PROJECT FINAL REPORT

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1 FINAL PUBLISHABLE SUMMARY REPORT

1.1 Executive Summary

Colon diseases are one of the most interesting chapters of public health. Every year millions of people around the world undergo to colonoscopy or other colon investigations. Although optical colonoscopy is currently the diagnostic gold standard for colonic diseases, however it is also invasive, with important limitations in terms of risks and patient acceptability: invasive minimally diagnostic procedures are required.

Market available video endoscopic capsules (VCE) explore the gastrointestinal (GI) tract proceeding by means of visceral peristalsis and gravity. Higher diagnostic accuracy, more extensive clinical application and shorter times of investigation would be achieved by controlling the VCE locomotion.

Some authors demonstrated that magnetic fields allow controlling the VCE movement.

However the cylindrical shape, while it may be suitable for the small intestine, esophagus and stomach, in the colon, due to its anatomical features, has intrinsic disadvantages as regard to VCE propulsion, surface friction and cleaning.

The EU-funded SUPCAM project (www.supcam.eu) addressed the development of an innovative active VCE (AVCE) whose design allows to safely and accurately guide it along the colonic lumen from the outside, using an innovative electromagnetic approach and an external compact assisted handle adapted to be transported and suitable for common outpatient setting. SUPCAM is able to investigate the colonic district, ensuring a high level of accuracy.

SUPCAM endoscopy represents a highly innovative and disruptive solution for colon diseases diagnosis and screening.

This innovative magnetically controlled AVCE, reducing clinical risk, improving tolerance, acceptability, territory availability and adherence to colorectal cancer screening programs, will provide significant benefits for patients and whole healthcare system.

After defining the technical requirements and target specifications for the system design, the overall architecture design was performed and a pre-competitive prototype of the SUPCAM system was realized. The prototype’s validation activities brought to demonstrate the feasibility of the overall SUPCAM concept.

1.2 Project Context and the Main Objectives

1.2.1 Project Context

Colorectal diseases, and in particular colorectal cancer (CRC), interest a huge number of people worldwide, with a strong impact on the public healthcare systems. It is the third most common form of cancer, after lung and breast cancer, and the fourth most common cause of cancer death in Europe[2].

Most cases of colon cancer begin as small, non-cancerous (benign) clumps of cell called adenomatous polyps and over time, some of these polyps become colon cancer. CRC can take many years to develop, and early detection greatly increases the chances of successful treatment[3].

Despite advances in the management of the colorectal cancer, the survival rate is still low. This is because only a very low number of patients are diagnosed when cancers are localized to the bowel wall. It is likely that with a widespread implementation of screening examinations these numbers might increase. Colorectal cancer screening is cost effective, irrespective of the methods used[4], and it is highly recommended in patients aged 50 years and older as well as in asymptomatic patients with family history of CRC.

Five-year survival from CRC is greater than 90% if caught in early stages of disease before the tumours infiltrate the bowel wall, but five-year survival falls to approximately 60% if lymph nodes are involved and below 10% when metastases are present. If CRC is detected once symptoms become apparent, the disease is usually well-developed. Late-stage disease is associated with high mortality; 40–50% of individuals die with metastatic disease[5].

The evidence for CRC screening demonstrates that if bowel polyps are identified and removed in early stages of development, progression to cancerous lesions can be halted. This was unanimously adopted by the Health Ministers of the European Union with the recommendation of bowel cancer screening.

Optical and virtual colonoscopy, double contrast barium enema (DCBE), faecal occult blood test (FOBT) and passive endoscopic capsules are the state-of-the-art technologies utilized for the colon exploration and the CRC screening.

State of the Art endoscopic devices have several disadvantages and limitations. Optical colonoscopy is the most common procedure for the evaluation of the intestinal diseases. It is also recommended for colorectal cancer screening and is considered the preferred screening modality by some organization. Although this technique is efficient, it has several disadvantages in terms of poor tolerability, pain, clinical risk and usually is performed under sedation. Clinical risks such as

[2]Clinical Biochemistry 47 (2014) 921-939, "Tests and investigations for colorectal cancer screening", Magdalen R.R. Carroll, Helen E. Seaman, Stephen P. Halloran
[3] Business Insights, "The Cancer Market Outlook to 2016", 2011
[4] Colorectal Cancer Prevention, Ernest T. Hawk and Bernard Levin, 2005 by American Society of Clinical Oncology
[5] http://www.who.int/cancer/detection/colorectalcancer/en/

perforation bleeding and cardiovascular events occur every 900 colonoscopies since pressure is exerted on the colon or on the curves during the examination[6].

