Horizon 2020

Call: H2020-PHC-2015-two-stage

Topic: PHC-11-2015

Type of action: RIA

Proposal number: 666906-1

Proposal acronym: IMMdoscope

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How to fill in the forms

The administrative forms must be filled in for each proposal using the templates available in the submission system. Some data fields in the administrative forms are pre-filled based on the previous steps in the submission wizard.

Proposal ID **666906-1** *Acronym* **IMMdoscope**

1 - General information

Topic PHC-11-2015 Type of action RIA

Call identifier H2020-PHC-2015-two-stage Acronym IMMdoscope

Proposal title* NEW 3D INMERSIVE REALISTIC ENDOSCOPE

Note that for technical reasons, the following characters are not accepted in the Proposal Title and will be removed: < > " &

Duration in months *42*

Fixed keyword 1 *Medical devices* Add

Free keywords *Diagnosis, imaging tool, In vivo, image-based intervention, Therapeutic novelty, Real 3D*

Abstract

IMMDOSCOPE will develop enhanced in-vivo imaging devices for real-time diagnosis of colonic polyps that will facilitate early screening for detection of colorectal cancer in both men and women. At the same time a therapeutic microsurgery toolset that enables bimanual versatile and intuitive tissue manipulation will be developed and tested taking advantage from the new 3D endoscopic imaging in order to increase the impact of this enhanced imaging technology on cancer prevention. Optimizing the efficacy of colorectal cancer screening and surveillance requires high definition colonoscopes with improved virtual technology that visualize the colon mucosa while maintaining optimal therapeutic capabilities, and keeping the procedural time as low and patient discomfort as optimal as possible.
A significant impact on achieving better informed clinical decisions will be obtained through the use of this novel technology when integrated in a picture archiving communication system and its association with the patient's electronic health record (HER). Formal core ontology will be defined and DICOM providing Interoperability with health information systems will be achieved by providing and open interface based on a service oriented architecture (SOA) enabling an easy integration into HL7 standard.
This new integrated technology will be develop through a business-led perspective, aiming impact on the growth and competitiveness of the companies that form the supply chain of the respective products and services to come. Companies related to endoscope products, optical development, sensors, therapy technologies, software located in the cloud, other visualization devices, etc will benefit directly from their cooperation to develop this new technology through a strong business case.

Remaining characters 208

Has this proposal (or a very similar one) been submitted in the past 2 years in response to a call for proposals under the 7th Framework Programme, Horizon 2020 or any other EU programme(s)? ○ Yes ◉ No

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Declarations

1) The coordinator declares to have the explicit consent of all applicants on their participation and on the content of this proposal.	☒
2) The information contained in this proposal is correct and complete.	☒
3) This proposal complies with ethical principles (including the highest standards of research integrity — as set out, for instance, in the European Code of Conduct for Research Integrity — and including, in particular, avoiding fabrication, falsification, plagiarism or other research misconduct).	☒

4) The coordinator confirms:

- to have carried out the self-check of the financial capacity of the organisation on https://ec.europa.eu/research/participants/portal/desktop/en/organisations/lfv.html. Where the result was "weak" or "insufficient", the coordinator confirms being aware of the measures that may be imposed in accordance with the H2020 Grants Manual (Chapter on Financial capacity check); or	◉
- is exempt from the financial capacity check being a public body including international organisations, higher or secondary education establishment or a legal entity, whose viability is guaranteed by a Member State or associated country, as defined in the H2020 Grants Manual (Chapter on Financial capacity check); or	○
- as sole participant in the proposal is exempt from the financial capacity check.	○

5) The coordinator hereby declares that each applicant has confirmed:

- they are fully eligible in accordance with the criteria set out in the specific call for proposals; and	☒
- they have the financial and operational capacity to carry out the proposed action.	☒

The coordinator is only responsible for the correctness of the information relating to his/her own organisation. Each applicant remains responsible for the correctness of the information related to him and declared above. Where the proposal to be retained for EU funding, the coordinator and each beneficiary applicant will be required to present a formal declaration in this respect.

According to Article 131 of the Financial Regulation of 25 October 2012 on the financial rules applicable to the general budget of the Union (Official Journal L 298 of 26.10.2012, p. 1) and Article 145 of its Rules of Application (Official Journal L 362, 31.12.2012, p.1) applicants found guilty of misrepresentation may be subject to administrative and financial penalties under certain conditions.

Personal data protection

Your reply to the grant application will involve the recording and processing of personal data (such as your name, address and CV), which will be processed pursuant to Regulation (EC) No 45/2001 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data. Unless indicated otherwise, your replies to the questions in this form and any personal data requested are required to assess your grant application in accordance with the specifications of the call for proposals and will be processed solely for that purpose. Details concerning the processing of your personal data are available on the privacy statement. Applicants may lodge a complaint about the processing of their personal data with the European Data Protection Supervisor at any time.

