MDevNet 2019

Catalog of medical device technologies with high potential of transfer to the market

MDevNet
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MDEVNET PROJECT

The new European regulatory framework for medical devices poses a new challenge for companies in this sector, as it introduces stricter obligations of conformity that aim to ensure greater safety for the users as well as greater transparency. In this new context, companies need to revisit their approach to the business as a whole and new developments will depend even more on a risk analysis relative to the regulatory requirements, which brings new challenges to the technology transfer processes that contribute for new product innovation.

These processes that empower companies to innovate will need to become more effective and agile if they are to keep up with the new regulatory scenario, with greater communication and transparency required between collaborative parties, most notably among scientific knowledge intensive entities and market oriented ones.

1. www.mdevnet.pt

It is in this context that the MDevNet Project[1]: National Network for Knowledge Transfer on Medical Devices, was created. Promoted by Fraunhofer Portugal AICOS, it aims to reinforce the economic value of the developed knowledge on Technology-based Medical Devices from the entities of the Portuguese Research and Innovation System through effective technology transfer processes to the industry.

The Project achieves this through several activities, such as a) the creation of a discussion forum (MDevNet network) for entities that participate in the process of research, development, certification or commercialization of medical devices for knowledge exchange, b) incremental technological improvements on selected medical device R&D results, c) testing and experimentation of said results in the real environment and d) activities of dissemination of the synthesized knowledge and medical device technologies (R&D results) identified during the project from the Portuguese knowledge intensive entities.

In this context, one of the key outputs of the MDevNet project is the Catalog of Technologies in the area of Medical Devices with High Potential of Transfer to the Market, presented in this document.

OBJECTIVE

The goal of this Catalog is to promote and disseminate the variety and quality of the R&D results developed in Portuguese R&D organizations which belong to the national research and innovation system (Sistema Nacional de Investigação e Inovação – SI&I), aimed primarily at companies and market oriented entities. The Catalog also aims to facilitate contact between potential licensees for the presented technologies and the respective Technology Transfer Offices and/or researchers, thus contributing to the transfer of the medical device technologies to the industry.

STRUCTURE AND ORGANIZATION

- This Catalog contains 26 medical device technologies from Portuguese organizations which belong to the national research and innovation system, identified in the course of the MDevNet activities;
- The technologies are organized by technological area according to their mode of operation and purpose;
- All the information displayed associated to the technologies was provided by the respective researchers and institutions.

The Technology Readiness Levels (TRL) presented follow the scale provided by the European Commission[2]:

G. TECHNOLOGY READINESS LEVELS (TRL)

Where a topic description refers to a TRL, the following definitions apply, unless otherwise specified:

- TRL 1 – basic principles observed
- TRL 2 – technology concept formulated
- TRL 3 – experimental proof of concept
- TRL 4 – technology validated in lab
- TRL 5 – technology validated in relevant environment (industrially relevant environment in the case of key enabling technologies)
- TRL 6 – technology demonstrated in relevant environment (industrially relevant environment in the case of key enabling technologies)
- TRL 7 – system prototype demonstration in operational environment
- TRL 8 – system complete and qualified
- TRL 9 – actual system proven in operational environment (competitive manufacturing in the case of key enabling technologies; or in space)

2. https://ec.europa.eu/research/participants/data/ref/h2020/wp/2014_2015/annexes/h2020-wp1415-annex-g-trl_en.pdf

1. Biomechanical and rehabilitation devices

Cleft Toothbrush

University of Porto

Description of the problem

The discontinuity of the oral cavity causes the accumulation of bacterial plaque and consequently gives rise to dental problems and infections.

Description of the technology

Add-on for conventional toothbrush, specially designed for patients with cleft lip and palate.

Intellectual Property Rights

Patent pending

Results and Clinical Evidence

Preliminary tests have been done with children with this malformation and significant improvements have been observed in bacterial plaque reduction.

Technology Readiness Level (TRL)

TRL5

Potential Applications

Application	Intended use	Class
Brush the area of discontinuity of the alveolar bone of the cleft lip and palate.	The cleft toothbrush can be adapted to any conventional toothbrush and allows access to difficult areas to improving significantly the dental health of these patients.	I

Training device to strength pelvic floor muscle

University of Porto

Description of the problem

Pelvic floor muscle (PFM) training exercises are a series of exercises designed to strengthen the muscles of the pelvic floor. They are recommended for women with PFM dysfunction. In addition, PFM suffer significant trauma throughout pregnancy and childbirth that sometimes may lead to urinary incontinence postpartum and, therefore, the National Institute for Health and Care Excellence guidelines recommends pelvic floor muscle exercises to all women during their first pregnancy as preventive strategy for urinary incontinence. A good awareness of the PFM function (voluntary PFM contraction and relaxation) is crucial to a successful conservative therapeutic approach of PFM dysfunctions such as urinary incontinence, anal incontinence, and sexual dysfunction.

This device allows: **i)** physiological strengthening of PFM through an innovative mechanical action; **ii)** correct placement during exercise execution; **iii)** correct contraction performing due to visual cues; **iv)** visual training and real-time feedback performance monitoring; **v)** adjustment of external load to achieve different training goals (muscular endurance, muscular strength, muscular power) for training optimization; **vi)** increase of muscle tonicity, endurance and strength in a short time. Moreover, this device is simple and user-friendly, cheap and re-usable and it can be used either in a clinical setting or at the patient's home.

Description of the technology

Mechanical device that allows monitoring the evolution of the strength-training program with quantitative and qualitative evaluations of pelvic floor muscle (PFM) contraction and relaxation.

Intellectual Property Rights

Provisional Portuguese Patent application

Results and Clinical Evidence

Two preliminary studies have been conducted:

Study I) on a sample of elderly women (device group n=3; no device group n=3) during 6 weeks, twice a week; training protocol: no device group: in standing, 3 set of 10 repetitions of PFM maximal voluntary contraction sustained for 8 sec.

Study II) on a sample of adult women (Device group n=4; Biofeedback (vaginal EMG) group n=3) during 12 weeks, twice a week. Protocol: 3 set of 10 repetitions of PFM maximal voluntary contraction sustained for 8 sec.

In both studies, better improvements were seen in PFM strength in the device group.

No adverse events were referred, no infection-related complications and no vaginal discomfort with the use of the device.

Technology Readiness Level (TRL)

TRL6

Potential Applications

Application	Intended use	Class
Training device to strength pelvic floor muscle	Improve urinary and anal incontinence	IIa
Awareness improvement of pelvic floor muscles function: strengthening training and voluntary relaxation	Improve sexual dysfunction	IIa

MechALife – – Exoskeleton for assistance of daily activities

INEGI

Description of the problem

MechALife is an active exoskeleton to assist daily activities such as gait, sitting or getting up and climbing stairs. The target market is people with some degree of muscle atrophy related to any dysfunction or aging, as long as there is no total loss of functioning of the lower limbs.

Description of the technology

MechALife is a low-cost active exoskeleton for walking and other day-to-day activities, such as sitting, getting up and going up or down stairs. The MechALife consists of a mechanical waist-to-feet structure in order to support the weight itself, and of a module with batteries, actuators and computer system placed above the waist.

Advantages

- Price: First estimations appoint to a highly competitive solution, when compared to commercially available solutions, typically targeting other markets.
- Weight/Volume/Low actuation loads are required due to the low-volume and low-density materials.
- Body Fitting: The system is designed to be adaptable to various forms of the human body, allowing the same exoskeleton to be used in people of different heights and body mass indexes. The just-to-the-body character of the system allows wear under clothing.
- Discretion: The only visible components would be the lower back module (which can be "hidden" beneath a backpack) and the exoskeleton extremity next to the floor. This low-profile feature reduces possible social awkwardness from using the device, which can considerably increase the users' predisposition to wear the system through several age spectrums and social classes.

Intellectual Property Rights

Know-how

Results and Clinical Evidence

Full system functionalities virtually validated (Computational biomechanics with integrated electromyography control). Electromyography-based control system experimentally validated. Full experimental validation planned for the short-term.

Technology Readiness Level (TRL)

TRL4

Potential Applications

Application	Intended use	Class
MechALife is the concept of active exoskeletons for rehabilitation applied to the mobility needs of elders, and assists daily activities such as gait, sitting or getting up and climbing stairs.	Rehabilitation	I

SHaRe

INEGI

Description of the problem

SHaRe, the System for Hand Rehabilitation in Dexterous Manipulation of Daily Objects, was developed in order to help individuals regain hand dexterity. The system is suitable for accessing, training and recovering patients who have difficulties in manipulating objects, particularly in respect to training grip force control.

