COBIOPHAD

Compact biophotonic platform for drug allergy diagnosis

H2020-ICT-2015-28a-688448

The COBIOPHAD project has reached a satisfactory conclusion. After more than three years working on the development and integration of different technologies and a preliminary validation of our system, we are proud to announce that the project has successfully finished, and finally we have a complete, portable and low-cost *in vitro* prototype for rapid detection of IgE mediated allergies to beta-lactam antibiotics.

During our final review meeting, the consortium had the opportunity to share the final results and conclusions, as well as some discussions about the future of our developments.

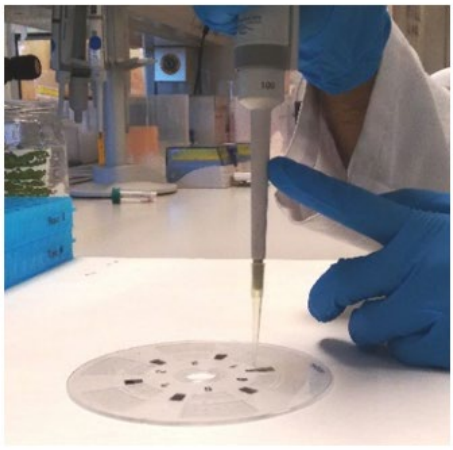
The problem addressed

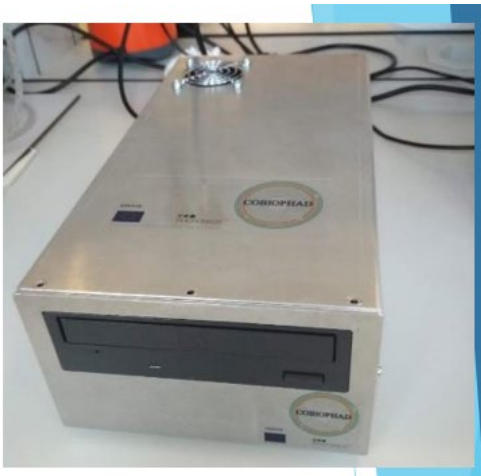
Over 2.5 million people in Europe and more than 5.4 million Americans suffer from hypersensitivity to β-Lactam Antibiotics (BLCs) and these figures increase every year due to the misuse and consumption of these antibiotics. Moreover, BLC allergy is the most frequent cause (47%) of drug anaphylaxis, and is an important public health problem with an estimated in additional hospitalization costs of 1750-4500 €/patient.

Drug hypersensitivity reactions are diagnosed by different approaches. In daily practice, few *in vitro* diagnostic (IVD) tests are available and only developed at the tertiary health services. The use of IVD tests for the detection of specific IgE associated to BLC hypersensitivity is a highly demanded solution to substitute the invasive and risky *in vivo* tests (gold reference).

The results of the COBIOPHAD project

COBIOPHAD has developed an innovative IVD solution for diagnosis of IgE-mediated drug allergies based on compact disc technology.





A device for performing the assay and reading the results has been designed and fully developed, including the hardware, firmware and software of the biophotonic device based on Compact Disc Technology. Also, the manufacturing of platform prototypes was completed, including a centrifugal microfluidic disc. On the COBIOPHAD disc there are six chambers for the simultaneous multiplexed analysis of six serum samples, based on the chemical interaction of the specific IgE with the determinants, revealing the presence and relative concentration of IgE. The integration of all parts and a preliminary validation was fulfilled within the duration of the project.

Now it is the time for a new plan for the COBIOPHAD system, as additional investment will be needed for its industrialization as well as for a complete technical and clinical validation.