Your personal data may be registered in the Early Warning System (EWS) only or both in the EWS and Central Exclusion Database (CED) by the Accounting Officer of the Commission, should you be in one of the situations mentioned in:
-the Commission Decision 2008/969 of 16.12.2008 on the Early Warning System (for more information see the Privacy Statement), or
-the Commission Regulation 2008/1302 of 17.12.2008 on the Central Exclusion Database (for more information see the Privacy Statement) .

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2 - Administrative data of participating organisations

PIC	***Legal name***
998696093	*INSTITUTO TECNOLÓGICO DE CASTILLA Y LEON*

Short name: ITCL

Address of the organisation

Street C/ López Bravo - Pol. Ind. Villalonquejar 70

Town Burgos

Postcode 09001

Country Spain

Webpage http://www.itcl.es

Legal Status of your organisation

Research and Innovation legal statuses

Public body ..... no
Non-profit ..... yes
International organisation ..... no
International organisation of European interest ..... no
Secondary or Higher education establishment ..... no
Research organisation ..... yes
Small and Medium-sized Enterprises (SMEs) ..... no

Legal person ..... yes

Nace code 721 -

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Department(s) carrying out the proposed work

Department 1

Department name	European Programs
	☒ Same as organisation address
Street	C/ López Bravo - Pol. Ind. Villalonqueja
Town	Burgos
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Country	Spain

Dependencies with other proposal participants

Character of dependence	***Participant***	

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Person in charge of the proposal

The name and e-mail of contact persons are read-only in the administrative form, only additional details can be edited here. To give access rights and basic contact details of contact persons, please go back to Step 4 of the submission wizard and save the changes.

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Proposal ID **666906-1** *Acronym* **IMMdoscope**

3 - Budget for the proposal

Total requested amount / €	5 597 887

Proposal template
(technical annex)

Research and Innovation actions

COVER PAGE

Title of Proposal: NEW 3D IMMERSIVE REALISTIC ENDOSCOPE

Acronym: IMMDOSCOPE

This proposal prepared in response to H2020-PHC-2015: Two-stage, PHC-11-2015. Topic: Development of new diagnostic tools and technologies: in vivo medical imaging technologies

List of participants

Number	Participant organisation name	Short Name	Organization Type	Country
1 (Coordinator)	Instituto Tecnológico de Castilla y León	ITCL	Research center	Spain
2	University of the West of England	CMV	University	United Kingdom
3	Optoelectronica 2001 s.a.	OPT	SME	Romania
4	St Georges Hospital	STGH	Clinical	United Kingdom
5	Philips	PHI	Industrial	Netherlands
6	GMV innovating solutions	GMV	Industrial	Spain
7	Ovesco	OVE	SME	Germany
8	Blaise Pascal University	BPU	University	France
9	University of Amsterdam	UA	Clinical	Netherlands
10	City University London	CITY	University	United Kingdom
11	Awaiba	AW	SME	Portugal
12	State University of Campinas	UNICAMP	University	Brasil

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1. EXCELLENCE

Every three minutes one adult in Europe dies of Colorectal Cancer (CRC). According to the most recent survey done by the United European Gastroenterology (UEG), CRC claims an estimated 214,675 lives (male and female adults) every year. More alarmingly, the UEG also predicts that this figure will rise by 12% by 2020 due to growth and ageing of the global population[1].

Although a number of technologies have been introduced in clinical practice to diagnose and treat the disease, CRC is still showing to be extremely serious and often lethal if allowed to progress in its advanced stages. The key to reducing the morbidity and mortality arising from CRC lies in its early detection and prevention.

Since 2003, several European nations have already introduced population-wide screening programs in a bid to fight CRC. While it is known that regular screening using Faecal Blood Test (FOBT) reduces the risk of dying from the disease by 20-30%, more recent studies have suggested endoscopic screening to have a more preventive effect than FOBT and could contribute to a substantial reduction in mortality due to CRC leading up-to a 90-95% survival rate[2]. So why a predicted rise of 12% in the mortality rate? Possible reasons to explain this would be:

(1) Current technologies used for screening have so far failed to reliably detect and facilitate the removal of precancerous polyps at the expected high level.

(2) Current screening programs are technology–oriented and have missed out on the need of a comprehensive cancer data platform. Representative data collection is an inevitable component for a successful screening program. Extensively gathered and appropriately presented data can raise the general public's awareness, guide politicians, and optimize health care.

In addition to the cost of endoscopic devices, the adoption of screening programmes depends heavily on the cost-effectiveness of CRC treatment. A recent study in Germany, reported that the different phases of CRC treatment (i.e. initial, intermediate and end-of-life phases) yielded mean incremental costs of €26,000, €2,300 and €51,700 yearly for every patient; there is also similar plausible data from other European countries[3]. In addition to these direct costs (including resources, infrastructure, drugs, and cancer-specific expenditure), CRC treatment also includes indirect costs such as resources lost due to inability to work, permanent disability and death before 65 years of age. The failure of current screening technology to detect polyps at an early stage means the CRC treatment life cycle is extended and so is the cost, with the advanced stage treatment (end-of-life) being considerably high.