Description of the technology

It is based on sensing the spatial orientation and grip force exerted on a device, and replicating it through a virtual model. This way SHaRe is capable of providing visual feedback by displaying on a virtual model: i) the force applied to the device, translated as the deformation of the model, and ii) the device's orientation. This device is integrated in a proprietary software platform (CORe) for storage and historical data access, as well as multi-user online interaction in real-time. A few serious games have been developed for this prototype to help balance the slowing of dexterous manipulation due to aging and for rehabilitation exercises, to be used in trial experiments within medical institutions.

SHaRe provides a wireless instrumented device, that can be shaped in distinct forms, allowing the use of augmented force and orientation feedback in multiple hand rehabilitation therapies.

Advantages

Past studies suggest that the use of augmented feedback can be helpful when evaluating and training grip force control. In this sense, SHaRe presents the following advantages:

- User-friendliness: The system can be shaped in different daily objects commonly used in hand rehabilitation. Virtual environments uses the Unity game engine to conduct therapy exercises enhanced by augmented visual and sound feedback in a serious games configuration.
- On-line assessment and training support
- Training precision: The device allows practicing hand exercises in fine manipulation movements.
- Load range and resolution: Measuring force range of 0-50 N, with high resolution.

Intellectual Property Rights

Know-how

Results and Clinical Evidence

A prototype of SHaRe is currently under test in a medical institution, in order to assess its usefulness in a real rehabilitation environment.

Technology Readiness Level (TRL)

TRL6

Potential Applications

Application	Intended use	Class
Monitoring, treatment, mitigation or compensation of an injury or disability.	Rehabilitation	I

WESt

INEGI

Description of the problem

WESt, the Wrist Evaluation system, is a device focused on wrist rehabilitation.

Description of the technology

The system has a physical structure linked to a software application (Android based) for real-time data acquisition and register from multiple users, through a cloud-based environment database during assessment and exercising.

It allows measuring the range of motion of pronation/extension, flection/extension and radial/ulnar deviation of the wrist, as well as conducting rehabilitation exercises.

Advantages

- Motion flexibility;
- On-line assessment and training support.

Intellectual Property Rights

N/A

Results and Clinical Evidence

A prototype of WESt was tested in laboratory, in order to assess its usefulness in a real rehabilitation environment.

Technology Readiness Level (TRL)

TRL3

Potential Applications

Application	Intended use	Class
Monitoring, treatment, mitigation or compensation of an injury or disability	Rehabilitation	I

Dental Prosthesis System for the use with at least two dental implants

University of Porto

Description of the problem

Due to different causes, the posterior areas of the mandible are often related with scarce bone volume. The proposed solution is a screw retained dental prosthesis system, developed for the oral rehabilitation of these locations, in the clinical situations where it is possible to place, at least, two short or extra-short dental implants. The reduced vertical bone volume results in an increased crown height space with deleterious effects at the marginal bone level. Thus, this prosthetic concept represents a bone protective solution.

Description of the technology

This invention represents a new and minimally invasive concept for the oral rehabilitation of the mandible posterior areas when the bone volume is scarce but enough to place short implants. This way, it is an alternative to the surgical procedures that intend to regenerate the lost bone volume and avoids healthy teeth extractions. It assumes that the so-called crown height space is increased when compared with the average measurement of the anatomical crowns of the natural teeth that are going to be replaced. Nevertheless, it may be considered for the application in different types of edentulism. Due to the configuration of the prosthetic system, and because the applied load during the masticatory function generates stresses potentially higher than bone's yield strength, the entire system has a bone protective effect, by the modification of the prosthetic design, allowing for the marginal bone crest maintenance over time, the success of the dental implants and therefore, the success of the rehabilitation.

Intellectual Property Rights

Provisional Patent Pending

Results and Clinical Evidence

The concept has been validated through mathematical models and experimental biomechanics.

Technology Readiness Level (TRL)

TRL4

Potential Applications

Application	Intended use	Class
Dental implant for situations where bone is scarce	Device for permanent dental replacement	I

Fall Prevention Technology

Fraunhofer Portugal AICOS

Description of the problem

A general decline in physical function and balance problems make older people more prone to falls which are one of the most common health related problems in the elderly population, representing more than 50% of the hospitalizations due to injuries in this age group. Falls are also considered one of the main causes for institutionalization and loss of independence. Exercises for balance control, mobility, strength and flexibility are effective strategies for fall prevention. However, older people lack motivation to perform these exercises at home, on a frequent basis, and fall prevention exercises based on scientifically accepted programs typically require the presence of a medical professional.

Description of the technology

Our fall prevention technology supports the senior population in the execution of specific exercises known to contribute to fall prevention. Multiple components of this technology can be combined to cover a multitude of scenarios for fall prevention. The developed components consist of the following:

- **A.** Hardware abstraction layer for sensor communication
- **B.** Movement evaluation algorithms
- **C.** Gamified fall prevention programs/exercises
- **D.** Interventions prescription and user profile management.

Component A comprises an interface for retrieving sensor data from a large array of supported and commercially available sensors (for example, inertial sensors from smartphones and smartwatches or depth sensors such as from Microsoft Kinect®), provided through a unified protocol (Kinteract). The employed architecture allows modules to be agnostic regarding the used sensors.

Component B can use different data sources to evaluate the movement of the user. Data from inertial sensors, gestures, body tracking or hand tracking may be used to evaluate different types of movements and extract multiple exercise properties. A focus has been on arms and legs movements during specific exercises. Exercises from the OTAGO fall prevention program (e.g. sit to stand, tandem walk, one leg standing, etc.), multiple dances and Tai Chi routines constitute examples of supported movements.

Component C may ideally be used in conjunction with component B, as exergames rely heavily on the ability to understand users' movement to control game progression. Component C consists of a set of gamified exercises for fall prevention that fully replicate the scientifically based OTAGO exercise program. Dance and Tai Chi based interventions are also presented as a game, which contribute to users' engagement and commitment, required to guarantee the efficacy of the interventions. Interactive games may also support a multi-player mode.

Component D consists of a backend server for storing users' profiles, movement performance adapt the intervention plans to the specificities and needs of the user. Personalized exercise plans can be recommended automatically by the system, which continuously adapts the intervention plan to the progress of the user.

Intellectual Property Rights

- Know-how
- Copyright (including software implementations, games animations and design)

Results and Clinical Evidence

The technology has been tested in senior care systems and the results showed that the game was easy to follow and most of the participants revealed interest in continuing using it.

The obtained results for all tested exercises were promising, constituting a valuable source of information for clinical practice or even for home-based rehabilitation solutions. More detailed information on these tests can be found through the following papers:

- J. Silva, E. Oliveira, D. Moreira, F. Nunes, M. Caic, J. Madureira and E. Pereira, "*Design and evaluation of a fall prevention group game for social care institutions*", 2018, p.12.
- J. Silva, D. Moreira, J. Madureira, E. Pereira, A. Dias and I. Sousa, "*FallSensing Clinical Tool: Technological Solution for Falls Prevention*", 2018, p.8.

Technology Readiness Level (TRL)

TRL6

Potential Applications

Application	Intended use	Class
Fall prevention system to install in Clinics, Nursing Homes or Health Service Centers	Prevent falls in the elderly population. Promotion of social activity and interaction among seniors	IIa
Exercise stimulation for seniors	Prevent falls and improve physical conditions of the elderly population.	IIa
Tool to support healthcare providers recording patients performance and progress for individually targeted support	Complement to physiotherapy treatment	IIa

2. Computer-aided Diagnosis Medical Technologies

EchoCAD – Carotid

INESC TEC

Description of the problem

Carotid atherosclerosis is an age-related disease and may present no symptoms or other signs whatsoever. Thus, measurement track of the carotid artery blockage using an ultrasound image is the common follow-up method and has to be frequently carried out. Consequently, there is a stated need for auxiliary tools that provide accurate and faster measurements of plaque and arteries' characteristics that can help physicians developing correct and personalised diagnosis and their corresponding treatments. The biggest limitation of the available solutions in carotid artery assessment is the short characterization of carotid artery structure, mostly based in the intima-media thickness (IMT) calculated at a limited region (far-wall). Therefore, there is a clinical need of improved carotid artery imaging at near-wall, ready to detect and quantify atherosclerotic carotid plaques. Expanding the carotid assessment to the near-wall demands new noise-resilient technologies, which also offer users images with quality to support accurate diagnosis and disease management.

Description of the technology

Developed at INESC TEC, EchoCAD – Carotid is a computer-aided diagnosis system for carotid ultrasound imaging.

This is the only solution ready to measure arterial features from both near and far walls of the carotid artery. In addition to IMT measuring, EchoCAD-Carotid supports the assessment of atherosclerotic plaques burden and texture as well as the degree of arterial stenosis along the entire field of view of the image. This is complemented with a fine-tune option allowing the physicians to do small adjustments towards more refined and personalised results. Overall, EchoCAD-Carotid speeds up the carotid ultrasound, allowing the physicians to dedicate more time to their patients' care.

