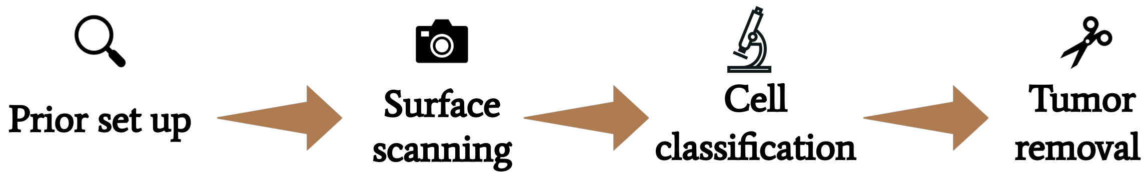
USER JOURNEY
SURGICAL FIELD

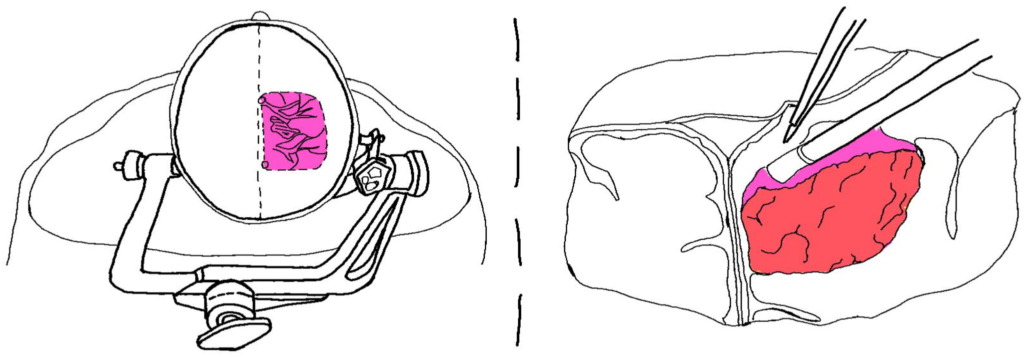


In the third step of the user's journey, the surgeon utilizes Hylight to classify cells. After conducting a surface scan, Hylight enables the surgeon to differentiate between tumoral cells and healthy cells. The fluorescent properties of the tumoral cells cause them to react differently to the light emitted by Hylight.

Additionally, Hylight is capable of detecting nerves, allowing for the creation of a comprehensive map of nerves, tumor cells, and healthy cells. During the classification process, the surgeon receives assistance from a trained AI system. This AI system recognizes the tumoral mass and provides guidance on identifying the specific area that needs to be removed. The combination of Hylight and the AI system enhances the accuracy and efficiency of cell classification, facilitating informed decision-making during surgical procedures.

USER JOURNEY
SURGICAL FIELD



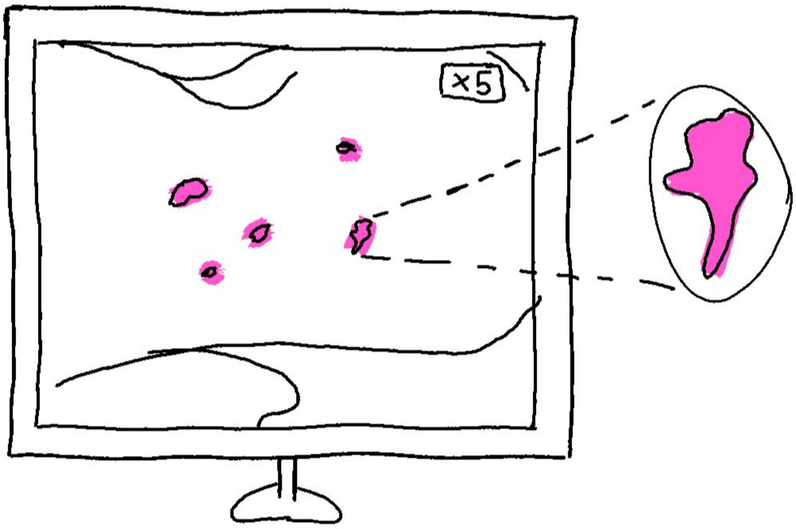


The laser technology utilized for tumor identification in the previous step can also be employed for high-precision tumor removal, known as laser ablation. Leveraging the precise mapping of the tumor, laser ablation enables complete removal of the tumor while minimizing damage to surrounding healthy cells.

Additionally, the mapping of nerves using the laser technology helps surgeons avoid any potential harm to these critical structures during the tumor removal process. This addresses a significant challenge in current surgical procedures and contributes to safer and more effective surgeries.

USER JOURNEY
SURGICAL FIELD

Prior set up → Surface scanning → Cell classification → Tumor removal → Follow-up scans



In this critical stage, Hylight plays a crucial role in the process of brain surgery. While the laser ablation is being performed, Hylight is used to conduct continuous scans of the brain surface. This continuous monitoring allows for the highest level of precision in tumor removal while minimizing the risk of damaging nearby nerves. By ensuring complete removal of the tumor, Hylight significantly enhances the effectiveness and success of the surgical procedure.