For the effective and successful screening of CRC, a proper and effective roadmap needs to be developed contributing to (1) provision of low-cost, high precision screening technology accessible to all European countries and (2) provision of a platform to cancer information which will benefit all stakeholders (endoscopists, patients, politicians and the general public). Hence a new approach which represents a quantum leap beyond state-of-the-art technologies is urgently needed for CRC prevention.

The IMMDOSCOPE project is a ground-breaking, multidisciplinary approach to CRC screening integrating a number of novel, synergistic technologies (3D Vision, Augmented Reality, computer-aided detection, sensors and cloud computing) into a ground-breaking form of enhanced in vivo 3D visualization and augmented diagnostic tool.

1.1 OBJECTIVES

The most important objectives provided by this revolutionary technology are listed below:

(1) Design of a hybrid 3D imaging system, suitable for endoscopic applications, that is capable of the accurate recovery of the important surface tissues attributes of reflectance and topography, that is able to provide precise metrology data in terms of polyp size and shape information from the colon wall in the presence of shadows and inter-reflections.

(2) Design of Computer-Aided Detection (CAD) and diagnostic tools to aid the endoscopist in screening the colon for polyps based in the surface data, allowing an increase of 25 - 50% in polyp detection and diagnosis.

(3) Development of immersive visualization and navigation tools for endoscopic screening and microsurgery by fusion of 3D high resolution images, endoscopic sensors and pre-interventional CT images (this also has application in training).

(4) New therapeutic endoscopic instruments and procedures that benefit from the 3D endoscopic imaging which will enhance the capabilities of doctors to treat large tumors, in a safer, faster and much more intuitive way.

(5) A new revolutionary data management and treatment procedure to improve diagnosis able to interoperate with health IT systems.

1.2 RELATION TO THE WORK PROGRAMME

The IMMDOSCOPE Project will accomplish the overall objectives set on the H2020 Societal Challenges by:

- Bringing together resources and knowledge across different fields, such us optical research, new sensors, computer vision, computer-based medical diagnosis, robotics, machine learning, clinical research, and big data management.
- Covering activities aimed at the market with the development of the new concept of both an improved diagnostic tool focus and an industrially led orientation, which will conclude with an operational business model and a new prototype demonstrator product close to the market.

[1] GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012.

[2] Winawer SJ, Zauber AG, O'Brien MJ. Randomised comparison of surveillance intervals after colonoscopic removal of newly diagnosed adenomatous polyps. N Engl J Med 1993; 328: 901-906

[3] Haug U, Engel S, Verheyen F, Linder R (2014) Estimating Colorectal Cancer Treatment Costs: A Pragmatic Approach Exemplified by Health Insurance Data from Germany. PLoS ONE 9(2): e88407. doi:10.1371/journal.pone.0088407

- Optimizing the efficiency and effectiveness of healthcare delivery, enabling enhanced and augmented visualization with a 25-50% increase in accuracy, enhanced by the use of adapted therapy tools that together facilitates polyps removal.
- Establishing links with the activities of the Group B3 of the EIP on Active and Healthy Ageing (AHA) or Joint actions such as the Development of the European Guide on Quality Improvement in Comprehensive Cancer Control ("CanCon") to:
    - Enable social innovation and inform decisions about implementation and delivery of integrated care.
    - Promote the Electronic Health / Care Record.
    - Collaborate to promote CRC screening thanks to the improvements obtained.

Contribute to objectives of the specific challenge Health, demographic Change and Wellbeing by:

- Improving our understanding of the causes and mechanisms underlying health, healthy ageing and disease; with the use of the PACS system (Picture Archiving Communication System) and its association with the patients EHR.
- Improving our ability to monitor health and to prevent, detect, treat and manage disease. Reducing cancer appearance and through the use of image management systems which will enable a better understanding of the disease.

And PHC-11-2015: Development of new diagnostic tools and technologies: in vivo medical imaging technologies by:

- Developing a diagnostic tool which will be more sensitive due to the enhanced mucosal visualization, more robust due to the improved surface definition and more selective due to the ability to differentiate hyperplastic vs adenomatous polyps - a clear advantage over existing tools and technologies.
- Improve clinical practice demands both in the context of polyps detected by standard endoscopy being assessed more accurately to guide resection and in the enhanced detection of previously missed polyps.
- Improved clinical decisions based on the development of a colonoscopy image big data management system approach and building the prototype taking into account standardisation and interoperability on: i) Colon imaging ii) creation of services and contents iii) data sources.
- Providing a new diagnostic tool to address €5.2 billion potential savings to the health care systems annually by 2018 through more accurate detection and treatment of colorectal polyps.
- The Project structure will contribute to the competitiveness of the European SMEs; the IMMDOSCOPE products are forecasted to reach an annual turnover of about EUR 150 Million, 50 % of which will benefit directly European SMEs.
- Translating multidisciplinary scientific & technological knowledge into clinical applications thanks to the consortium structure.