The main advantages of EchoCAD-Carotid are:

- Provide a unique solution for plaque measurements and characterisation both in near and far walls;
- Perform accurate measurements even with lower-quality images;
- Execute a 1-minute real time computer analysis of an ultrasound image;
- Detect large, hypoechogenic, and irregular plaques, giving a better insight of the risks it can bring;
- Automatically measure the IMT of the near wall of the carotid artery, being a solution with a good performance in scenarios of poor contrast between layers;
- Allow manual adjustments of the automated measures by the physicians;
- Be compatible with different image file formats (DICOM, PNG, TIFF and JPEG);
- Integrate easily into different devices;

The system processes both single and multi-frame B-mode longitudinal ultrasound images (US) and automatically segments media-adventitia and lumen-intima interfaces of the near and far carotid walls. The EchoCAD - Carotid system outputs vascular biomarkers such as the intima-media thickness (IMT), plaque burden, plaque echolucency/echogenicity and plaque gray-scale median, as well as, the degree of stenosis of the artery. Intima-media thickness and plaque quantifications are performed at both near and far wall. Because the EchoCAD - Carotid is a CAD system, automatic segmentations can easily be adjusted by the medical doctors.

Intellectual Property Rights

Copyright

Results and Clinical Evidence

This software has been developed focusing its application in the diagnosis stage of carotid atherosclerosis by automatic detecting carotid artery layers. The EchoCADCarotid was tested at a partner hospital in 20 ultrasound images and benchmarked against the manual annotation of two medical experts.

Technology Readiness Level (TRL)

TRL5

Potential Applications

Application	Intended use	Class
Viewing, manipulation, communication, and storage of ultrasound medical images	Automatic/semiautomatic segmentation and characterisation of the image in terms of IMT, plaque and stenosis quantifications in a matter of few seconds, helping neurologists in the assessment of carotid artery atherosclerotic disease.	IIa

Choroidal Thickness App

INESC TEC

Description of the problem

The choroid is a vascular layer of the eye globe located between the retina and the sclera and its thickness is affected by a range of diseases such as retinitis pigmentosa and serous chorioretinopathy. Choroidal evaluation is carried out through OCT imaging but current software solutions require excessive inputs from ophtalmologists and present poor performance in lower quality images. Automatic segmentation of eye regions eases medical evaluation but the technology available in clinical arena is not able to fulfill the required level of accuracy. Moreover, there is a gap in solutions that allow the combination of two sets of OCT scans, for a better estimation of the choroidal thickness or analysis on the thickness progression.

Description of the technology

Choroid CAD is a software that improves the diagnosis and clinical follow-up of ocular diseases by supporting the evaluation of choroidal membrane. This computer-aided diagnosis system was designed to automatically calculate the choroidal thickness of patient's eyes using EDI-OCT videos. The algorithms embedded in Choroid CAD are able to identify the different layers of the eye globe and calculate the choroidal thickness in the regions of interest defined by ophthalmologists. This software was designed to deal with lower quality OCT images, including an easy way to output the thickness results (interpolating and mapping them). Although automatic, Choroid CAD allows manual fine-tuning adjustments by the user. The metrics delivered by Choroid CAD are clinically relevant for diagnosis and disease progression assessment, impacting clinical decisions. The visualization and data integration options present in Choroid CAD saves time to ophthalmologists, provide clinical registries and makes easier the communication with patients.

The Choroid CAD has the following unique technological features:

- Construction of a 3D map of the choroidal thickness by integrating multiple sets of OCT B-scans;
- Ready for large scale screening;
- Follow-up of choroidal thickness variations;
- Option of calculate choroidal thickness in specific areas of the eyes;
- Perform accurate measurements even in lower-quality images;
- Parallel or perpendicular integration of OCT scans sets;
- Allow manual adjustments of the automated measures by the physicians.

Intellectual Property Rights

Copyright

Results and Clinical Evidence

Choroid CAD is under testing in the Ophthalmology department of Centro Hospitalar Universitário de São João (CHUSJ) in order to validate the software. The developed software was evaluated on 152 manually segmented B-scans from 8 OCT tests by two independent ophthalmologists. The clinical results are promising showing a small mean relative error of 3,62+/- 4,67%) when compared with experts' measurements. Further developments intend to combine the mapping of two videos from the same eye to improve the estimation of the 3D choroidal thickness.

Technology Readiness Level (TRL)

TRL4

Potential Applications

Application	Intended use	Class
Support the diagnosis and clinical follow-up of variations in choroidal thickness	Visualization, processing, segmenting and calculating the choroidal thickness of patients eyes using EDI-OCT videos, helping clinicais to follow-up ophthalmologic diseases such as retinitis pigmentosa and serous chorioretinopathy.	I

EyeFundusScope

Fraunhofer Portugal AICOS

Description of the problem

The increasing prevalence of diabetes in the population is associated with several health issues, one of them is the development of diabetic retinopathy (DR), where a diabetic patient will experience cumulative changes to his retina, which ultimately may lead to blindness. Diabetic retinopathy progression is mostly asymptomatic until the later stages of the disease, when vision loss settles in, and at that point it is very difficult to reverse. The incidence of retinopathy is rarely detected in the first few years of diabetes, but the incidence increases to 50% by 10 years, and to 90% by 25 years of diabetes. The asymptomatic profile of the initial progression and the high effectiveness of early treatment have motivated the implementation of extensive screening programs covering the diabetic population, in which images of the patient retinas are acquired and subsequently analysed by an expert. However, this requires the use of relatively expensive and cumbersome equipment to acquire the retinal images as well as a time consuming analysis of those images by ophthalmologists.

Description of the technology

Following Fraunhofer AICOS contribution to reduce the prevalence of avoidable blindness in the world, the EyeFundusScope includes a mobile application that employs parallel computation and artificial intelligence (AI) offline, to control and simplify the handheld image acquisition of the retina through real-time user guidance and evaluation of the right moment for auto-capture. Computer-Aided Diagnosis running on-device can be used to rate the risk level of DR, visualize computer-detected annotations of exudates and microaneurysms, and classify them between pathology-free and eye-disease cases.

The EyeFundusScope technology aims to simplify, anticipate and increase the coverage of retinal screening as a powerful image acquisition and pre-diagnostic tool. Currently, the EyeFundusScope technology comprises:

1. A low-cost, 3D-printed and handheld non-mydriatic fundus camera device with FhP-AICOS' optical and mechanical design coupled with:
   a) FhP-AICOS' dedicated electronics and firmware for light control and dual power-supply, allowing continuous acquisition and processing in rural scenarios/ ICT4D, even on smartphones that do not support charging and power delivery at the same time;
   b) A smartphone combined with FhP-AICOS' mobile image processing software taking advantage of the faster and more efficient processing units increasingly available, by empowering:
      1. AI software for user guidance based on sensor fusion and dedicated Graphical User Interface (GUI) for effective Human Computer Interaction during the retinal alignment;
      2. The evaluation of the right moment for auto-capture. This evaluation is performed by analysing in real time the stream of frame previews in the camera. The implementation automatically triggers an acquisition whenever a fixed number of consecutive preview frames are considered as retina;
      3. Quality control with quick feedback when the user should repeat the acquisition;
      4. The central processing unit of the apparatus is the smartphone.

2. FhP-AICOS' EyeFundusScope App: a mobile application that employs parallel computation (all of this can be done offline):
   a) To rate the DR risk level based on number, type and size of structures;
   b) To visualize computer-aided annotations of exudates and microaneurysms automatically detected;
   c) To classify between pathology-free and DR cases, based on AI software for telemedicine and decision-support use cases.
3. FhP-AICOS' Anonymized data repository of mobile acquisitions;
4. FhP-AICOS' web portal for quick image annotation and classification by specialists (ground truth generator).

Alternatively, the EyeFundusScope software is compatible with Welch Allyn PanOpticTM ophthalmoscope via adapter and dedicated light source that can be operatively coupled with the smartphone processor. However, the field-of-view is much smaller and some features such as non-mydriatic acquisition or improved usability are not possible. In this type of images, EFS-Image Stitching is applied to combine multiple images for a wider composed view. In addition, the EyeFundusScope technology has the potential to be extended to other eye diseases and stand as a useful tool for eye health screening in developing countries where even lower number of specialists in Orthotics and Ophthalmology are available.

Intellectual Property Rights

Copyright (includes: software implementations of Android Application and Decision Support System (Software and Algorithm) and the optical fundus camera hardware).

Results and Clinical Evidence

The current results achieved with EFS Artificial Intelligence DR component have so far reached the following outcomes:

- Tested in 350 images of the EyePACS-1 dataset with new ground truth generated by 3 experts using Fraunhofer AICOS annotation tool;
- Sensitivity 82% , Specificity 97%.