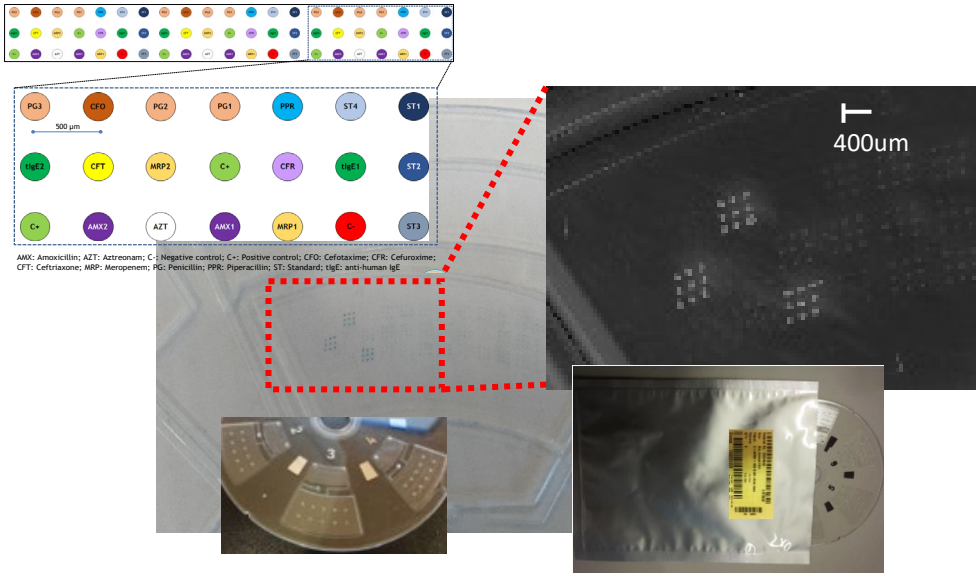
In the COBIOPHAD project (http://www.cobiophad.eu), participated ten partners from seven European countries, including research institutions, manufacturers and hospitals. This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 688448. It is an initiative of the Photonics PPP (www.photonics21.org).

COBIOPHAD results in detail

The COBIOPHAD system integrated a low cost and portable processing and reading unit, performing the multiplexed assay in 60 minutes and providing the results in 15 minutes, a microfluidic platform capable to analyze 6 different samples and determine specific IgE for 9 different beta-lactam antibiotics simultaneously.

The whole system has been tested by the developers and by a hospital, partner of the project. In the future, additional efforts will be needed to industrialize the devices and to pass through a complete and final clinical validation of the system.

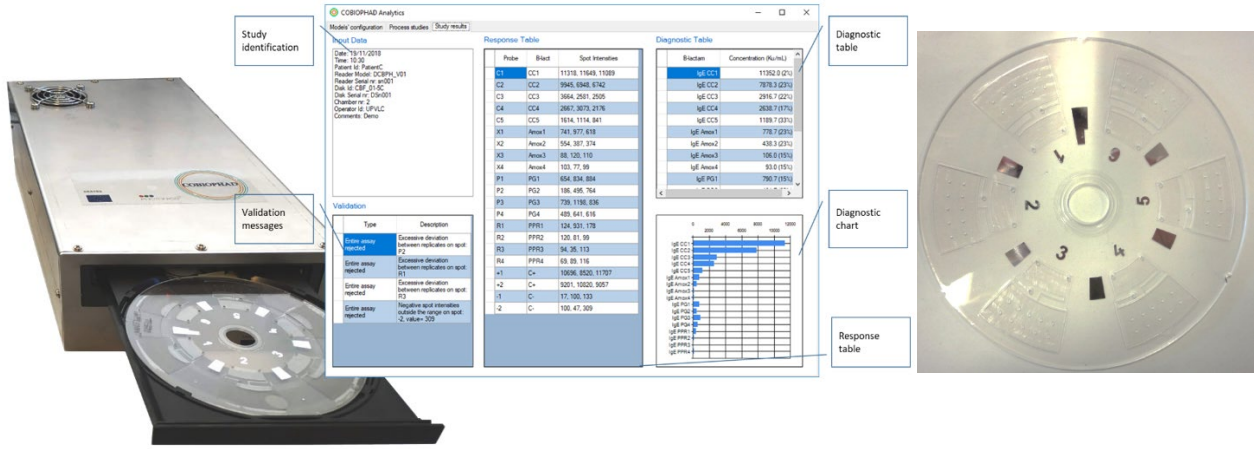
The COBIOPHAD hardware is user friendly, portable and simple to operate by locally trained healthcare staff. Regarding the assay, the recognition and detection take place in the reaction chambers of the microfluidic disc. In the device, the assay protocol is automatically managed by the reader.



Regarding to the optical measurement, the final software is able to perform signal capture, data analysis and quality control, following an automated protocol. The final version includes a user-friendly interpretation tool for reporting results, with minimal participation of the operator (end-user interface), just for sample traceability. Also, an expert interface has been developed for advanced modification of assay protocol.

A successful application of the COBIOPHAD system has been performed at hospital facilities by trained healthcare staff. In summary, the device can be operated under user-friendly conditions.

The COBIOPHAD system has been proven as an integrated biophotonic device based on compact disc technology for *in vitro* diagnosis of drug allergy to antibiotics by determining human specific IgE levels in serum for hypersensitivity to β-lactam antibiotics.