1.3 CONCEPT AND APPROACH

Overall concept

IMMDOSCOPE aims at overcoming current limitations in endoscopy which is widely accepted as the gold standard for screening, surveillance, and treatment of lower GI diseases. Endoscopy has not changed significantly in decades and interval cancers still regularly occur. Up to a quarter of polyps and adenomas are missed during colonoscopy due to poor visualization caused by occlusion behind folds and the inner curves of flexures. In addition the presence of flat or depressed lesions can be particularly difficult to detect Also standard colonoscopes are unable to adequately visualize the entire mucosal surface, as due to occlusions, significant portions of the surface are not visualized.

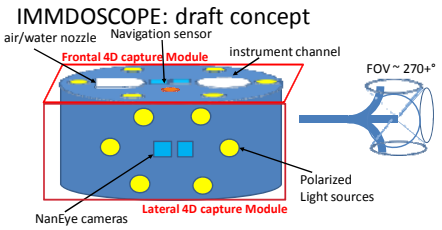
In a tandem study[4] a pooled miss rate for polyps of any size was reported as high as 22%. Current endoscopy devices have failed to receive wide acceptance from surgeons/clinical environments due to their lack of accuracy in providing precise measurement of lesions. This is mainly due to the fact that most endoscopes are restricted to provide only abstract two-dimensional images and leave surgeons to identify potential polyps based on their experience and knowledge. Some newly developed endoscopes provide stereo images for better visualization, but don't retrieve depth data. Recently approaches using time-of-flight sensors and photometric stereo were used in endoscopes, but the depth resolution is poor or the reconstruction inaccurate. Most of these approaches have not materialized into commercial endoscopic products as they have not been able to improve on the accuracy of detecting polyps in the GI tract.

Our proposed approach could lead to a decrease of the miss rate of adenomas by up to 50% based on previous studies, For example Leufkens et al.[5], report an increase of 29.8% in polyp detection rate using a specialized endoscope that provided forward and retrograde imaging of the colon and large increases in accuracy were reported with a full spectrum endoscopy system with three cameras[6]. These systems demonstrate that with increased coverage of the colonic surface during screening, a higher detection rate is possible.

The IMMDOSCOPE project proposes to develop a novel 3D imaging system for endoscopes using the fusion of data obtained by advanced Photometric Stereo (PS) and Stereo Vision (SV) approaches. The capture system embedded in the endoscopic head will comprise of two 4D capture modules composed each by six polarized lights and two high-resolution stereo cameras situated with one module in front and one the side of the endoscope head. The head itself will be rotatable so as to capture the colon wall in its entirety. Our Multi-scale Polarization based PS approach aims to reduce inter-reflections, adapt to tissue deformations and different absorption rates, retrieving high definition 3D surface texture, reflectance information and surface normal data, using six lights to ensure robustness. In order to complement missing information from the PS (data location of

[4] van Rijn JC, Reitsma JB, Stoker J, Bossuyt PM, van Deventer SJ, Dekker E, "Polyp miss rate determined by tandem colonoscopy: a systematic review,"Am J Gastroenterol. 2006 Feb;101(2):343-50.
[5] Leufkens AM, DeMarco DC, et al., "Effect of a retrograde-viewing device on adenoma detection rate during colonoscopy: the TERRACE study," Gastrointest Endosc. 2011;73:480–489
[6] Gralnek IM, Siersema PD et al., "Standard forward-viewing colonoscopy versus full-spectrum endoscopy: an international, multicentre, randomised, tandem colonoscopy trial," Lancet Oncology, 15(3), 2014: 353-60

discontinuities, occlusions and obtain the depth in metric scale), data such as coarse 3D structure, discontinuity and occlusion regions, will be estimated in a calibrated metric scale by robust stereo matching methods such as fast ZNCC or iSGM. A high resolution 3D image will be then achieved by multi-scale fusion and refinement, providing an accurate representation of the colon wall, suitable not only for visualization but also for navigation (and in training). As quality measure: where inspection has not been fully possible, we will be able to present the 3D anatomy of the colon based on the images and indicate in the reconstruction the shadow areas. If available these shadow areas will be linked to imaging scans made on CT to allow for additional inspection.



This system will also prevent disease by the removal of detected polyps thanks to a toolset which will enable complex manoeuvres in laparoscopic surgery, on a micro scale within the digestive tract through triangulation of two interchangeable instruments. Bimanual control, triangulation and extended degrees of freedom are benefiting from as well as complementing to the 3D vision capabilities of the IMMDOSCOPE.