More detailed information on these tests can be found through the following paper: Gonçalves, J.; Conceição, T. and Soares, F. Inter-observer Reliability in Computeraided Diagnosis of Diabetic Retinopathy. In Proceedings of the 12th International Joint Conference on Biomedical Engineering Systems and Technologies - Volume 5: HEALTHINF, ISBN 978-989-758-353-7, DOI: 10.5220/0007580904810491. A10, pp. 481-491, 2019.

Usability tests with the image capture device were performed by 10 medical doctors (in which 6 are general practitioners), 5 nurses, and 1 physiotherapist, in laboratory and hospital setting. Only a subset of participants presented slight difficulty handling and stabilizing the fundus image in first-time use, which improved significantly in subsequent acquisitions. Participants revealed no difficulty interfacing with the Android Application and demonstrated willingness to use the device in their clinical practice.

Technology Readiness Level (TRL)

TRL6

Potential Applications

Application	Intended use	Class
Clinical Decision Support Tool	Automated diabetic retinopathy detection	IIa
Application for widespread/ large scale screenings of diabetic retinopathy, without the need of ophthalmologists' specialists on site.	Determination of the diabetic retinopathy risk level for the images collected	IIa

Mobile Dermatology Support System

Fraunhofer Portugal AICOS

Description of the problem

Skin cancer corresponds annually to about one-third of all cancers detected in Portugal, affecting one in seven people throughout their lifetime. Although Malignant Melanoma (MM) accounts for a small percentage of skin cancer, it is responsible for most skin cancer related deaths. Early diagnosis of MM is, therefore, extremely important considering the high success rates of recovery if the malignancy is detected during the early stages of its development.

There has been a growing interest on Telemedicine and other ICT solutions for their ability to improve efficiency and ease the burden on health services, such as dermatology services, but a great potential still lies unexplored.

Smartphones, in particular, are well suited to maximize the accessibility of solutions to early detection of pathologies due to their ubiquity, relatively low cost and growing technological capabilities like high quality image acquisition.

Description of the technology

The presented system is comprised of 3 modular components:

Referral mobile application of skin lesions for healthcare professionals (SLR)

Using this mobile application, general practitioners from Local Healthcare Units are able to acquire relevant dermatological information through the usage of a smartphone, the application itself and an optional adaptable dermatoscope. This technology presents a simple and intuitive workflow that uses real time image processing algorithms to improve image acquisition (automatic focus and capture) and ensure image quality.

Teledermatology system for patient-doctor communication (TSC)

This sub-system is comprised of 3 parts: the Patient Mobile Application, the Back--End server and the Web Interface.

Using the Android Patient Mobile Application, the patients can capture images of their skin lesions or load them from the mobile image gallery, and record associated information, such as location and size. Dermatologists may then use the Web Interface to consult and validate the check-up images sent by the patients, and can consult the automatic analysis results provided by IPM (see below), where it is possible to agree or correct the evaluation given by the automatic analysis. The Back-end Server hosts the system database and the Image Processing Module (IPM) and ensures communication between the user interfaces.

Image processing module for automatic risk assessment (IPM)

This is a machine-learning algorithm based on image processing to automatically assess the risk of skin lesion images with images collected through a smartphone without additional accessories. This software automatically processes and performs extraction of significant features for risk assessment purposes, with the goal of assisting the specialists in the triage process. The algorithm currently runs on a server but may also be adapted to run locally on the phone.

Intellectual Property Rights

- Know-how;
- Copyright (SLR; IPM; TSC).

Results and Clinical Evidence

The mobile application of skin lesions has been tested in clinical environment, namely in Local Healthcare Units, and proved to be easy, intuitive and capable to automatically acquire images with quality.

The automatic risk assessment of skin lesions achieved 77.3% of sensitivity, 90.3% specificity. These results were achieved using a dataset of 1648 images classified as suspicious (including pre-cancer and cancerous lesions) and non-suspicious lesions (benign lesions).

Technology Readiness Level (TRL)

TRL7

Potential Applications

Application	Intended use	Class
Clinical Decision Support Tool	Aid for diagnosis	IIb
Application for widespread/ large scale triage of skin cancer, without the need of dermatology specialists on site.	Determination of risk level for the clinical images collected	IIb
Teledermatology solution to bridge communication between patient and doctor One particular example is the scenario where the patient is advised by the dermatologist to selfmonitoring between face-to-face consultations, being the TSC solution used to support and improve this process with the dermatologist involvement.	Aid for diagnosis	IIb

MalariaScope (powered by the uSmartScope)

Fraunhofer Portugal AICOS

Description of the problem

Malaria is a leading cause of death and disease in many developing countries, where young children and pregnant women are the most affected groups. In 2016, there were an estimated 216 million cases of malaria in 91 countries, which caused approximately 445 000 deaths.

Microscopy examination has been the pillar of malaria diagnosis, being the recommended procedure when its quality can be maintained. Around 90% of all malariarelated deaths occur in Africa, where the lack of access to malaria diagnosis is largely due to shortage of expertise and equipment. These drawbacks are closely related with the increasing interest in the development of computer-aided diagnosis systems based on Artificial Intelligence (AI), particularly distributed solutions that provide access to complex diagnosis in rural areas. Promising advances have been reported in the area of computer-aided detection of malaria parasites during the past few years. However, the majority of the proposed approaches in the literature are based on two main requirements unsuitable for most malaria-endemic areas: images acquired under wellcontrolled conditions and the need of proper microscopic equipment. Both criteria are difficult to accomplish in those areas, where this type of equipment and the know-how to maneuver it are scarce or non-existent.

The search for suitable alternatives for these scenarios has been the main driving force behind the MalariaScope project. Our main goal is to develop an AI-powered mobilebased framework that supports the pre-diagnosis of malaria in medically-underserved areas, being simultaneously low cost and easy to use, even for non-experts in microscopy. By merging software and hardware innovative technologies, we believe that the lack of highly trained microscopists on malaria diagnosis in rural areas could then be complemented by a significantly less specialized technician that knows how to operate the MalariaScope solution and prepare blood smears.

Description of the technology

The MalariaScope solution is an AI-powered mobile-based framework that supports the pre-diagnosis of malaria in medically-underserved areas, being simultaneously low cost and easy to use, even for non-experts in microscopy. To achieve a solution with realistic chances of being effectively used in the field for malaria diagnosis, we soon realized that we needed to explore the development of both hardware and software components.

Particularly, the solution is composed by 3 main components:

1. **uSmartScope:** a fully automated 3D-printed smartphone microscope with a motorized stage. This prototype (termed µSmartScope) was the first proposed smartphone-based alternative to conventional microscopy that allows autonomous acquisition (without human interaction) of a predefined number of images at 1000x magnification with suitable resolution, by using a motorized automated stage fully powered and controlled by a smartphone. All the components of the device were properly evaluated, in order to validate it as a reliable alternative to conventional microscopy. Particularly, we evaluated the SmartScope performance in terms of: resolution; field of view; illumination; motorized stage performance (more specifically the mechanical movement precision/resolution and power consumption); and the proposed automated focus procedure.

2. Artificial Intelligence for malaria parasite detection: Software modules for the automated detection of malaria parasites (MPs) via Computer Vision and Machine Learning approaches, on microscopic blood smear images acquired using 1. This component consists of two main modules: (a) Module to detect the presence of MPs on thick blood smears; (b) Module for the determination of MPs species and life cycle stage on thin blood smears. The automatic detection of WBCs in thick blood smears achieved 98.2% of sensitivity and 72.1% specificity, while the P.falciparum trophozoites detection achieved a sensitivity of 80.5% and a specificity of 93.8%, being used a dataset of 194 images manually annotated by an experienced parasilogist. Regarding the automated analysis of thin blood smears, results of 73.9-96.2% sensitivity and 92.6%-99.3% specificity, using a dataset of 566 malaria-infected thin blood smear images.

3. Smartphone application: envisioned to be used by technical personnel without specialized knowledge in malaria diagnosis. The user collects and prepares a blood sample of the patient, introducing it in a slot of 1. Using the companion mobile application, installed in the smartphone that is coupled to 1, the user starts the automated image acquisition process described in 1. The images are acquired with the smartphone's camera, being subsequently analyzed by the algorithms described 2, which also run locally on the smartphone. After the image analysis is completed, a report is generated and the correct procedures and medication can be administered accordingly.

   As a final note, we are improving the performance of our AI modules by increasing our training data through image datasets acquired in laboratory tests with clinical partners. In the future, we plan to move to field trials in Africa with the same partnership, in order to assess the performance and practical usefulness of the MalariaScope solution.

Intellectual Property Rights

- Know-how;
- Copyright (includes: 1. uSmartScope; 2. Artificial Intelligence for malaria parasite detection and 3. Smartphone application);
- Patent pending (related with uSmartScope).