Less invasive exams such as virtual colonoscopy, double contrast barium enema, faecal occult blood test and passive endoscopic capsules have disadvantages in terms of level of accuracy. For example, virtual colonoscopy has sensitivity and specificity reduced for lesions < 1 cm and for flat lesions.

Minimally invasive as well as more accurate techniques for the colon investigation have long been expected and requested by patients themselves as well as health care system.

In this framework SUPCAM project addressed the design and development of an innovative "medical device" intended for clinical investigation, which ensures a high level of navigation accuracy and enhanced diagnostic capabilities.

The less invasiveness of the SUPCAM exam may increase the number of patients who undergo CRC screening, with an early detection and a consequent likely reduction of the colorectal cancer miss rate. This is a very important issue, also for the optimization of the colorectal cancer screening programmes.

1.2.2 Main Objectives

The SUPCAM project aimed at developing a minimal invasive **medical device** able to investigate the colonic mucosa, ensuring a high level of **navigation accuracy**, **enhanced diagnostic capabilities,** as well as a substantial **reduction of discomforts** typical of current diagnostic practices.

The SUPCAM concept is based on an innovative endoscopic device whose the structure and novel design allow to safely and accurately guide it along the colonic lumen from the outside, through an electromagnet, completely wireless.

The completely new mechanical configuration of the capsule allows the medical examination through an external control system with a simple structure, inexpensive, with reduced bulk and usable in normal outpatient settings, able to ensure an accurate vision of the colonic mucosa.

Within this framework, the SUPCAM project addressed the development of the medical device that foreseen three principal components:

- a medical grade, biocompatible and optical grade **outer capsule**;
- an **inner body** free to rotate with respect to outer capsule;
- an **external control system** (i.e., electromagnet).

Inside the inner body there are all the main capsule components: i) image capturing (i.e., vision system), ii) power supply system, iii) data transmitting-receiving system and iv) a permanent magnet that enables the movement of the capsule.

[6] Gut 2004;53:277-283

1.3 Main S & T results/foregrounds

After defining the SUPCAM desired system performances, technical requirements and target specifications for the SUPCAM system design, the Consortium focused on the development of a pre-competitive prototype of the medical endoscopic device.

The main results achieved within the SUPCAM project consist of:

- **prototype of the capsule** with all the miniaturized subcomponents integrated within the capsule (i.e., frame, permanent magnet, image system, vision and control boards, illumination board, telemetry board, RFID, recharging coil, and battery);
- development/implementation of the **image acquisition and processing chain** for the endoscopic wireless SUPCAM capsule;
- **locomotion system** based on the internal permanent magnet and on an external electromagnetic system composed by a robotic manipulator used for supporting and manoeuvring an heavy and bulky electromagnetic source; it consists in a electromagnet with an integrated cooling system;
- **localization system** is achieved by image-based and RFID feedback processing (scanning procedure for raw detection of the capsule position);
- **wireless recharging system** to increase the lifecycle of the SUPCAM capsule in order to reduce the cost related to each endoscopic procedure.