VALUE STATEMENT
SURGICAL FIELD

Pursuing this direction is important to:

Surgical Precision

Minimized Complication

Advanced Surgical Techniques

Impact:

Improved Patient Safety

Surgeon Empowerment

In the realm of surgical procedures, the integration of Hylight as a nerve recognition tool holds immense significance. By incorporating Hylight into the surgical workflow, surgeons can augment their ability to identify nerves before tissue cutting, leading to enhanced surgical precision. This advanced technology reduces the potential for nerve damage, consequently improving patient safety and mitigating the risk of post-surgical complications.

The implementation of Hylight's nerve recognition technology brings about tangible benefits in terms of improved patient safety. By accurately identifying nerves before tissue cutting, Hylight minimizes the risk of unintended nerve damage, safeguarding the well-being of patients. Furthermore, Hylight empowers surgeons with a laser ablation probe specifically designed for nerve recognition, enabling them to perform peripheral surgical operations with heightened precision and efficiency.

END OF THE PROJECT

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CONVERGENT PHASE: IDENTIFY 1 APPLICATION

After the second milestone the team was left with two choices:
drug development or surgical assistance.
The first option was pretty straight forward, as there was little to be changed in Hylight technology to apply it. However, at the same time the improvement in the field was not "market disruptive".
The latter option came with higher risks, as there were still some unknown variables - technology itself needed to be altered, therefore it would have taken a considerate amount of time to introduce the product to the market. Despite this, it would have been something unseen, something that could change the current way of surgeries.

Thus, as a team with ambition, it was chosen to work further on the surgical field!

SURGICAL FIELD: CRUCIAL COMPONENTS

To have a successful device for microsurgeries, the team had to satisfy the needs of surgeons and to provide the required conditions for a successful surgery.

The further paragraphs will explain this necessities in detail.

NERVE IMAGING

According to interviews with surgeons and research in the literature, there is no non-invasive method to observe nerves in patients. This is a huge problem, because it is crucial to observe them during operation, as their damage could paralyse the patient.
For this reason a surgeon would greatly benefit if there would be a device that could show the exact location of the nerves.

Recently, it has been published a paper that explored the capabilities to observe nerve autofluorescence in near UV on animals [4].
Although Hylight operates in NIR, the article shows the potential of using the technology during surgeries in a non-invasive way.
Apart from that, there are many ways to use binding fluorophores in NIR that can also be used for nerve imaging [14-15].

Thanks to its capability of nerve recognition, Hylight would be able to classify the cells into 3 types: healthy cells, target cells (tumours etc.) and nerves.

LASER ABLATION

Laser ablation is a surgical technique that involves the use of laser energy to precisely remove or destroy tissues. It is commonly used in various surgical procedures, including neurosurgery, where it can be employed for tumor removal, tissue ablation, and other therapeutic purposes.

The process of laser ablation involves the delivery of high-energy laser light to the target tissue. The laser emits a concentrated beam of light that interacts with the tissue, causing thermal energy to be absorbed. This energy absorption leads to the rapid heating and vaporization of the tissue, resulting in the removal or destruction of the targeted area.

This procedure could be performed with Hylight!
The NIR laser used for imaging can be adjusted to serve the purpose of cell destruction [12]. With the combination of precise information of target cells, for example the fact that tumoral cells increase the temperature in a faster manner (therefore are destroyed before healthy cells), the target can be removed with great accuracy and without damaging the nearby tissue.

AUTOMATIZATION

In the operation there is an open surface where the target is concentrated.
What is left is to accurately locate all the target cells and remove them with great precision.

This process could be automated with Hylight, thanks to the combination of the previously mentioned techniques!
Firstly, the surface area can be scanned with an adaptive grid basing on the information gathered before the operation. In this way it is possible to save for scanning all the layers, which is very important for real time target removal.
Secondly, the target is removed with laser ablation: from the previous step a precise map has been acquired with a location of all the healthy, pathogenic and nerve cells.
Therefore human intervention can be minimal, as the laser can do the removal on its own following the coordinates, and then performing subsequent scanning to remove the remaining target cells.

BENEFICIAL PARTIES

PATIENTS

- **Higher success rate** - the success of the surgery is increased, thanks to the reduction of damage to nerves and the improvement in the accuracy of target removal.
- **Shorter operations** - as the operation can be done faster, there are less possible complications due to exposure of the surface as well patients time is saved.
- **Availability** - prospect of automatization means that the operations will be more accessible, hence allowing to get the treatment faster.

SURGEONS

- **Shorter surgeries** - allows surgeons to help more people in need.
- **Higher success rate** - possibility of nerve recognition, as well as automated target removal eliminate human error possibility.
- **Assistance** - the assisted process allows the surgeon to do less mechanical and more intellectual work during surgeries, such as decision making.
- **Mental health** - less toll on surgeons allows them to be mentally healthy, which increases the productivity of their work and personal well-being.

ATTRACT EXPO

On the 16th of June the team had an opportunity to present their work in an expo. A prototype had been made and people from different backgrounds came to the booth to know more about the idea.
Most of them were impressed and saw great potential in Hylight!