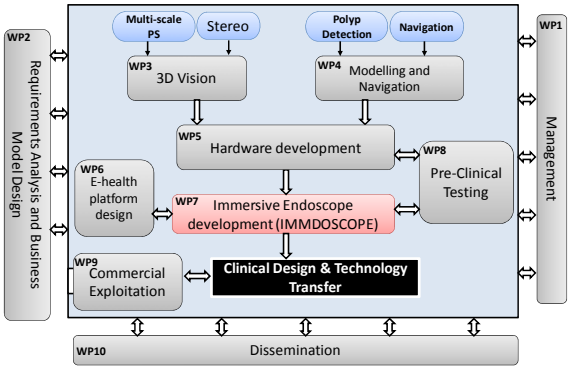
In addition a medical data management system, will be implemented that is able to benefit from the promise of cloud computing, especially fault tolerance, availability, elasticity, in a pay-as-you-go manner. This will make it possible to store large amounts of 3D image data while limiting the costs. The system will focus on the DICOM standard (http://medical.nema.org). The primary objectives of this standard are to achieve inter-operability between medical imaging systems and to make it easier to exchange and store large amount of medical data while limiting the costs. Furthermore, colonoscopy domain ontology and common terms will be defined to enable image annotation and retrieval. In particular, multilingual access will be studied.

The IMMDOSCOPE project is based on a strong partnership among different industrial partners with deep interest in the development of an improved Diagnostic Tool. Phillips will act as the commercial of the final endoscope to be developed, while Ovesco will benefit from the creation of additional therapy tools, able to operate with this technology. Optoelectronica and Awaiba will be able to improve the capability of their optical and miniaturized solutions for any type of Image device tool. The clinical aspects of the proposal will be supervised by the collaboration with strong and well positioned partners, such as Saint Georges Hospital (part of the NHS in England) and University of Amsterdam, who are strongly linked with the European Society of Gastrointestinal Endoscopy. The development of the 3D tissue modelling and visualisation system will benefit from the expertise and Knowledge of investigation groups from University of the West of England Bristol, ITCL, City University and UNICAMP. Standardization and operational development will also be commercially focused thanks to the collaboration between GMV and Blaise Pascal University

Positioning of the project

- TRL3 in software development, associated with limited research in 3D reconstructions of mucosal surfaces[7], so within the project the feasibility of using this data for detection, diagnosis and navigation will be established.
- Hardware development will be at TRL6 due to the developments required in new optical and lightning solutions.
- On standardization and interoperability will be at TRL6 considering the different operational environment.

Overall approach and methodology



The multidisciplinary nature of IMMDOSCOPE with shared inputs and responsibilities by various parties requires a special and dedicated effort to ensure the success of the different activities. To meet this challenge, our proposal should undertake the following activities, aligned to its work planning framework.

WP1 MANAGEMENT subsumes the management activities at the project level.

In the context of ***WP2 REQUIREMENTS ANALYSIS AND BUSINESS MODEL DESIGN*** consortium partners will adapt their specific needs to the requirements of a new device development using the House of Quality approach. Focus on an in-depth understanding of customer needs and wants performing a voice of customer analysis. During this phase factors defining the preclinical test will be designed. The preclinical phase will help determine how well the technology can meet demands in terms of improving detection accuracy of polyps (i.e. finding polyps that are missed by surgeon) and the characterizing polyps using 3D surface texture data (pit patterns).

WP 3 3D VISION SYSTEM DESIGN will develop the system to capture the 3D surface texture and geometry of the colon wall in real-time (moving 3D or 4D Capture System). Two different sources of 3D information will be generated. One using a photometric stereo (PS) based method to recover high-resolution 3D surface texture information and secondly a stereo-triangulation based method offering complementary low-resolution 3D data - not feasible to be retrieved by the first approach alone. Graphical Processing Unit (GPU) acceleration will be used to provide real-time capture and recovery of 3D surface data.

[7] Emrith *K*, Slabaugh G et al, *"Photometric stereo reconstruction for surface analysis of mucosal tissue,"* Medical Image Understanding and *Analysis* 2014.

In *WP4 MODELLING AND NAVIGATION SYSTEM DESIGN*, Data from polyps excised during colonoscopy procedures as well as CT colonography and phantom data will be acquired and analysed in terms of their geometric shape, fine scale topography, and colour – all captured using the 3D vision system. Computer-aided detection algorithms will be developed to run in real-time and to identify 'lesion signatures' in the data. An optical biopsy algorithm will be developed to characterize a detected lesion based on its colour, geometry, and pit pattern. An odometry/visualization system will reconstruct the shape of the colon and provide navigational support to the endoscopist. Finally, enhancement of surface details, tracking and enhancement of regions with polyps (potential or detected), using surface relectance mapping, virtual relighting and manipulation of the 3D data (shape amplification) will be achieved for advanced and augmented visualization of the data.

The essential components of the IMMDOSCOPE include the viewing camera, the lens system, the steering and navigation toolset and the integration path towards a scope. This work package addresses the component development within the agreed form-fit factor of the delivery system capable of doing in vitro as well as preclinical studies. Further surgical tools will be updated to take full benefit of the added value of the new visualization provided by the scope. All these will be developed under *WP5 HARDWARE DEVELOPMENT.*

WP6 E-HEALTH PLATFORM DESIGN will develop a medical image data management system focus on the DICOM standard. Ontology and common clinical terms will be defined. SOA services will provide an integration bus in order to easily incorporate the IMMDOSCOPE system into the Hospital/Health Information Systems in terms of standard DICOM 3D diagnostic images and clinical reports to be part of the patient's EHR. The platform architecture will be ready for cloud deployment.