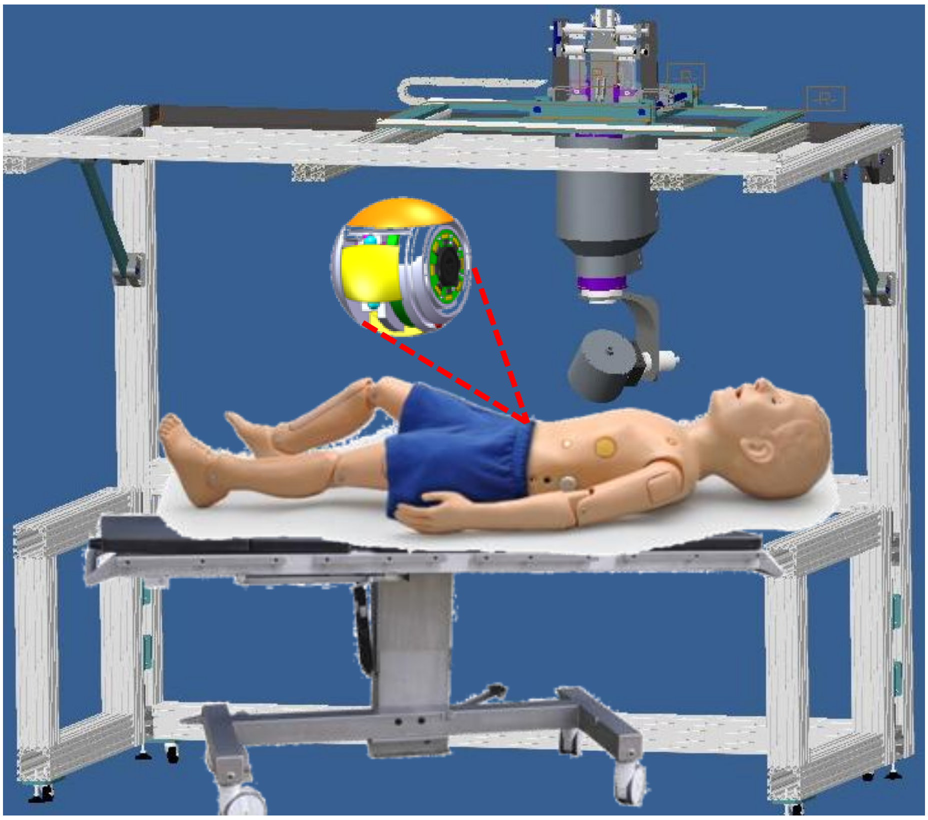

Figure 1: SUPCAM overall architecture

1.3.1 Capsule prototype

The SUPCAM concept is based on a wireless endoscopic capsule whose structure and innovative design allow safely and accurately guiding it along the colonic lumen from the outside, through an external electromagnet. This innovative active capsule is composed by an inner body (i.e., frame) that allows coupling and ensuring a 360° rotation of the inner body with respect to the external shell.

The capsule is composed by three principal components:

- an outer shell;
- an inner body (called mechanical frame) free to rotate with respect to the outer shell;
- sub-components.

Whenever possible, commercial available components were identified after a benchmark analysis; other components, such as the imager and the optics, were developed during the SUPCAM project.

The capsule is equipped with a **vision system** composed by a commercially available image sensor (by AWA) integrated with a tailored optic and an illumination system for capturing images of the colon during colonoscopy; a **permanent magnet** to enable the locomotion and a **RFID** that (together with a image-based localization strategy) allows the capsule localization. The embedded electronics (i.e., control and transmission electronic boards) enables the management of the integrated modules. An on-board battery is used as power source.