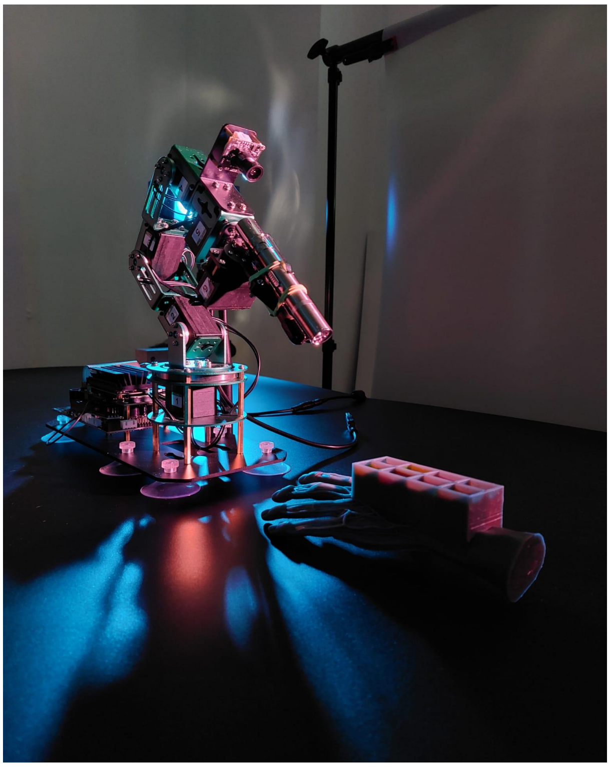
PROTOTYPE

Entered in the prototyping phase, the first step was to identify the main goal.
With that level of knowledge, time and materials, it was impossible to build something that could replicate any of the functions the team thought. However, it was possible to create a simulation of them. That became the aim of the end product.

The crucial components included in the prototype are:

- cell classification in the target;
- ability to observe nerves;
- ability to show the promise of automatization.

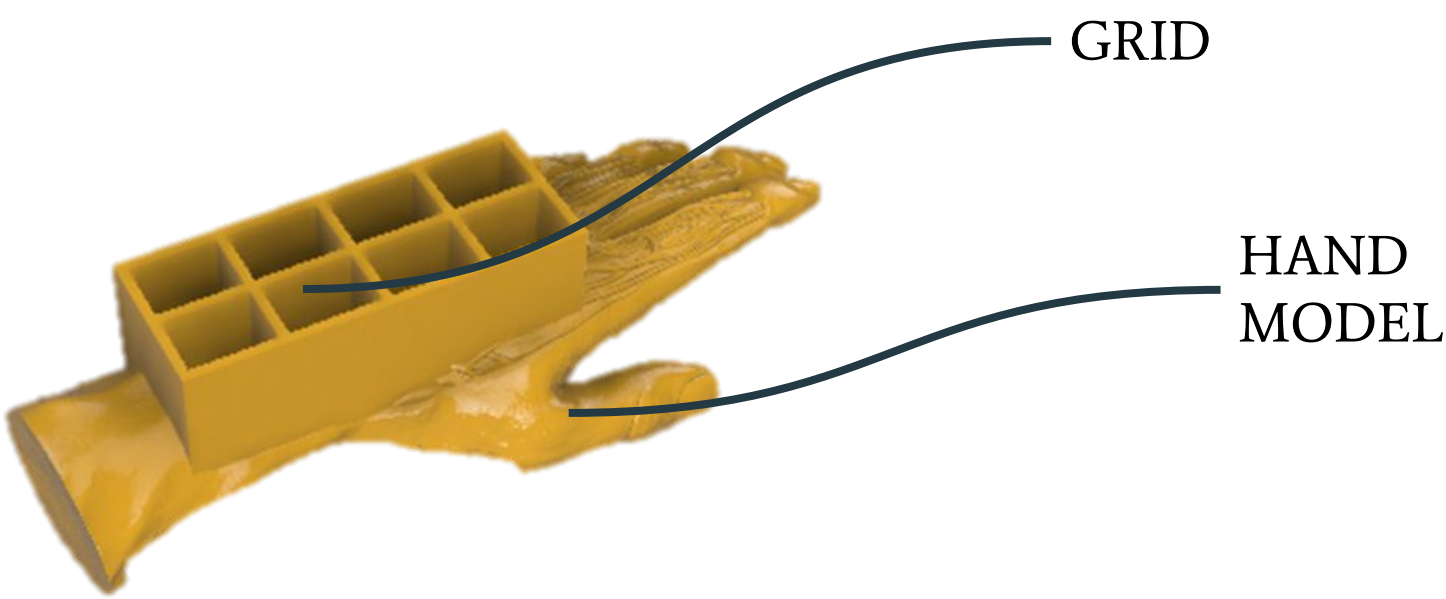
The following image shows the obtained result:



PROTOTYPE
HAND

Firstly, the team needed to identify the “object of the operation”.
A brain was an obvious choice, but in that case it was not possible to show the full capacity of the technology.
Therefore a hand was chosen.