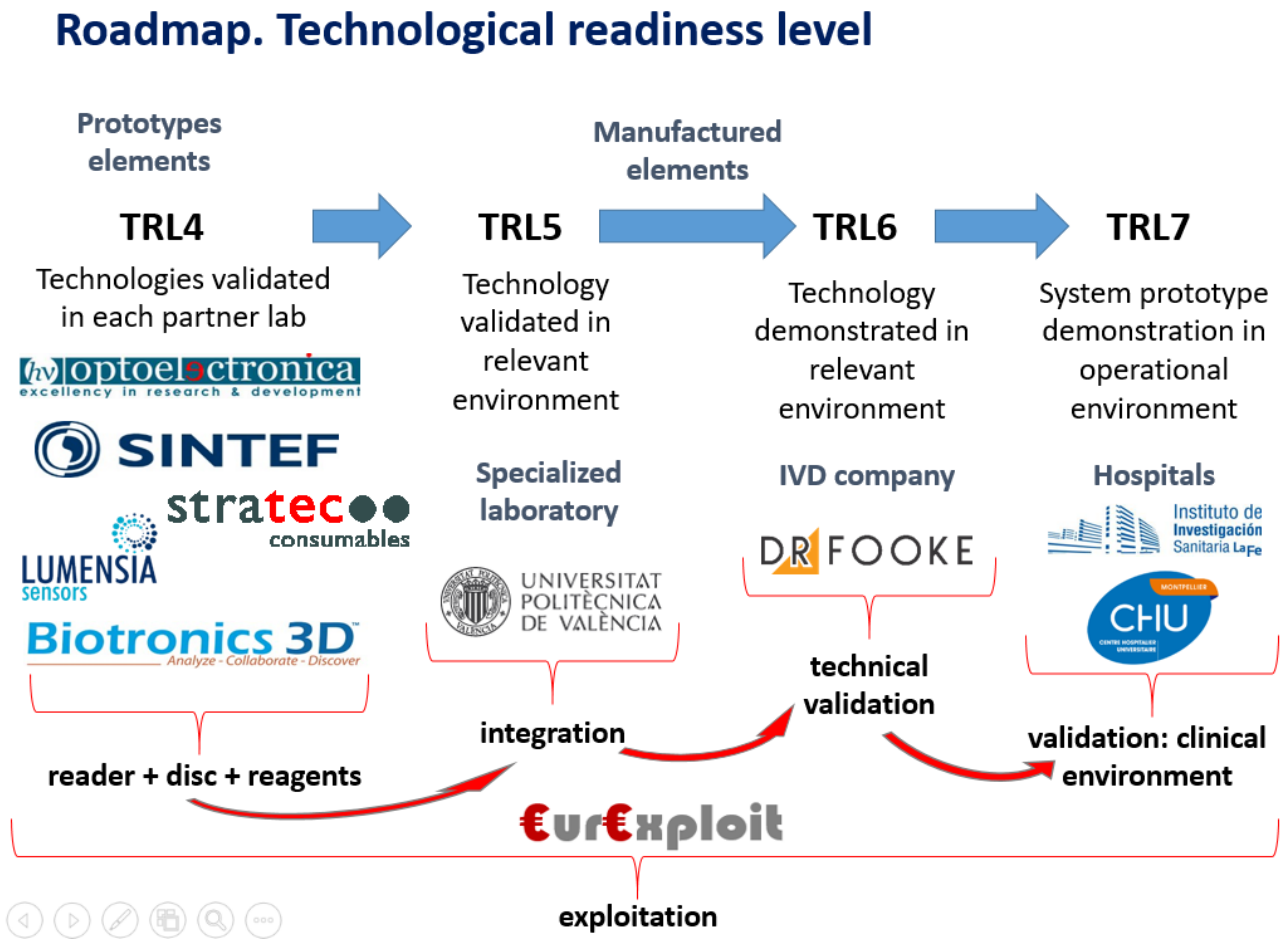


The test can operate autonomously both in clinical or mobile lab environments. A centralized database allows the research and development of more optimized drug specific decision thresholds. All the needed software modules (Clinical Analysis, Imaging software) are complete and ready for optimization during clinical validation. The integration of the software components was implemented in terms of data flow and integration of processing, completing the automation of the device. The local application operates autonomously from the cloud system. The cloud platform enables telemedicine and collaboration and can be

used for research applications. Complete development of SW and databases were achieved with the pre-validation of the system.