Results and Clinical Evidence

- **uSmartScope:** In order to validate the prototype as a reliable alternative to conventional microscopy, the µSmartScope performance was evaluated in terms of: resolution; field of view; illumination; motorized stage performance (mechanical movement precision/resolution and power consumption); and automated focus. The results showed similar performances when compared with conventional microscopy, plus the advantage of being low-cost and easy to use, even for non-experts in microscopy.
- **Malaria detection on thick blood smears:** The automatic detection of WBCs in thick blood smears achieved 98.2% of sensitivity and 72.1% specificity, while the P. falciparum trophozoites detection achieved a sensitivity of 80.5% and a specificity of 93.8%. This results were achieved using a dataset of 194 images acquired from 6 different thick blood smears infected with P.falciparum.
- **Malaria detection on thin blood smears:** Eight different species-stage combinations were considered, with an automatic detection performance ranging from 73.9% to 96.2% in terms of sensitivity and from 92.6% to 99.3% in terms of specificity. This results were achieved using a dataset of 194 images acquired from

5 different thin blood smears infected with P.falciparum, P.ovale and P.malariae.

Technology Readiness Level (TRL)

TRL6

Potential Applications

Application	Intended use	Class
Clinical Decision Support Tool	Automated detection of malaria parasites species and life cycle stages on blood smear	IIb
First triage tool for isolated laboratories, where a technician collects blood from a patient, prepares the blood smear, and uses the system to analyze the blood sample.	Malaria-infected blood smears digitalization, visualization and automated pre-diagnosis, so the correct medication can be provided	IIb

3. Therapeutic/ Surgical Planning Technologies

Microcooler Device for Drug-Resistant Epilepsy

University of Minho

Description of the problem

The cooling systems currently available are too large and complex to allow for their use, both in thermal neuro modulation viability studies and in systems for chronic application.

Description of the technology

Device that allows the focal cooling of neuronal regions.

Intellectual Property Rights

Patent filed

Results and Clinical Evidence

N/A

Technology Readiness Level (TRL)

TRL3

Potential Applications

Application	Intended use	Class
Epileptic patients whose medication treatments failed.	This is a technology that allows the development of an alternative solution to electrical neuromodulation for the control of medicationresistant epilepsy.	N/A
Thermal stimulation (cooling) of peripheral nerves.	Treatment of pain pathologies where electrical neurostimulation may not be effective.	N/A
Cold technology could be used to replace the ice used by athletes.	Aiding the treatment of injuries.	N/A

Medical device for objective cataract characterization and optimal phacoemulsification energy estimation

University of Coimbra

Description of the problem

Phacoemulsification is the most common surgical procedure using an ultrasound device to fragment the lens into small pieces that are subsequently aspirated. In order to emulsify the cataract, the selection of the optimal energy level is fundamental to avoid damage of the corneal endothelium and the rupture of the posterior lens capsule. The evaluation of the type and hardness of cataract as well as the determination of the optimum energy level of phacoemulsification in real time will allow to optimize the surgical procedure, minimizing the risks of complications and reducing the surgical time, with a considerable socio-economic impact.

Description of the technology

Non-invasive medical device, by ultrasound to support cataract surgery in real time. On the diagnostic side the device performs a subclinical cataract detection. Concerning to the surgical extraction of cataract, the developed device provides real-time information about the cataract hardness, and the optimal energy of phacoemulsification to be used in its extraction.

Intellectual Property Rights

Portuguese Patent 109646: "SISTEMA ULTRASSÓNICO DE EXAME OCULAR PARA DETEÇÃO PRECOCE E CLASSIFICAÇÃO DA CATARATA EM TEMPO REAL".

Results and Clinical Evidence

Validated in animal models. Human validation ongoing.

Technology Readiness Level (TRL)

TRL4

Potential Applications

Application	Intended use	Class
Subclinical diagnosis of cataract and inclusion of the developed device in a surgical environment, in Phacoemulsification Workstations.	For use in the diagnosis and surgery support of cataracts.	IIa

Accurate-BV

INESC TEC

Description of the problem

Among the different surgical techniques that can be used in breast reconstruction surgeries, Deep Inferior Epigastric Perforator (DIEP) flap emerges as the top choice when autologous tissue is used as a longstanding and natural solution. DIEP flap requires a challenging pre-operative planning based in a contrast-enhanced Compute Tomography (CT), which is evaluated by a radiologist to identify the best donor abdominal location according to its vascular features.

The gold standard approach consists in a time-consuming and manual procedure to radiologists, resulting in work overload and wrong clinical decisions concerning the volume and location of the donor tissue that should be used in DIEP flap. The incoherencies between the imaging studies and the surgical findings presented by the current manual methods implicate higher healthcare costs.

Solutions based on 3D imaging software have been tested in DIEP flap planning, but they provide inaccurate information on perforator location and properties, which is critical for a thorough surgical planning. Moreover, conventional methodologies for blood vessel segmentation have a poor performance in tracking blood vessels perforators, especially in the intramuscular portion where the signal-to--noise ratio is low.

Description of the technology

Accurate-BV is an image processing algorithm that automatically tracks and retrieves clinically relevant features from perforator blood vessels within a volume of interest. When applied to the DIEPs, which are relevant for the state-of-the-art method for autologous tissue-based breast reconstruction, Accurate-BV's precision is at voxel-level (~1 mm) and the software calculates caliber, tortuosity, exit point at fascia, subcutaneous course orientation, and intramuscular course length.

The main advantages of Accurate-BV are:

- Reduce DIEP flap surgery and recovery duration, as well as overall complications;
- Increase the quality of breast reconstruction and patients' satisfaction;
- Avoid surgery rescheduling due to incorrect preoperative assessment of blood vessels;
- Support analysis of perforator blood vessels, reducing radiologists' workload and facilitating the tracking of blood vessels in regions of difficult evaluation (i.e., intramuscular).

Intellectual Property Rights

- EP3352135, patent pending
- US2018199997, patent pending
- CN108324300, patent pending
- JP2018134393, patent pending

Results and Clinical Evidence

A preliminary study on annotated Computerized Tomographic Angiography data from twenty patients was conducted in collaboration with the Champalimaud Foundation. Accurate-BV was able to reach an average error of 1.35mm and 1.06mm regarding the extraction of subcutaneous and intramuscular DIEP vessel paths, respectively. Besides, caliber was estimated with an average error of 0.35mm and the location where the perforator leaves the fascia was reported with an average error of 1.4mm in height and 1.72mm in width. More recently, we improved our algorithms achieving errors of 0.64mm and 0.50mm regarding the detection of subcutaneous and intramuscular paths, respectively. At the moment, reports generated with the aid of the software are being compared with manually generated ones, also in cooperation with the Champalimaud Foundation.

Technology Readiness Level (TRL)

TRL3

Potential Applications

Application	Intended use	Class
Accurate-BV is an image analysis software for evaluating enhanced CT images, especially devoted for preoperative planning of DIEP flap surgery	Visualization, processing and evaluation through the characterisation (length, diameter, tortuosity) of subcutaneous and intramuscular portions of perforator blood vessels, helping physician to select the better blood vessels and surrounding tissue that should be used as graft in DIEP flap surgery.	I

Breast Cancer Conservative Treatment. Cosmetic Results (BCCT. core)

INESC TEC

Description of the problem

Cosmetic outcome of breast cancer conservative treatment (BCCT) remains without a standard evaluation method. Subjective methods, in spite of their low reproducibility, continue to be the most frequently used. However, subjective evaluation when performed by a panel of observers, which is the most frequent approach, has very low reproducibility values and it is both a difficult and time consuming procedure. Self-assessment on the contrary is easy but usually translates Quality of Life (QOL) issues more effectively than a reproducible value of cosmetic outcome. To address these limitations, we present the BCCT.core, a system to automatically evaluate the aesthetic outcome of BCCT.

Description of the technology

The BCCT.core is a data collection, image processing and aesthetic modelling system that predicts and optimizes the outcome of an individual patient's breast after oncoplastic surgeries.

By analysing several parameters related to asymmetry, color differences and scar appearance, BCCT.core helps at increasing the quality of breast reconstruction and patients' satisfaction with the final outcome. After positioning the reference points on the patient face view image, the program simulates automatically asymmetry, color and scar features, reducing patient's anxiety. Machine learning techniques are used to find the best subset of measures and the best relation between them, classifying each case in one of four classes (excellent, good, fair or poor). The software can be used either to extract individual or multiple measurements or to make use of the created algorithm to calculate the final classification of cosmetic outcome.

Intellectual Property Rights

Copyright

Results and Clinical Evidence

The patient meshes used in this research were obtained from MRI data of 6 patients scanned during data acquisition of European PICTURE project.