All the technologies designed during the development of WP3,4,5,6 will be integrated to create the envisioned use-case application within *WP7 IMMERSIVE ENDOSCOPE DEVELOPMENT (IMMDOSCOPE).* Once the components on HW level and SW level have been completed, these parts will be integrated into one operational system for verification testing and prototypes will be manufactured to be used in *PRE-CLINICAL TESTING WP 8* The accuracy of the capture system will initially be tested in ex-vivo models using images captured from porcine gut tissues and human GI tract tissues extracted for histopathology (In UK and Netherlands). Once shown feasible, prototype systems will be repeated for in-vivo testing in Germany to get first feedback on the proposition in an animal study; all the gathered experiences will be collected to inform decisions for future human trials. International standards and norms to make assessment data applicable for future regulatory approval will be considered. Specific study protocols will be defined according to the performance of the prototypes and the biomedical task to be fulfilled.

WP9 COMMERCIAL EXPLOITATION will lay the basis for the commercialization of the IMMDOSCOPE after the project is finished based on the Business Model Canvas, while *WP10 DISSEMINATION* will devise methods for the protection of the intellectual property (IPR) generated during the project. Further work, is concerned with the dissemination to the general public via social media, medical communities via ESGE and to the scientific community through workshops at major conferences.

Gender analysis

Women have a lower risk of CRC than men of the same age; in general, there is a 7 years difference per 100000 population between an average-risk man and woman[8]. Also in Europe there is a marked age effect for men[9] in death due to CRC and men had more adenomas than women[10]. WP2 will consider these differences in the definition of specifications and in WP 8 Pre-clinical data will be anonymized, but patient's gender will be retained to be analysed to accommodate gender differences.

Research and innovation activities linked with the project

Projects carried out under European framework programs that will be linked to the proposed project have been studied. All of them produce new imaging technology, but not specifically offer valuable 3D reconstruction, nor the recovery of discriminating fine surface texture. There are a number of projects ongoing to enhance polyp detection and lesion characterisation based on the modification of standard endoscopy equipment but not a completely novel approach as in our proposal.

1.4 AMBITION

The American Society of Gastroenterology Endoscopy has identified real time poly diagnosis as one of the next major technology driven changes in endoscopy (Rex et al. Gastrointest Endosc 2011;73:419-22). The IMMDOSCOPE approach to endoscopy development has the potential to revolutionise real time endoscopic diagnostics and impact on the well recognised problem of missed polyps; Is a research action that boldly addresses the improvement of polyp diagnosis and treatment to decrease colorectal cancer that is based on based in the following pillars:

New 4D imaging technology for endoscopes

In order to offer the maximum amount of discernible detail during a screening and so improve diagnosis, intense research has recently been undertaken, to provide tri-dimensional visualization from images captured from an endoscopic head. Two main complementary approaches showed to be promising: Photometric Stereo (PS) and Stereo Vision (SV). While PS has already been applied to recover the surface properties of mucosal tissue[11] [12], the highly reflective nature of the colon surface has been completely ignored leading to poor characterisation and visualization of the mucosa. Moreover, since PS is a monocular approach, the 3D surface recovered cannot be used for accurate metric measurement of polyps. To retrieve surface geometry

[8] Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ, Cancer statistics, 2007. CA Cancer K Clin 2007; 57 : 43-66
[9] The State of Men's Health in Europe
[10] American Journal of Gastroenterology 102, 856–861
[11] Collins T. and A. Bartoli. 3d reconstruction in laparoscopy with close-range photometric stereo. MICCAI 2012, pp. 634–642, 2012.
[12] Durr N. J. et al. "Imaging colonic surface topography with photometric stereo endoscopy", In Digestive Disease Week; American Society for Gastrointestinal Endoscopy, 2014.

in metric scale SV approaches have been proposed[13] [14]. SV uses matching regions over epipolar lines from two images of calibrated cameras displaced horizontally or vertically to recover realistic 3D geometry of a surface. Existing SV approaches are still unable to obtain high resolution depth information of highly reflective and unstructured surfaces such as the mucosal tissue. Real-time applications of SV in endoscopy have failed leading to poor visualization and navigation.

The novel approaches proposed will advance and revolutionise the way in which 3D colon imaging is performed. Our multiscale six-source PS approach will use information from different spectral bands and filter out inter-reflections through polarised lights to recover fine 3D texture information from the highly specular colon tissue. The proposed SV method will provide significantly realistic 3D geometry of the mucosal tissue through an augmentation process based on the photometric images captured. Taking advantage of the potential synergy between the proposed PS and SV approaches and using optimised superposition methods we will combine the 3D surface geometry of the colon surface with the dense 3D surface texture of the mucosal tissue to provide a highly accurate and unique representation of the colon wall. Such a representation will significantly improve polyp detection and their removal. In addition, a metric scale accurate measurement of 3D polyps shape will be provided for better diagnostic and monitoring purposes. Moreover, this representation has the potential to be used for odometry and the extraction of a model of screened area for comparison and post-procedural analysis (and potentially in clinical training). Our proposed vision system will capture 3D frames in real-time (4D Vision) and through state-of-the-art GPU acceleration and novel registration methods will enable enhanced and realistic visualization of the colon. As such our 4D Vision system will provide an integrated and enhanced platform to facilitate endoscopists and significantly improve the accuracy of CRC screening.