The model of the hand was made in “Fusion 360 “and then printed with a 3d printer.
To show the cell classification, for simplicity reasons, the team decided to use as grid: each square of the grid represented a cell, that could be either a nerve, a healthy or a target cell.
In order to help the observer in distinguishing them, they were colored with fluorescent dye.



PROTOTYPE
CELLS

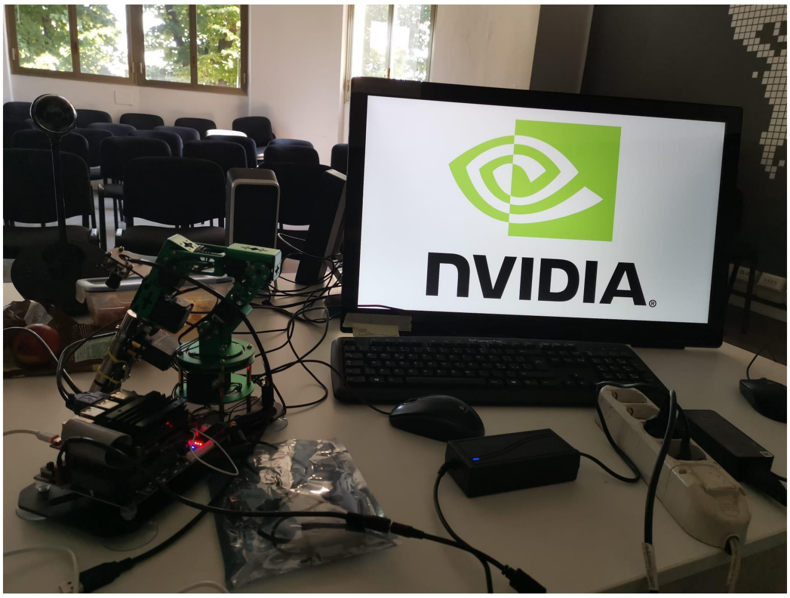
Secondly, the team focused on how to visualize the cells.
To simulate Hylight, that exploits autofluorescent properties of the target, two different fluorescent dyes were bought: Rhodamine and fluorescein sodium.
In this way it was possible to obtain three different colors/cells (the third was mixture of both).

To simulate their excitation, UV light was used.
With the laser turned off, there isn't a clear distinction between the cells: this situation represents what a surgeon would see without any imaging technique.
Once the UV light is used (although Hylight uses NIR), a clear distinction is visible: this allows a cell classification with great precision.

PROTOTYPE
ROBOTIC ARM

Lastly, there was the need to use a probe or a robotic arm to perform all the tasks, including laser ablation (yet to be added).

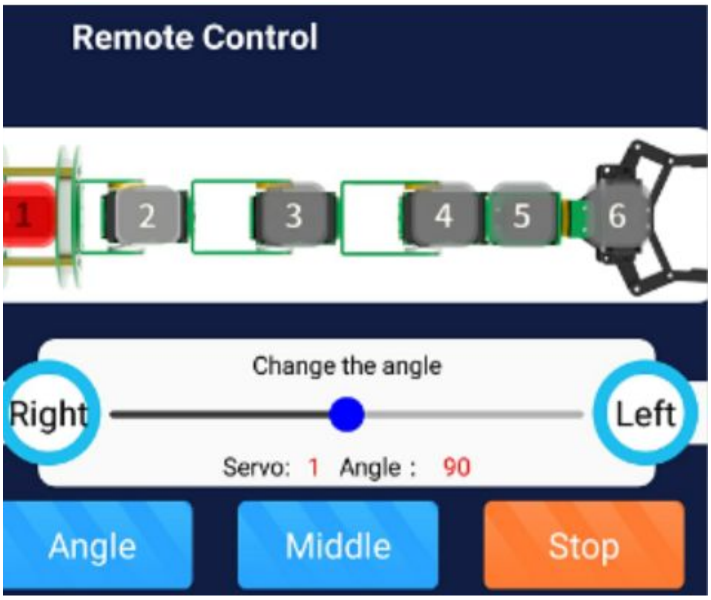
For this function, a programmable robotic arm with Jetson Nano B01 was used. Thanks to its six degrees of freedom, it could be moved in sophisticated ways, replicating as close as possible the needs of an actual surgeon.



To install the system in the robotic arm, it has been necessary to download the appropriate system image and boot file from: DOFBOT-Jetson (yahboom.net).

Then, using a virtual machine of Ubuntu not newer than 18.04. the system was installed according to instructions.