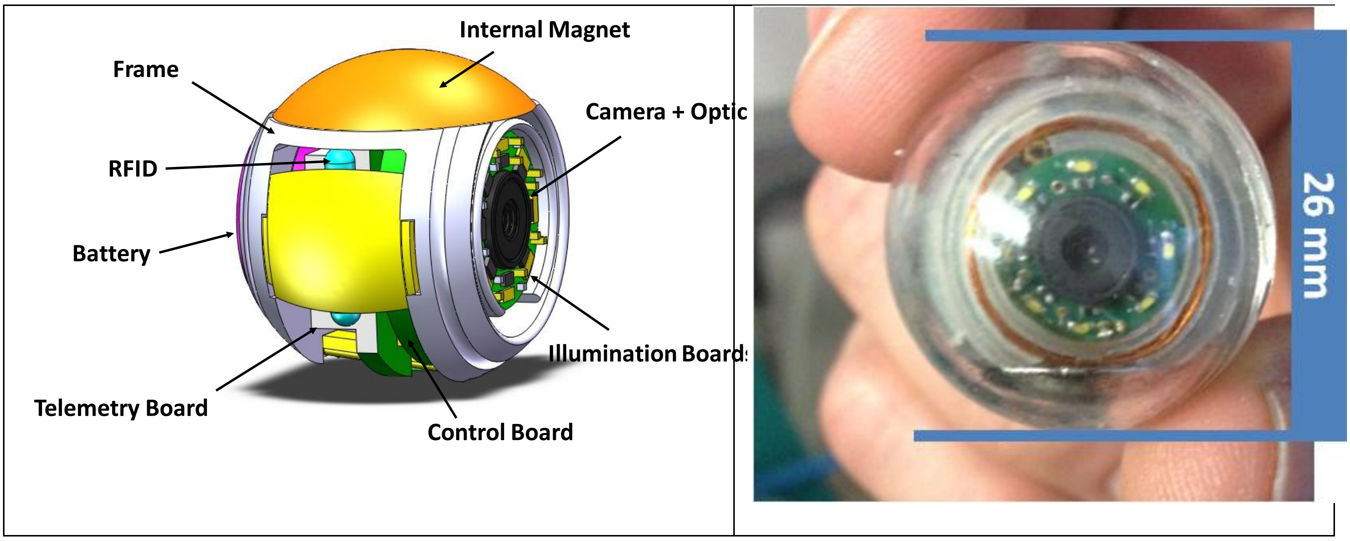

Figure 2: final capsule prototype

During the SUPCAM project a pre-competitive prototype was tested and validated in order to evaluate the capsule performances in terms of locomotion, ability of orientation, functionality of image capturing system (micro-camera) and of image transmission system.

1.3.2 Image processing

The image acquisition and processing chain is a crucial aspect for endoscopic capsules and the integration of many operations in the workflow is very challenging due to the limited number of operation that can be performed on board.

During the SUPCAM project, an image-processing pipeline was developed in order to identify specific processing actions for obtaining the best image quality for endoscopic applications with the minimum bit rate transmittable via wireless by a commercial telemetry system.

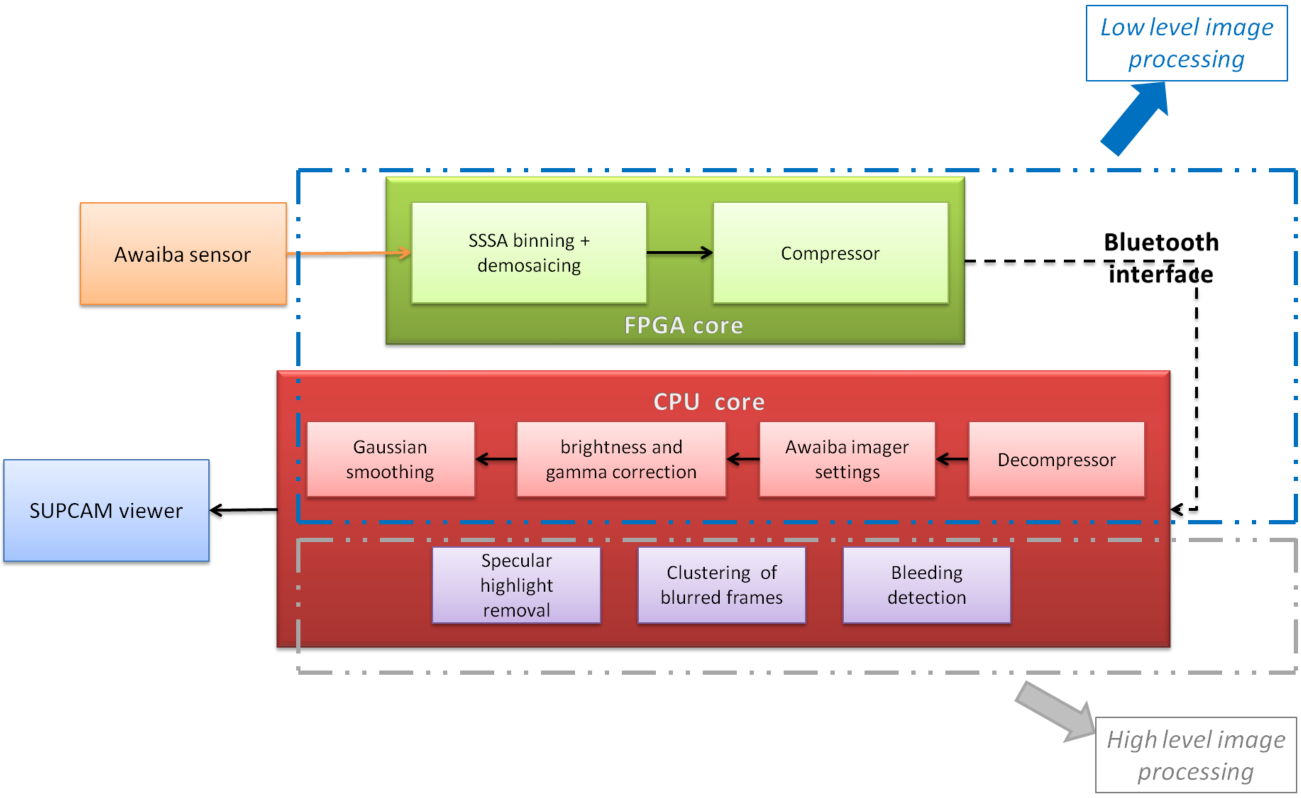

Figure 3: Image processing pipeline (high level and low level)