Use of New Hardware solutions

Endoscope images present some unique challenges and opportunities. The small diameter of the instrument and cramped operating conditions limit the linear separation between the light sources to a few millimeters.. On the other hand, the typical operating range is also very short, so the angular separation of the lights as seen from the surface will be several degrees. This variation is too small for adequate perception of relief by the unaided eye, but sufficient for PS algorithms — meaning that a 3D-enhanced endoscope can provide useful data. The small angular separation between the objective and the light source, as well as the nature of the targets, will also minimize the occurrence of cast shadows, which are a major problem in other applications. As a quality control the system will be able to know what amount of the colon has been inspected using the tracking information as well as the image information and identify by that the shadow areas where polyps might be hidden still. The use of stereo cameras in an endoscope, on the other hand, is a technology already present in advanced commercial endoscopes, thus it is feasible to be seamlessly incorporated in our PS capture tool although new lenses with smaller focal length will have to be developed and included in the nano sensors within the project. Thanks to the anticipation in size and shape information retrieved by the scope it will be developed a 3D micro-surgery toolset, a device that enable bimanual, versatile and intuitive tissue manipulation capabilities via a transanally or transorally deployed for the flexible instrumentation carrier.

Standarization and Interoperability with health information systems

The use of a standard data management system for 3D colonoscopy clinical image data (PACS) will create a durable in time device able to interoperate with the current and future Health Information Systems. Also, the incorporation of the novel 3D colonoscopy PACS of interoperable features based on semantical standard information (SNOMED-CT, CIE10, etc.) and clinical image exchange protocol DICOM, as well as the clinical report generation fully compatible with the EHR, make the IMMDOSCOPE system a cutting edge interoperable system.

Patent research carried out

Under a detail search of Patents related to the use of Photometry in Endoscopes, we state that several describe using photometric information to control the brightness in the captured image. However, none relate to photometric stereo for 3D endoscopy. On the consortium already patented products linked with the research of the proposal are:

- Schostek S, Ho CN, Rieber F, Schurr MO. Medical Appliance. European Patent EP1886620
- Schostek S, Prosst R, Rieber F, Schurr MO. Surgical manipulator means. European Patent EP2286756
- GMV has a patent for an image guided intraoperative radiotherapy planning, with id WO 2009/127747 A1

Other products in the market linked with the project is the Standardization and interoperability systems “Syseo”, from Yansys

2. IMPACT

2.1 EXPECTED IMPACTS

The IMMDOSCOPE Project aims at improving actual screening methodologies by creating new in vivo diagnostic tools that are:

More accurate, being able to detect different categories of colonic polyps at an early stage, irrespective of their geometric size and shape. Capturing both fine and coarse polyps, will have major impact in reducing the lesion miss rate.

Less invasive. Current screening programs are based on routine optical colonoscopy (OC) or virtual colonoscopy (VC). OC involves examining the patient’s colon with a flexible video camera, due to the lack of unique visual landmarks, it is possible to lose track of the endoscope’s position. VC exposes the patient to ionizing radiation, and if a lesion is found, a follow-on polypectomy is required. Our approach will provide better visualization and navigational support in real-time, without exposing the patient to radiation.

[13] Chang, Ping-Lin,Stoyanov,Davison. "Real-time dense stereo reconstruction using convex optimisation with a cost-volume for image-guided robotic surgery." –MICCAI 2013, 2013. 42-49.
[14] Totz, Johannes, et al. "Fast Semi-dense Surface Reconstruction from Stereoscopic Video in Laparoscopic Surgery." IPCAI2014. 206-215.

More reliable. With a more robust system, more advanced visualization and augmentation techniques and some variables collected from the patient; the detection rate can be increased and thus the polyp removal percentage. Shadow areas will be linked to imaging scans made on CT to allow for additional inspection.

Earlier disease diagnosis, prediction or response to therapy, IMMDOSCOPE will help oncologists establish early detection to prevent cancerous regions spreading; providing more precise diagnosis, reducing patient's exposure to aggressive treatments and avoiding the risk of side effects. Recording of data has important application to surgical planning for complicated lesions for which routine snare polypectomy may be counter-indicated. 3D surfaces reconstructed from the sensor can be reviewed and discussed for surgical options as well as used in training.