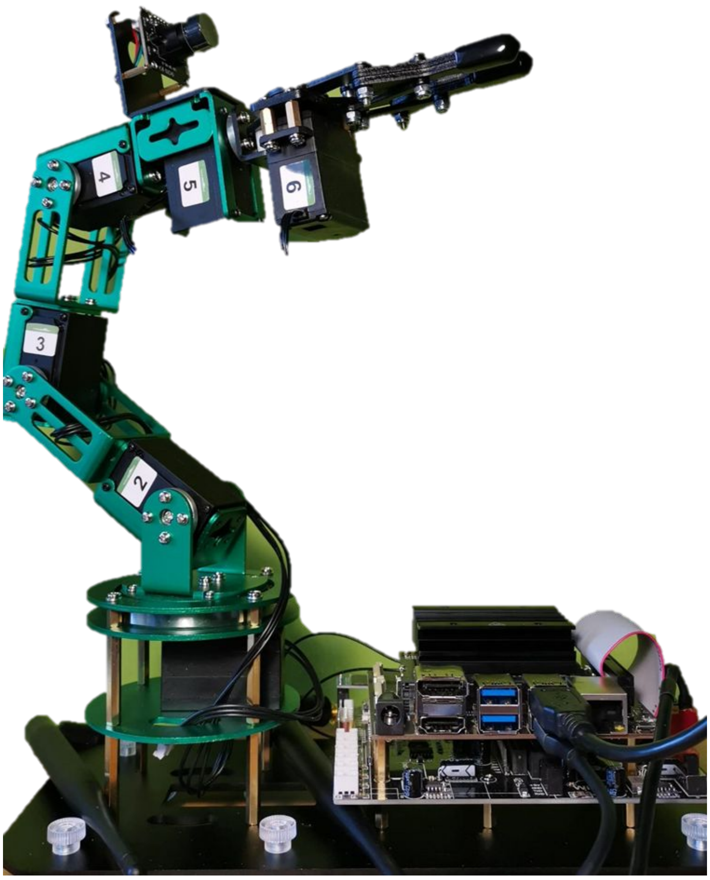
PROTOTYPE
ROBOTIC ARM



The robotic arm can be moved with an application of the manufacturer - Yahboom (picture to the right) - which includes several predefined functions, such as gesture recognition, in-built movements and other actions.

It can also be programmed with computer vision in Python, using OpenCV to perform automated tasks. This option could be exploited to simulate automated surgical engagements.

To reproduce laser ablation, representing NIR laser from Hylight, the team used a red laser, which could be grabbed by the robotic arm.

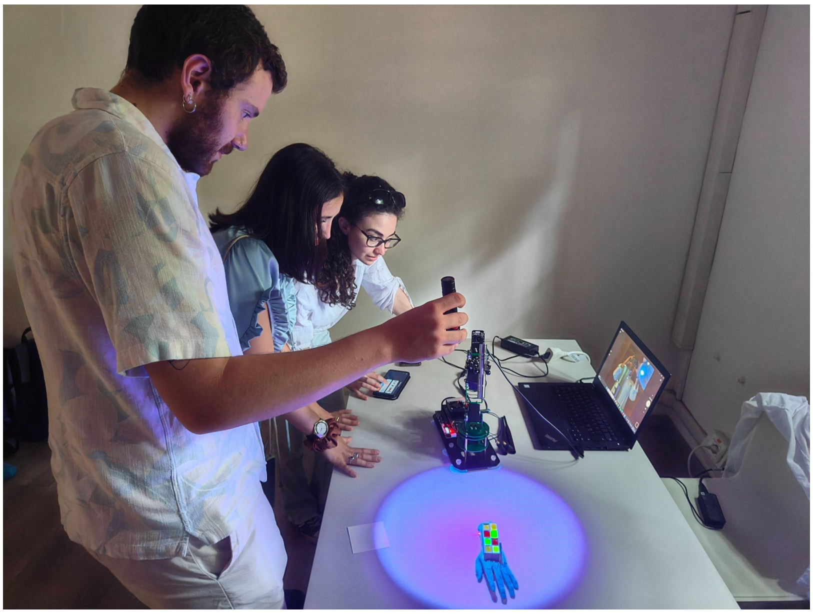


PROTOTYPE
THE FULL EXPERIENCE

Following the passages above-mentioned, it is possible to obtain the full user experience of using the prototype. The steps to follow are:

- Try to differentiate the cells without UV light (which is very hard)
- Turn on the UV lamp and see the three different cell types shown in the grid (now it is possible to distinguish them).
- Thanks to a mobile application, take control of the robotic arm (the idea is to automatized the next steps of the process).
- Turning on the red laser (laser ablation) and pointing it towards the targeted cells.

In doing this procedure, the user (surgeon) can observe every movement from a monitor, that shows what is recorded by a camera installed on the robotic arm (see image below).



In the future, to improve the overall experience, the movements of the robotic arm will be automated. Moreover, with the help of computer vision, the device will be able to detect the different cell types just by the color, and then move the arm accordingly to do the laser ablation or, in this case, pointing the laser at target cells.
The user would only have to confirm the procedure: assessing the accuracy of the target identification and ablation.