The overall image-processing pipeline has been implemented and the image processing methodologies validated in a real scenario. In particular, the main achievements can be summarized as follows:

- a **low-level image acquisition and processing methodology** (including the acquisition of the images from the AWAIBA sensor, the binning and the demosaicing operations, the compression and decompression steps, the gamma and brightness correction and gaussian smoothing) have been implemented, tested and validated with the final SUPCAM camera, obtaining a good-quality images;
- the **high-level intra-operative and post-operative methodologies** for image processing and 3D reconstruction have been successfully implemented for further improve the image quality applying specular highlight removal, clustering of blurred and poor quality frames and

bleeding detection algorithms. Moreover, a reconstruction of the 3D structure of the visualized scene from the capsule camera stream was implemented using shape-from-shading techniques, for qualitative post-operative tissue reconstruction and lesion evaluation.

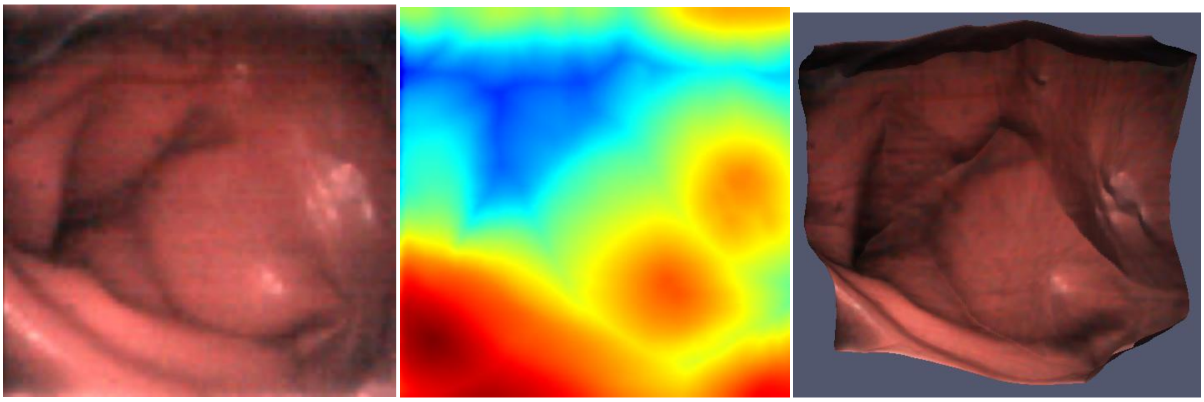

Figure 4: Original image, the relative depth map and the 3D reconstruction obtained using the shape from shading implementation

1.3.3 Locomotion system

A tailored locomotion system for endoscopic capsule were developed within the project. The locomotion source is based on an electromagnetic field generated by an external electromagnetic system (i.e., electromagnet), designed according to the permanent magnet's features embedded inside the capsule (i.e., NdFeB N52).

The design of the external magnetic system was performed considering that i) **5 degrees of freedom** (DoFs) for capsule navigation and steering are needed, ii) a **suitable forces and torques** have to be generated in a range of distance (that are related to the different abdominal thickness), iii) the electromagnet needs to match with normal outpatient setting (i.e., **compactness**) as well as the electromagnet has to be portable and easily controllable by the physician.

The external electromagnet has been designed and produced and an experimental evaluation demonstrated that the external magnetic system cannot be continuously used due to overheat issue; therefore cooling system was designed and integrated into the SUPCAM locomotion scenario.

Moreover, due to the consistent weight and encumbrance of the electromagnetic system (around 13 Kg), a 5 DoFs robotic manipulator has been designed for holding and accurately moving the electromagnetic source by the physician.