Contribution to the sustainability of health care systems. A recent study[15] performed a population-based cost analysis of cancer in the EU member states, and determined that colorectal cancer accounted for €13.1 billion in the year 2009, in terms of healthcare costs in primary, outpatient, emergency, and inpatient settings, drugs, unpaid care provided by relatives, missed wages, and lost earnings after premature death. Assuming an average 3.4% increase in historical (2000 – 2011) healthcare costs[16], colorectal cancer is estimated to cost the EU member countries annually €17.1 billion by 2018.

In the clinical literature, it is well accepted that more than 95% of colorectal cancers arise from adenomatous polyps[17], which are the primary target in programmes that screen the colon for pre-cancerous lesions. Therefore, there by 2018, the cost of undetected polyps in the EU will be €16.2 billion annually. If use of the IMMDOSCOPE results in 50% fewer missed polyps (the lowest expected rate), then the potential financial cost savings would be €8.1 billion annually by 2018. However, this assumes that all individuals who develop colorectal cancer are screened. Experience[18] suggests patient uptake of approximately 65%, so the total addressable market in terms of healthcare savings in the EU is **€5.2 billion** annually for the device by 2018. This amount is expected to increase with further adoption of colorectal screening programmes, via patient awareness and compliance along with an ageing population. Other direct impacts of our system will be to reduce the cost not only by avoiding repeated FOBTs or CTCs but also through savings in other aspects such as the elimination of histopathology analysis of the exscinded tissues through computer-aided diagnosis tools[19].

Innovate healthcare delivery. The project will cover all the administrative and support aspects of a regional, national or corporative health system thanks to the adaptation of their standards. The standard will guide multimode therapy (surgery, radiotherapy and chemotherapy) in a personalized and effective manner. The system will feed from a retrospective database with information of a scalable number of patients with colorectal cancer that integrates patient data as DICOM attributes along with image data and applications for presenting, conveying and extracting information using the database: Interventions, costs and outcomes will be measured and recorded in the same way. IMMDOSCOPE will create a relationship among old 2D systems and 3D systems biomarkers and so, a better understanding of cancer and its consequences and relationship with lifestyle. Data and information improves the relationship between individuals and their health allowing more informed choices

Build the healthy cities and countries of the future by Building a pan-European collaborative approach to digestive cancer screening collaboration with the European Society of Gastrointestinal Endoscopy (ESGE) will engage, through workshops, a wider set of stakeholders to contribute to better health for all. Health system leaders will work with policy-makers, industry heads and other multi-sector actors trying to promote the use of screening programs through Europe with the use of new technologies and overcome data privacy concerns in order to avoid patients' possible resistance to the system.

Growth of the European diagnostics sector, in particular for SMEs. The consortium includes the full value chain, starting with universities and research organizations delivering breakthrough technology building blocks, via relevant industry specialized in key components of the system that will serve as suppliers of those components in the market phase, and medical device companies willing and able to sustainably deliver resulting medical devices into the market. The consortium is designed to conduct all commercialization activities from within the consortium and create a competitive European player in the endoscopic digestive diagnosis market, ensuring that the investment of the European Community to be a catalyst for boosting competitiveness through innovation and technology advancement. The global GI endoscopy equipment market is worth almost USD 40 Billion in 2018, and continuous to grow. Growth is driven by the increasing need for healthcare delivery of the aging population (in 2030, the life of more than 25% of the population will be impaired or threatened by digestive diseases), and by the innovative framework that continuously delivers technologies enabling the transfer from invasive to non-invasive endoscopic techniques. A market analysis of the IMMDOSCOPE products has been conducted. Provided the market preconditions explained above, with product finalization and regulatory approval achieved within two years after the project, the IMMDOSCOPE products are forecasted to reach an annual turnover of about EUR 150 Million with a market potential of about EUR 440 Million. This represents a very lucrative niche market that constitutes about 1% of the entire GI endoscopy market. Furthermore, this would enable the consortium to extend their business further through their innovation capacity in the European framework. The development of this new device will enable Philips to establish itself as one of the main companies worldwide with one of the most relevant types of Endoscope.

[15] Luengo-Fernandez R, Leal J, Gray A, Sullivan R, "Economic burden of cancer across the European Union: a population-based cost analysis," The Lancet Oncology, 2013, 14(12); 1165-74
[16] Bujanda L, Cosme A, Gil I, arenas-Mirave JI, "Malignant colorectal polyps," World Journal of Gastroenterology, 2010, 16(25); 3103-11.
[17] OECD, "Health at a Glance", 2013: OECD Indicators, OECD Publishing
[18] Lo, SH, Halloran S, et al., "Colorectal cancer screening uptake over three biennial invitation rounds in the English bowel cancer screening programme," Gut, 2014, pre-print ahead of publication.
[19] Dachman AH, Obuchoswki N, et al. Effect of Computer-aided Detection for CT Colonography in a Multireader, Multicase Trial, Radiology 2010; 256(3): 827-35; Lawrence EM, Pickhardt P, et al. Colorectal Polyps: Stand-alone Performance of Computer-aided Detection in a Large Asymptomatic Screening Population, Radiology 2010; 256(3): 791-8

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