Technology Readiness Level (TRL)

TRL6

Potential Applications

Application	Intended use	Class
Breast surgery planning	Vizualizing, processing, simulating, and 3D reconstruction of breast region using MRI images	IIa

4. Biosignals and Medical Imaging Technologies

Microwave imaging impedance matching surface

INESC TEC

Description of the problem

There is a need for non-ionizing and cost-effective medical imaging solution. Although X-rays, CT, US, and MRI offer a wide range of applications, microwave imaging (MWI) is affordable, uses safe radiations and delivers functional images by assessing bulkelectrical tissue properties.

However, a major problem facing microwave imaging is the reflection of energy from the air-skin interface, which may be orders of magnitude larger than the reflected tumor response. Currently, this matching problem is overcome by immersing both the antenna array and the skin in a liquid having a permittivity close to the human tissue so as to reduce the impedance mismatch and thus, the reflected power at the interface.

However, the liquid is not practical to handle, is uncomfortable for patients, has a complicated maintenance and requires replacement to avoid contamination. Additionally, the liquid does not provide an optimum (wideband) impedance matching, compromising the MWI resolution.

Description of the technology

To solve the mentioned limitations of the liquid-based matching, INESC TEC developed the METAMat MWI, a new meta-material based impedance matching surface.

Using the proposed impedance matching surface technology, MWI becomes more comfortable to the patients since they avoid placing their head or breast in the matching liquid, more attractive to the clinicians and patients since the results can be more accurate, avoiding false positives or negatives, and it eliminates the handling and maintenance of the liquid.

Intellectual Property Rights

- Copyright
- Trade secret

Results and Clinical Evidence

Lab Simulations

Technology Readiness Level (TRL)

TRL2

Potential Applications

Application	Intended use	Class
Medical Imaging	Functional (electrical) imaging; Breast and brain cancers detection, and brain stroke classification and follow-up are preferential use cases.	N/A

Medical Thermography

University of Porto

Description of the problem

In order to ensure the normal functioning of the vital organs, the human body temperature is, under normal conditions, axisymmetric and kept within a very tight range regardless of the ambient temperature. Thus, changes in skin temperature, or the presence of asymmetric patterns, can be interpreted as being originated by changes in the circulatory system, derived from pathological situations, local inflammation or muscular activity.

Description of the technology

Medical infrared thermography is a complementary diagnostic and therapeutic method characterized by the ability to obtain a color map image corresponding to the temperature of each pixel. This technology does not use ionizing radiation nor is invasive, thus not poses any risk, both to the patient and examiner.

Thermal cameras are small and portable devices able to record thermal images and videos, with typical resolutions from 500 mK to 18 mK, and matrix sensors sizes from 80x60 to 1024x768.

Intellectual Property Rights

N/A

Results and Clinical Evidence

This technology has proven results in all situations where there is a change of the skin temperature.

Technology Readiness Level (TRL)

TRL7

Potential Applications

Application	Intended use	Class
Hyperhidrosis, Diabetic Foot Ulcer, Skin Cancer, Raynaud's Syndrome, Temporomandibular disorders (TMD), Mass fever screening.	Aid for diagnosis and evaluation of treatment effect. Screening tool.	I
Sports, Music Performing Arts, Occupational Medicine	Monitoring Tool	I

Digital stethoscope

University of Porto

Description of the problem

Digital stethoscopes are well established in the medical devices scenario but usually they rely solely in acoustic data acquisition, namely Phonocardiography (PCG). Some approaches integrate also Electrocardiography (ECG), albeit modifying the standard form factor of the stethoscope.

Furthermore, it acquires inertial measurement unit (IMU) data, as a way of integrating the relative position of the stethoscope head in relation with the electrical axis of the heart.

This invention proposes to integrate ECG and IMU data acquisition in the form factor of a standard stethoscope, and to complement it with fNIRS. This last technology is already being used to check, for example, brain oxygenation. This invention can open a new approach to the evaluation of cardiopathies and potentially save lives.

The main advantage is that, besides providing signals with higher reliability and in the form factor of a standard stethoscope, it will give an optimal solution for doctors and other health professionals to add this device to their existing set of medical devices, thus accessing to three extra analysis technologies (IMU, ECG and fNIRS) in a single device that can reveal crucial information for the pre-screening of cardiopathies.

Description of the technology

A new digital stethoscope is proposed that, synchronously, measures phonocardiographic (PCG), electrocardiographic (ECG), inertial (IMU) and functional near infrared spectroscopy (fNIRS) signals using a standard electronic stethoscope or a purpose-built device.

Intellectual Property Rights

Provisional Portuguese Patent application

Results and Clinical Evidence

An initial prototype has been developed and validated in a laboratory setting, to define the form factor, electrode materials, sensor dimensioning, and comparison of the collected signals against an established gold standard. It has resulted in an MSc thesis and a journal submission to an established Q1 journal in the field of biomedical engineering.

Technology Readiness Level (TRL)

TRL3

Potential Applications

Application	Intended use	Class
Cardiopathy pre-screening	Doctors or other health professionals that can integrate this invention in most of the existing analogue stethoscopes used by them to diagnose cardiac pathologies	IIa
Telemedicine and home hospitalisation	Remote monitoring of cardiovascular dynamics either by an informal carer or the subjects themselves to support the remote monitor and follow-up of their health status	IIa

NeuroKinect

INESC TEC

Description of the problem

Currently, for a good diagnosis and therapy planning (including surgery), physicians need to admit patients into an Epilepsy Monitoring Unit (EMU) where video-EEG monitoring is carried out. Despite the establishment of several automatic methods that help to analyze brain electrical activity, seizure semiology is still widely interpreted by visual inspection.

2D monitoring systems have been considered to replace visual inspections but their limitations are obvious: difficulty of tracking the erratic movements of interest, frequent marker occlusions and instability of the attached intrusive reflectors or sensors.

Other proposed 3D systems and non-camera approaches have limited widespread use due to their high associated costs, heavy maintenance demands (calibrations, reflectors placing), and complex set-up. NeuroKinect offers a more accurate and fast body motion assessment in epilepsy, unlike the generic few systems based on depth images.

Description of the technology

In clinical practice, neurologists usually rely on direct visual observation (or through a video) to evaluate motor symptoms following subjective methods of evaluation based on clinical scores. To address these limitations, INESC TEC developed NeuroKinect, a portable and low-cost 3D video system designed to provide quantitative data on human motion in the context of neurological diseases with movement impairment.

Based on synchronized EEG-depth video, a few of patients' joints are tracked during epileptic seizures in the EMUs, and relevant metrics for understanding its disease are calculated. The physician can then analyse these metrics on parallel with the brain's electrical activity better understanding, characterizing and quantifying the epileptic seizures.

Intellectual Property Rights

- Copyright
- Trade secret

Results and Clinical Evidence

NeuroKinect was successfully tested in the University of Munich Epilepsy Monitoring Unit, and is continuously recording data in 3 beds. Over 300 seizures from more than 300 patients have now been recorded. There are published results showing the analysis of 42 seizure movement of interest found in different parts of the patients' body – 19 from temporal and 23 from extra temporal brain region seizures. These findings show that it is possible to differentiate seizures occurring in the extratemporal and temporal brain regions using NeuroKinect technology.

Technology Readiness Level (TRL)

TRL5

Potential Applications

Application	Intended use	Class
Clinical continuous monitoring units (i.e. epilepsy units)	Provides a user-friendly and comfortable system for both patients and clinical professionals; Is less expensive than previous approaches based on non-camera or 3D systems; Offers a reliable and accurate tool to support human body motion assessment of Epilepsy patients.	IIa
Gait analysis in neurological diseases	Several neurological diseases have changes in gait that can be directly correlated with the severity of the disease. Objective gait analysis can help characterize different patient groups and help assess improvements in the disease and its management with changes in the treatment.	IIa

5. Bioengineering & Biomaterials Technologies

Heart at Tech

University of Aveiro

Description of the problem

Acute Myocardial Infarction (AMI) is currently the leading cause of death and disability in the world. Every year, more than 7 million patients in the United States come to the emergency department with complaints of chest pain. The screening of patients who are suffering from an AMI episode from other causes is of vital importance: the rapid distinction between benign and severe cases allows a more adequate management of emergency services, with cost reduction effects and better management resources. Current diagnostic solutions are accurate (high sensitivity) or portable, but none effectively combines these features into one device.

Description of the technology

The device that is being developed combines high sensitivity and reproducibility with the portability of an optical biosensor for the detection of cardiac markers (notably Troponin). This unique combination will allow faster results, with reliable precision and next to the patient bedside. The device will consist of a portable system divided in two parts: a cartridge containing the optically active zone that will receive the patient's blood sample and handheld optical reader per se where the cartridge is inserted.