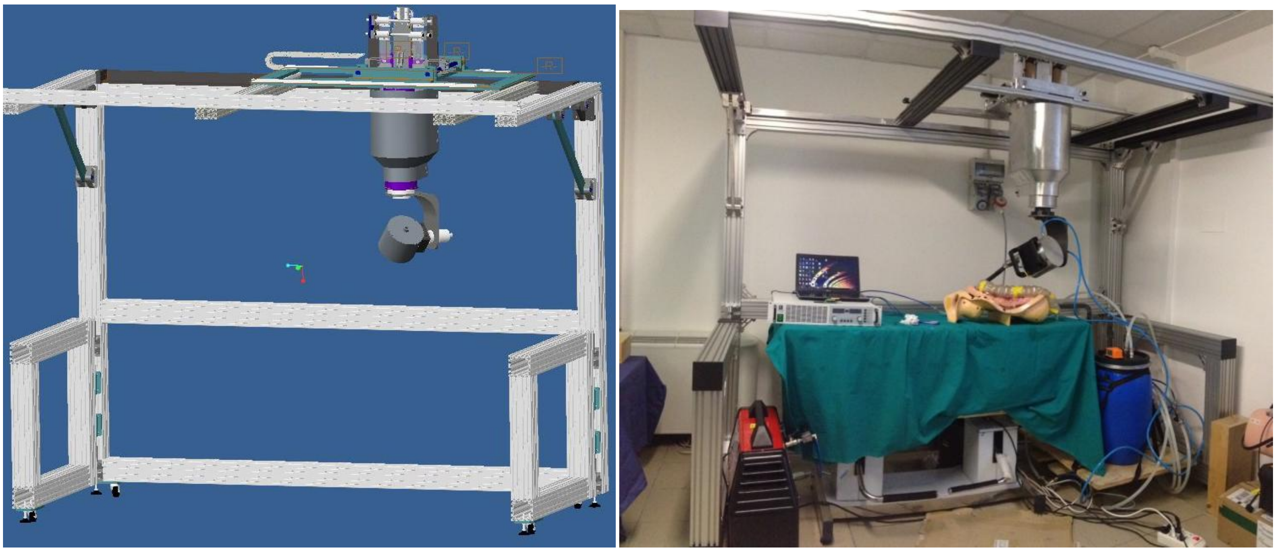

Figure 5: external electromagnetic, manipulator and cooling system

1.3.4 Localization system

A localization system has been implemented and it is based on two different approaches: i) an image and ii) a RFID-based strategy. These two strategies, used alone or combined, would allow for a discrete-time detection of the position of the capsule under a scanning procedure.

A vision-based algorithm, based on a Shi-Tomasi features detector and a Lukas-Kanade optical flow computer vision methodology, was implemented and exploited for the implementation of a localization strategy of the capsule using the already embedded capsule camera as the sensing source. A scanning procedure of the diagnostic area has been performed and the attraction of the capsule is received as a downward movement of the environment (i.e. surrounding tissue); this event can be monitored and provide information about the establishment of the magnetic link (thus localization of the raw position of the capsule).

In addition, a RFID-based system was exploited for the implementation of a localization strategy of the capsule using a specific external antenna and embedding a small RFID seed inside the SUPCAM capsule. This feedback gives information about the position of the capsule with respect to the external antenna (attached to the external electromagnetic system), thus allowing for the localization of the capsule itself (again, under the performance of a scanning procedure).

An experimental evaluation was carried on, demonstrating that the position of RFID tag has to be perpendicular to the magnetization axis of the hemispheric internal magnet. These considerations have been taken into account during the capsule design and integration.

1.3.5 Wireless recharging system

In order to increase the number of procedures with the same SUPCAM capsule. A wireless recharging system has been developed. The wireless powering for battery recharging is based on electromagnetic induction, specifically on an inductive coupling between two coaxial coils in offline mode. The wireless recharging system has been developed, integrated into the SUPCAM platform and tested within the project. Through this system, it is possible to recharge the battery enclosed into the capsule and to utilize the capsule more than once time.