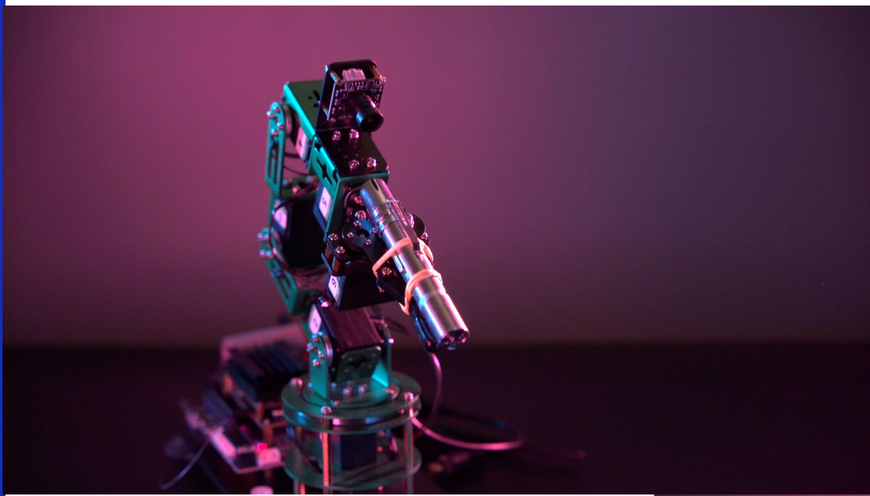
This changes would bring the prototype closer to the actual experience of the surgeon (the potential user of the device).

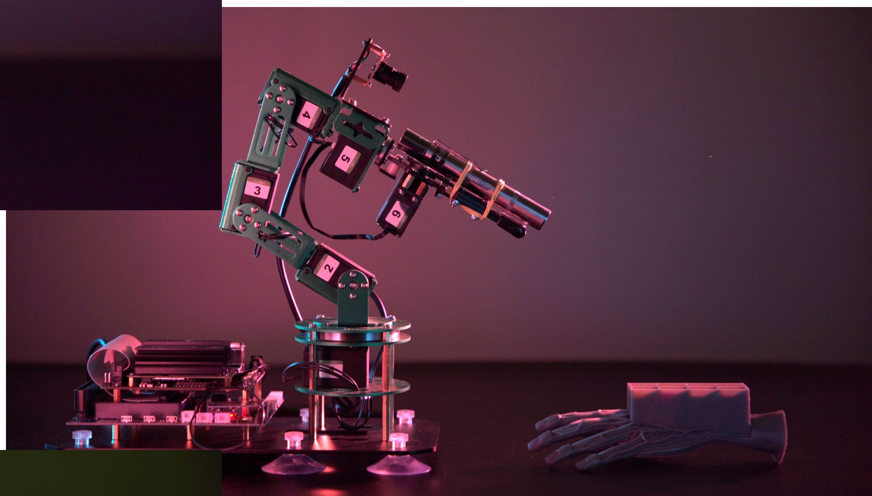
PROTOTYPE
THE BIRTH OF HYPER-EYE

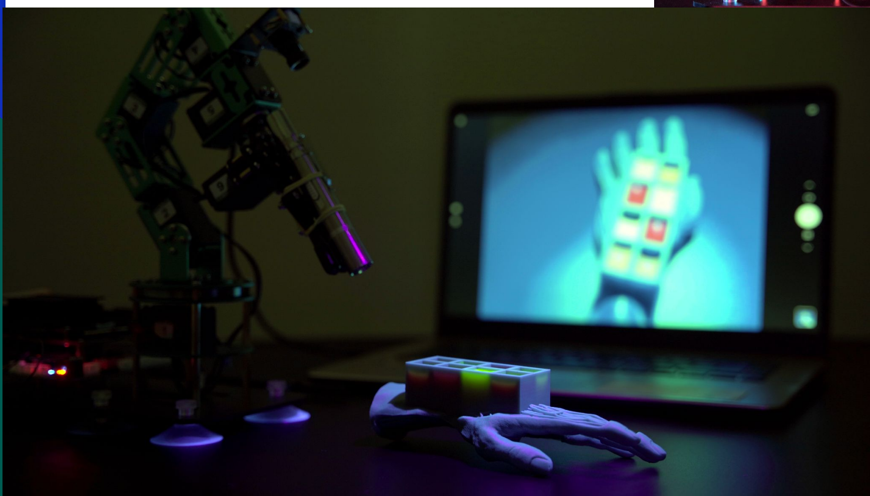
Hyper-Eye assistant is the name the team decided to give to the whole process. For the first time, we have the passage from Hylight technology, developed by IBEC, to *Hyper-Eye assistant* solution.

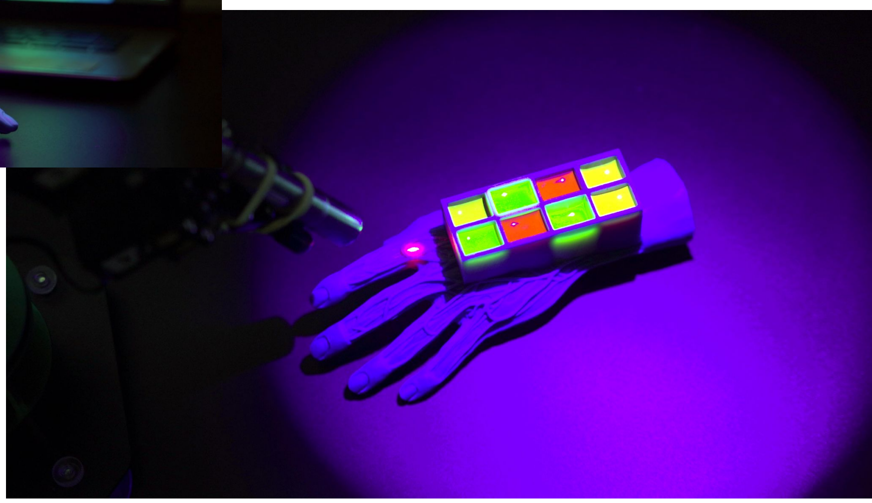
To help better understand the solution, the team created a video:
Hyper-eye assistant - YouTube