The required power supply of device is low compared to other IVD systems. The dimensions are also reduced (180 x 180 x 200 mm, 1.7 kg), compatible to different medical scenarios. The COBIOPHAD system technology was demonstrated in operational environment.

During the last year of the project the integration of COBIOPHAD elements (reader, software, disc and reagents) has been achieved. The complete system worked properly in different environments, starting in research laboratories up to the hospitals' facilities, a real operational environment. For that, 317 serum samples from allergic patients and controls were analyzed in three different scenarios. The results have been validated to an IVD reference method, reaching a TRL level 7.

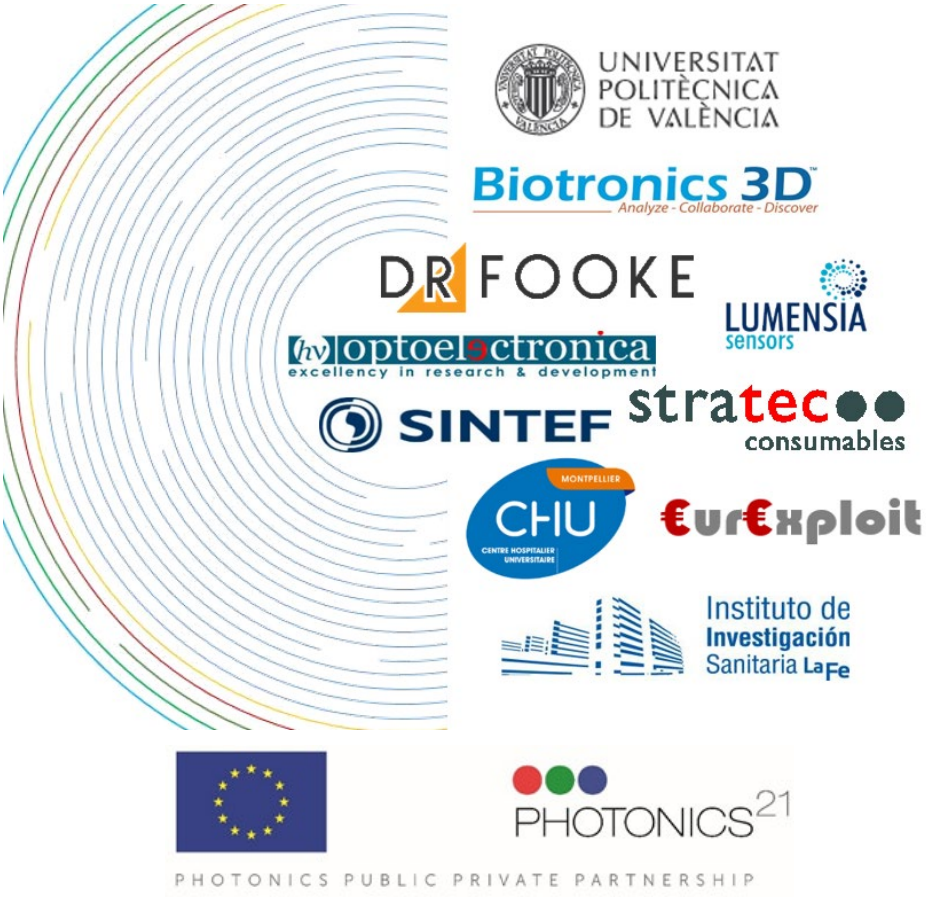


The limit of detection of the COBIOPHAD system was 0.1 IU/mL in serum, which allows the quantification of very low amount of specific IgE. The clinical sensitivity achieved was 89% for amoxicillin and penicillin; while the specificity was 94% and 84% respectively. The multiplex nature of the system allowed the determination of allergic patients to other less prescribed BLCs such as cefuroxime, ceftriaxone, meropenem, aztreonam; for these BLCs, there are not any commercially available in vitro systems, what confers an additional added value to COBIOPHAD system.

The reduction of costs of the COBIOPHAD approach will result in cheaper diagnostics tests, as well as global medical costs considering also reduction of practitioners' time. In addition, as the developed IVD device is simple and user-friendly, the required training is reduced.

The COBIOPHAD technology, assay method and results management is able to incorporate new target BLC drugs in short time. It is also possible to open the system up to allergens of different nature as other drugs, food and environmental.

Finally, the knowledge developed, reagents, discs analytical platform, and data management, are ready to be industrialized for a future exploitation, being a powerful alternative to in vivo tests that could give way to a new generation of in vitro tools expected by patients and the market.



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