Intellectual Property Rights

Patent submission in the near future

Results and Clinical Evidence

- Prototype assembly of measuring device
- Validation of measurement capacity of the active substrate contained in the disposable cartridge.

Technology Readiness Level (TRL)

TRL3

Potential Applications

Application	Intended use	Class
Circulating blood troponin measurement in the acute patient with suspected acute myocardial infarction	Early diagnosis of acute myocardial infarction	IIa
Measurement of circulating troponin in the blood of a patient that arrives to the emergency department with acute chest pain	Rapid and reliable exclusion of acute coronary syndrome	IIa
Circulating troponin measurement in the blood in ambulatory patients with stable chest pain or with acute pathology, but without chest pain	Individual risk stratification	IIa

Cream for allergic contact dermatitis

University of Coimbra

Description of the problem

Allergic contact dermatitis (ACD) is one of the most common skin diseases with a high prevalence rate of 15-20% over the general population. This high prevalence not only results in large costs for the healthcare system but also greatly impacts the quality of life of the affected patients. One main concern about this pathology is that once sensitized the individual will always develop ACD after the contact with the allergen, highlighting the relevance for the development of preventive strategies. From a pathophysiological point of view for an immune response to be induced, and for skin sensitisation to be acquired, the contact allergen must gain access across the stratum corneum and reach the viable epidermis and beyond. Here, a variety of important events take place, including the formation of immunogenic complexes following the stable association of the chemical with proteins, which is thought to be the molecular initiating event responsible for the development of skin sensitisation. These assumptions were the starting point for the design of this innovative proposal, which envisioned the development of a skin medical device able to prevent the development of ACD by inhibiting the formation of the immunogenic complexes.

This project is the first step in proof-of-concept work that will generate important insights in the preventive value of new medical devices, acting as skin barriers, for Allergic Contact Dermatitis.

Description of the technology

- Medical device for preventing Allergic Contact dermatitis
- A medical device that will consist in a “chemical barrier cream” or a “chemical glove” against skin allergens.

The medical device we are developing includes several molecules with the capacity of reacting with skin allergens thus rendering them unable to further establish covalent bindings with skin proteins, which is considered the early molecular event responsible for the development of skin sensitization and allergic contact dermatitis. Until now, the industry does not use any similar technology. Indeed, for ACD preventive purposes, the industry has, for instance, latex gloves. However, studies on using gloves to prevent the development of occupational contact dermatitis are limited and the observed benefits were not exclusively attributable to wearing gloves, because they were only one part of a comprehensive prevention strategy. Concerning barrier creams, water resistant barrier creams contain hydrophobic substance such as silicone, which protects skin against water soluble substances such as acids, alkali and dye. On the other hand, oil or solvent resistant barrier creams protect against dust, oils, greases and solvents, but their clinical effectiveness in preventing ACD is controversial and unsupported by clinical studies. Furthermore, barrier creams should be used on normal skin as they cause aggravation of dermatitis if applied to inflamed skin. Among the ingredients used in topical formulations there is fair-quality evidence that the topical skin protectant quaternium-18- bentonite can prevent dermatitis and diethylenetriamine penta acetic acid can prevent nickel, chrome, and copper dermatitis. There is also fair evidence that pentoxifylline is not effective in preventing nickel allergy. Of utmost importance, the mechanism of action of barrier creams and of all the ingredients listed above is quite different from the molecules we intend to commercialize as a medical device, which constitutes the innovative character of this proposal. Therefore, and focused on the market demand, we envisage the development of a skin medical device enriched in

molecules, not yet available on the market, capable of chemically sequestering skin allergens thus avoiding its interaction with skin proteins (the first adverse outcome pathway for skin sensitization) and consequently preventing the development of allergic contact dermatitis.

Intellectual Property Rights

Trade Secret

Results and Clinical Evidence

- Currently, and among the panel of molecules investigated for their potential to chemically sequester extreme and strong skin allergens, we found 3 molecules very promising and able to abolish several key events crucial for the development of skin sensitization, namely the maturation of dendritic cells evoked by well-known allergens;
- Molecules already available on the market for other purposes;
- Low cost product;
- User friendly.

Technology Readiness Level (TRL)

TRL3

Potential Applications

Application	Intended use	Class
If successful, this project will allow the development of a medical device able to prevent the development of allergic contact dermatitis.	Avoid the onset of the disease allergic contact dermatitis	Not determined
Besides the main application of this proposal (the development of a medical device able to prevent the development of allergic contact dermatitis) another potential application is that the more promising ingredients could also be incorporated in any other cosmetics already commercialized on the market, allowing the claim of cosmetic for ultrasensitive or allergic skin with the capacity to prevent/rescue the development of skin allergy in individuals with some propensity to develop this pathology.	Development of cosmetics with anti-allergic properties	Not determined
The allergens' sequestering molecules could also be introduced into "selfproducts" enhancing the effects of products already available in the market	Enhance the effects of products already available in the market	Not determined

TESty - Typing Easier

Polytechnic Institute of Coimbra

Description of the problem

Data from 2017 indicate that in Portugal there are more than 130 thousand regular donors - donors who give blood between 2 to 4 times a year. These data lead us to a number of gifts from 250 to more than 500,000 donations per year in Portugal alone. Associated with this, we have more than 300,000 transfusions per year that may require more than one unit of blood. All of these units, before being given, and all patients before they are subjected to a blood transfusion or even a transplant, must be properly identified as to their blood type. Currently, and for the determination that TESty intends to make, the standard technique (in tube) requires that at least 8 tubes be used per individual and the widely used device today requires that 2 per individual, also requiring the purchase of expensive laboratory equipment specifically for this purpose. Although these solutions present a high reliability of results, these methods are performed through a complex protocol, requiring access to laboratories with specific equipment without any other use (e.g. centrifuges for cards) and with the need to be performed by specialized healthcare professionals.

Description of the technology

TESty consists of a 96-well microplate coated by an agarose gel soaked with antisera at a certain concentration that it intends to develop and present a new method that allows AB0 (cellular and reverse) and Rh blood groups to be made in a simple, easy way and inexpensive, without the need for expensive specific laboratory equipment (e.g. centrifuges). TESty can be a key device for gift and harvest centers by providing the same results as the options currently on the market, but at a lower cost associated with them. In addition, TESty also presents a profile for the developing countries market, since it allows grouping 12 individuals at a time, without the use of specialized equipment and at low cost, being determinant to increase transfusion safety and avoid fetal incompatibilities in the countries mentioned above.

Intellectual Property Rights

Results and Clinical Evidence

Currently, we have a prototype developed in the laboratory that has already proved to be efficient in allowing to obtain the same results as the standard technique (tube) and the technique most used today (card). Some known samples were tested and in all we obtained the expected results.

Technology Readiness Level (TRL)

TRL3

Potential Applications

Application	Intended use	Class
Developing countries	Because it is a simple and easy to use method of interpretation and interpretation of results, it is easy and inexpensive to allow the analysis of a larger number of samples in the same period of time as conventional methods, without the use of specific high cost equipment. a business idea that can revolutionize the current context of transfusion medicine, thus comprising a strong force of our business idea that could allow a greater acceptance of our product by the target market.	IIa
Centers for donations and harvests, blood services in the laboratory routine	In Portugal alone, there are more than 350,000 benevolent donations and 300,000 transfusions. For each of the samples involved in these situations, it is mandatory to perform the AB0 and Rh determination. Nowadays, the most commonly used options (tube - standard technique - and card) allow the grouping of only one sample/individual. In this way, our microplate is presented as a more favorable option in that it allows the grouping of 12 samples or individuals in a single device.	IIa

PhotoAKI: Photonic Biosensor for point of care and Early Diagnostics of Acute Kidney Injury

Polytechnic Institute of Lisbon

Description of the problem

The goal of the PhotoAKI project is the development and characterization, of a disposable photonic sensor for point of care detection of biomarkers of Acute Kidney Injury (AKI). Achieving this target would be of great impact in the disease management.

It is in fact widely accepted that after an episode of AKI there is a significant risk of death and progression to chronic kidney disease and despite recent improvements in diagnosis, the mortality of AKI remains unacceptably high. Early diagnosis of AKI is often problematic, due to the lack of suitable early biomarkers of renal damage and kidney function. Neutrophil gelatinase-associated lipocalin (NGAL) as an early marker of AKI partially overcomes such limitations making possible diagnosis of AKI in its early stages.