HYPER-EYE









FROM HYLIGHT TO HYPER-EYE

To make Hyper-eye not only a prototype, but a properly working device, a few steps need to be taken:

1. MICROSCOPE IN A PROBE

It is essential for the light-sheet microscope to have a 90 degree angle with the target, but it is very hard to do so on a surface for a human tissue. Not only that, now the device has the size of approximately cubic meter, which is hard to compress.

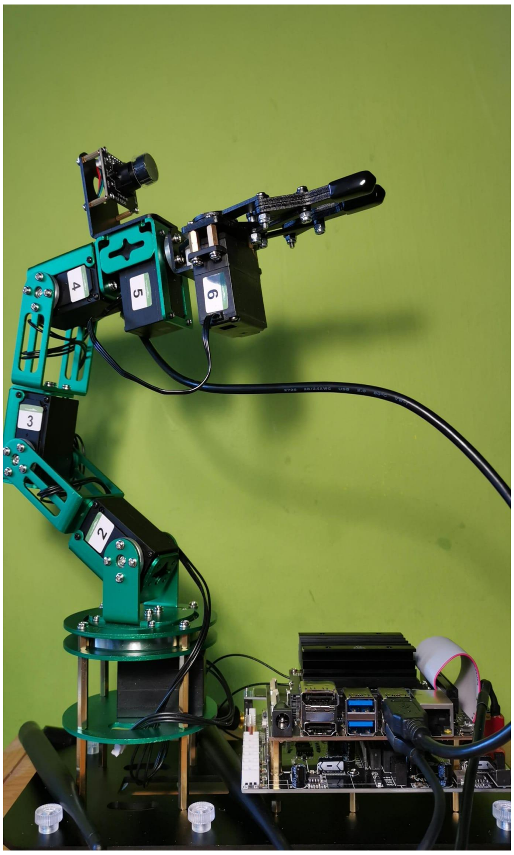
The 90 degree issue can be solved by using confocal microscope, but then the cells can be damaged and the technology losses one of it's key properties. Otherwise a clever engineering solution is needed.

2. PROGRAMMABLE ROBOTIC ARM

The device must perform certain tasks in automated manner. Here it is mostly about the laser ablation, as in the previous steps accurate coordinates of target cells have been acquired. Now the goal is to move the laser to the target cells, remove them using thermal ablation, and leaving the nerve cells and other healthy cells intact.

It should be straightforward with the information that it has, but as people lives are on the line, you can never be too sure. For that reason surgeons will have an interactive software for accepting or denying actions that Hyper-eye wants to perform, such as laser ablation and repeated scanning.

Other automated tasks include scanning functions, such as changing the adaptive grid, focusing on certain parts more (for example, where target boundaries might be) or altering the depth.



3. AI FOR CELLS CLASSIFICATION

"It is possible to use hylight to differentiate between myelin, tumoral cells and other types of tissue. If you train the system to make this distinction it could be an innovative application of your work."

Researcher at Neurologic Institute Carlo Besta

This is the most important feature of Hyper-eye - classifying cells with autofluorescence non-invasively. With the subcellular resolution, it is possible to even observe metabolic processes of cells, which can quite clearly differentiate between healthy and tumoral cells.

The spectra differs for different tumors in different stages, which means that there are many variables, why AI classification is needed in this case.

To train the AI model, a large training set is needed with the target cells (where tumor is only one of them). For that reason it is possible to use, for example, "The Cancer Imaging Archive", "Genomic Data Commons", University of California, "Irvine (UCI) Machine Learning Repository" and more yet to be published.

4. LASER ABLATION

"If you increase the power you can use the same laser to detect the tumoral cells and then to kill them with pulses of light that are very short and intense"
Samuel Ojosnegros, Hylight

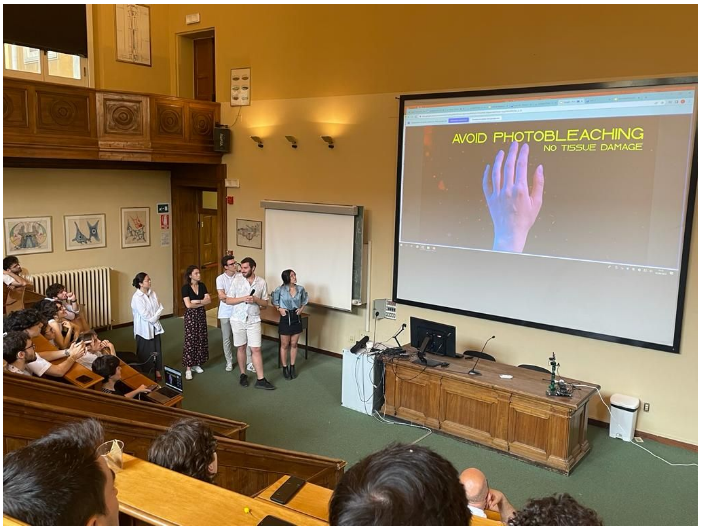
Laser ablation has been used in surgeries for several decades. But mostly it has been done using optical fibers that are inserted in to the target tissue. There are also probes or needles from which the laser energy is delivered. But with Hylight technology it is presumably possible to move the robotic arm close enough to the target tissue, aim the laser and deliver the energy through air.