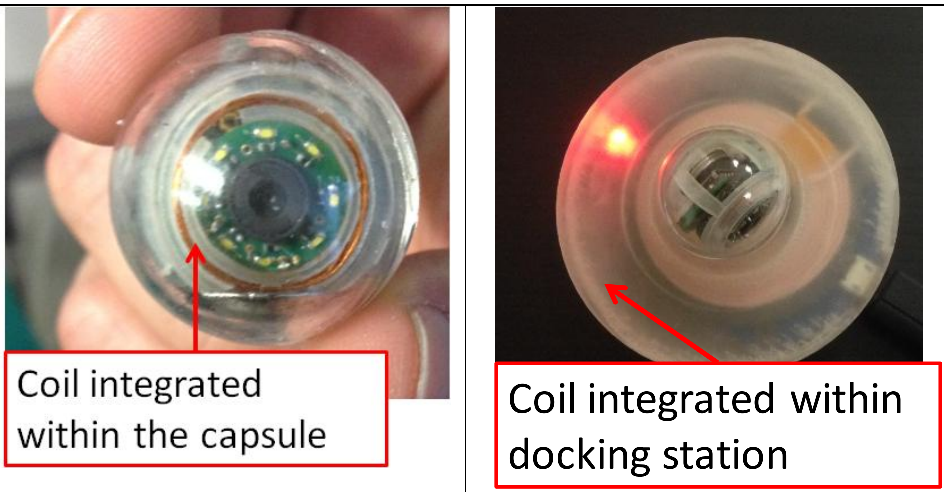

Figure 6: Wireless recharging system

1.4 Potential Impact of Results

Current diagnostic practices for the colo-rectal diseases, and mainly optical colonoscopy, have relevant negative impacts on the patients, who are usually reluctant to undertake colorectal examinations. This is mainly due to the fact that colonoscopy is seen by the patients as highly invasive, usually painful and risky, as complications may occur. Clinical risk related to colonoscopy is quite important, as perforation could occur in one case over 900[7].
Furthermore, patients are not feeling comfortable undertaking colonoscopy, which is seen as highly embarrassing: this is one of the reason, together with the physical pain, that leads to the wide use of sedation in many European Countries as France and UK. Pain and emotional factors plays in fact a crucial role in the good outcome of the examination, as well as in the occurrence of complications.

In this framework, once on the market, SUPCAM capsule will provide an accurate, less invasive, less embarrassing and more reliable early disease diagnostic tool.
De facto SUPCAM will meet important needs in terms of tolerability and clinical risk reduction, most likely improving cultural acceptability of screening CRC programs as well. It is expected to increase the survival rate from CRC, by detecting it in very early stage and improving clinical decisions. If CRC is only detected once symptoms become apparent, it usually means that the disease is already well-developed and the survival rates decrease significantly (the late-stage disease has a high mortality rate of 40–50%)[8].
According to the market analysis performed during the project, SUPCAM could penetrate the market of screening (i.e. CRC programs) and surveillance colonoscopy.

Moreover, the cost per exam performed with SUPCAM was estimated by the Consortium to be 125 € per exam taking into account that a single capsule can be used up to 6 times. This cost is slightly cheaper in comparison with the traditional optical colonoscopy with a cost per exam equal to 150 €[9] without sedation, and up to 300 €, if sedation is needed with significantly cost due to personnel costs.
Considering that SUPCAM could replace or complement traditional colonoscopy in 200 000 cases per year; the total potential economical impacts can be evaluated by comparing the total cost of the optical colonoscopy exam (50% without sedation, 50% with sedation) and the total cost of SUPCAM exam. The potential saving for the European healthcare system can be 20 M€ per year.
Considering that in 2013, the European markets for gastrointestinal endoscopic devices were collectively worth over 948 M€ [10], it was estimated that the new medical exam allows a cost saving of the 2% of the overall costs, with a total saving of 100 M€ in 5 years.

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[7] Gut 2004;53:277-283
[8] Clinical Biochemistry 47 (2014) 921-939, "Tests and investigations for colorectal cancer screening", Magdalen R.R. Carroll, Helen E. Seaman, Stephen P. Halloran
[9] Christine Krizaa et al., "An international review of the main cost-effectiveness drivers of virtual colonography versus conventional colonoscopy for colorectal cancer screening: Is the tide changing due to adherence?", European Journal of Radiology 82 (2013), 629–636.
[10] European markets for gastrointestinal endoscopic devices". iData Research Intelligence Behind the data (2014), page 1.

With reference to the commercialization of the SUPCAM capsule, the future income for the SUPCAM supply chain stakeholders such as the SMEs member of the Consortium representing producers of the system or subparts of it as well as the distributors will be around 21 M€.

1.5 Contact Information

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1.6 Consortium

D'Appolonia S.p.A.

Special Electronic Design SRL

Awaiba Consultadoria, Desenvolvimento e Comercio de Componentes Microeletrônicos, LDA

Meqnordic AS

Scuola Superiore di studi Universitari e di Perfezionamento Sant'Anna (the BioRobotics Institute)

Fraunhofer- Gesellschaft Zur Foerderung der Angewandten Forschung e.V. (IOF)

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