Description of the technology

The PhotoAKI project targets the implementation of a low-cost method for fast diagnosis, monitoring of disease and patient status: a label-free, high-throughput approach for quantitative analysis of NGAL based on a low cost photonic sensor based on amorphous silicon technology. The sensor profits the capability of a-SI:H to produce tunable surface plasmonic resonance (SPR) effects, when used jointly with metal interfaces, metal nanoparticles and graphene multilayers. The proposed sensor structure is based on a a-SIC:H waveguide, coupled to an Aluminium surface capable to produce SPR affects at visible (red) wavelength. The metal surface is functionalized with antibodies against NGAL. Coupling between the waveguide mode and the surface plasmon generated at the semiconductor-metal interface produces a light intensity modulation of the guided light that is dependent on the NGAL concentration. The output is measured by an a-SI:H thin film photodetector. The waveguide, the SPR coupler and the photodetector are integrated into one unique system targeting the fabrication of a compact device.

As a second alternative, we propose the development of a plasmonic structure based on the Localized Surface Plasmon Resonance (LSPR) interaction of metal nanoparticles with an embedding amorphous silicon matrix. After proper functionalization with selective NGAL antibodies, the efficiency of light extinction (scattering and absorption) is controlled by the slight changes in the refractive coefficient induced by the NGAL concentration. Direct integration with an a-SI:H photodetector allows the quantification of the NGAL presence on the sensing surface. Even if less efficient, this second configuration allows lower production cost. From the point of view of a disposable sensor it is very important the realization of the two structures and a following comparison about efficiency and costs.

As a further improvement, for both the proposed sensor structures, we propose the use of a functionalized surface based on multilayer graphene. This choice would allow an improvement of the biocompatibility of the surface to be functionalized and a cost reduction for the sensor production.

Intellectual Property Rights

Know-how

Results and Clinical Evidence

Not yet available

Technology Readiness Level (TRL)

TRL2

Potential Applications

Application	Intended use	Class
Measuring Ngal concentration in human urina as an indicator of Akute Kidnay Injury risk.	Disposable photonic sensor for point of care detection of biomarkers of Acute Kidney Injury. This problem is of a major importance, as the absolute incidence of AKI has increased over the last decade. Almost 10% of hospitalized patients can develop AKI and incidence is even greater in the intensive care unit (ICU) and emergency department (ED) settings, respectively attaining 30% and 20% in Portugal	I

BB-SPECTRAL

INESC TEC

Description of the problem

Blood test offers crucial information for diagnosis, treatment and disease monitoring. Still, current technologies lack rapid and accurate analysis at the point of care. Also, blood collection causes particular discomfort in risk groups (neonates, children, elderly and debilitated patients) and is impractical where critical high-frequency tests are essential (oncology, chronic diseases, intensive care, and emergency settings). Furthermore, wet lab technologies, such as microfluidics and related nanotechnologies make use of reagents, which has major drawbacks for its application in harsh environments. By only using light, we can disruptively eliminate all previous art limitations, for a real miniaturized POC where is needed the most, anytime, anywhere.

Current approaches for spectral analysis comprise artificial neural networks (ANN) and non-linear support vector machines (SVM), which attempt to create complex function models that fit to all data. This strategy fails at analysing complex samples, requiring large amounts of data, being unable of detecting outliers, and encompassing high computational costs.

BB-SPECTRAL was developed to overcome these technical problems using a local and global approach to provide medical-grade accuracy and precision, quantifying and identifying any chemical compound in highly complex samples like blood.

Description of the technology

BB-SPECTRAL is an artificial intelligence (AI) technology for quantify and categorised chemical compounds using spectral information of highly complex samples (e.g. blood). Avoiding the use of reagents, BB-SPECTRAL is able to predict compounds concentrations with an accuracy of about 90% in comparison to the laboratory results (gold standard).

Explaining to humans the spectral data extracted from samples, BB-SPECTRAL is unique at establishing its own knowledge base, indicating 'a priori' the predictability, accuracy and precision of new estimates. This technology is applicable to all regions of the electromagnetic spectra used in spectroscopy analysis, or with any other type of spectroscopy where complex multi-scale interference and chemical/biological variability is present.

Intellectual Property Rights

Patent pending (WO)

Results and Clinical Evidence

The most complete study was performed for human samples (blood, serum and urine). The study was developed in two phases: i) initial exploration for proof-of--concept; and ii) blind testing for total error determination of the technology for several clinical analysis parameters. Blind tests were set to test the system in real world conditions: i) usage in clinical environment by nurses; ii) samples from different locations and types of patients than the training dataset; iii) inter-laboratory results. Results from blind tests were performed for blood and serum to the following parameters: erythrocytes, hemoglobin, hematocrit, MCV, MCHC, leucocytes, platelets, bilirubin, creatinine and CRP.

The technology was further successfully tested for veterinary applications (dogs and cats) in 2016 and 2017. BB-SPECTRAL, with the name VetPAT, was awarded with the "Prémio Startup Montenegro" in 2017 (https://www.veterinaria-atual.pt/naclinica/vencedores-do-premio-startup-montenegro-querem-revolucionar-mercadodas-analises-clinicas/).

Previously, the technology was validated in precision agriculture. In 2010 won the I2P Global competition. Today is being transferred into autonomous metabolic robots for agricultural management."

Technology Readiness Level (TRL)

TRL6

Potential Applications

Application	Intended use	Class
Clinical Chemistry and Clinical Toxicology Devices	The BB-SPECTRAL system is an in vitro diagnostic product for the calibration of the analytes on the system. The analytes measured are erythrocytes, hemoglobin, hematocrit, MCV, MCHC, leucocytes, platelets, bilirubin, glucose, myoglobin, creatinine, CRP, triglycerides, urea, and uric acid.	IIa / IIb

Injectable hydrogel-forming polymer solution for a reliable EEG

University of Porto

Description of the problem

EEG has been used for the investigation of pathophysiological conditions of the human brain, but also extended to non-clinical applications. Silver/silver-chloride electrodes (Ag/AgCl), used together with an electrolytic gel, have been the gold standard for EEG acquisition. However, the gels are a source of many problems, as a non-negligible risk of electrode short-circuits exists, particularly in high density EEG. Furthermore, the gel strongly sticks to the hair and scalp and the patient is forced to thoroughly wash the hair after the exam. The need for a more expeditious EEG system, combining the performance of the actual Ag/AgCl electrodes with electrolytic gel with a faster and easier application protocol, has translated into a high number of technical solutions.

This product may be applied with a syringe into the electrode cavities of many commercial EEG cap systems and it allows for a faster and easier cleaning of the scalp after the recordings. On the technical side, its semi-solid nature substantially reduces the risks of electrodes short-circuiting due to gel running, hence increasing EEG data reliability and higher mechanical stability of the electrodes, particularly in high density. In addition, the isotonic salt concentration and the use of mild, dermatologically approved skin hydration agents, make this gel suitable for sensitive skins and allergy prone patients.

Description of the technology

This invention relates to an electrolytic gel for EEG recording, which can be applied into the electrode cavities of common EEG caps. The product forms a solid hydrogel shortly after application. When the cap is removed, the hydrogel either remains inside the electrode cavities or breaks into small pieces and is thus easily removed with a comb; hence, the patient does not need to wash the head. The new formulation will contribute to make EEG easier, faster and more comfortable to the patients.

Intellectual Property Rights

Patent pending application in Europe, USA, China, Japan and Australia

Results and Clinical Evidence

The gel was tested for the setting time (which can be adjusted by changing the formulation), mechanical properties and electrochemical properties in contact with a saline solution. The impedance modulus proved to be similar to that of a commercial gel tested in the same conditions. In-vivo tests were carried out in three volunteers, using a 128 electrodes cap, where half of the electrode cavities were filled with a commercial gel and the other half with the alginate gel. EEG signals from adjacent commercial gel and alginate gel electrodes proved to be indistinguishable for all tests performed. After the exam, the average cleaning time was about 3 minutes and the patients did not need to wash the head.

Furthermore, when the recording time was extended for 3.5h the impedance even decreased, unlike commercial gels where the impedance becomes too high to continue the measurements after 3-4h.

Besides these tests, some successful demonstrations were performed for companies to show the potential of the new product.

Technology Readiness Level (TRL)

TRL7

Potential Applications

Application	Intended use	Class
Non-invasive EEG imagiology	Studies of brain functioning and diagnosis of brain disorders	I
EEG/MRI exams (simultaneous EEG and magnetic resonance imaging exams)	Studies of brain functioning and diagnosis of brain disorders	I

CONCLUSION

This Catalog presents several research results in the area of medical devices developed by various entities of the national research and innovation system (Sistema Nacional de Investigação e Inovação – SI&I). The document is directed at companies and market oriented entities to whom these results may bring a competitive advantage, as well as potential research partners for further scientific developments. These entities are invited to contact the institutions directly for more information on the technologies of interest.

Overall, the presented results reveal the significant evolution and quality of the research done in Portugal, in this field, contributing this Catalog not only to disseminate this knowledge but also to facilitate the adoption of these technologies by the market and, ultimately, to promote a greater benefit to society."