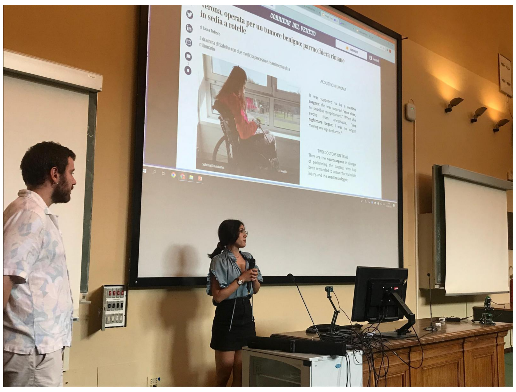
The enginerical issues to be resolved are precision - can the laser be moved with enough accuracy to the given coordinates? And can it be used safely, not affecting the surrounding tissue? These are the questions that need to be addressed developing this feature for Hyper-eye.

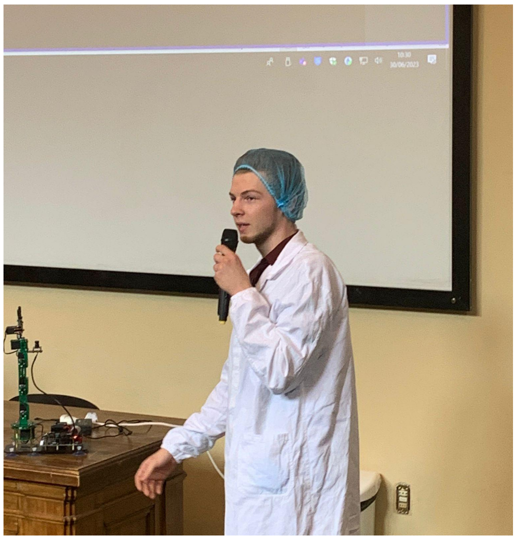
HYPER-EYE STRENGHTS

- No photobleaching - as the method is not using dyes and a laser of NIR light, there is no damage to fluorescent capabilities of the cells. Not only that, but also dyes do not falsely attach to the healthy cells or not attach to the tumorous cells. Hence there are multiple advantages of not using fluorescent dyes.
- Nerve imaging - first method that could non-invasively detect them, allowing the surgeon to avoid any damage to them, which results in a higher success rate of the operation.
- Imaging and laser ablation - Hyper-eye not only can make accurate images in different depths of the tissue of different cells, but also remove them with laser ablation. Such combination would be a new addition to the surgical field.
- Automated surgery - automated surgeries is the future of medicine, that will improve the result of operations and allow doctors to have improved mental health.

FINAL PRESENTATION







FINAL CONSIDERATION

The past four months working on this innovation program have been an incredible journey for all of us.
We faced numerous challenges, encountered obstacles, and even stumbled along the way. But instead of letting those difficulties discourage us, they became the driving force to complete this project.

Let's be honest - it wasn't always smooth sailing. We had our discussions, misunderstandings, and, sometimes even quarrels. However, what truly mattered was the commitment to supporting one another and working together towards our common goal.

Throughout this experience, we had the privilege of meeting and interviewing several experts, researchers, and teachers who generously shared their time, ideas, and knowledge with us. Their help, advice and contributions proved to be crucial in reaching the final outcome, and we sincerely thank them.

Moreover, we formed deep connections with our fellow colleagues, who turned out to be not just exceptional professionals, but also incredible individuals and friends.
We shared anxieties, fears, and hopes, growing together as we navigated uncharted territory. It has been a pleasure to share this experience with them.

To everyone who supported us along this remarkable journey, we want to express our deepest appreciation.
Firstly, thanks to Samuel, Anna and all the members of IBEC who developed Hylight: you gave us the possibility to work and innovate with the technology and we are grate for this.
Then, thanks to Giovanni for his patience and his commitment: your guidance and insights have been of great help!
Last but not least, thanks to Lucia, for listening to our complaints and for supporting us during the whole experience: you started as a coach, and you became a genuine and loyal friend.

We start this journey working with a technology we did not know and collaborating with people we had never met.
Together, we explored numerous possible applications where Hylight could be used to generate a great impact.
Through careful considerations, we identified the microsurgical field as the most promising option, conceiving to use Hylight as an assistant for the surgeons.
We firmly believe in the potential of this idea, even though we are conscious of the necessary adjustments and improvements required to test its feasibility thoroughly.
As we conclude this journey, we do so with the awareness that we have built something truly important.

The Hylight Team

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