Innovative multiphotonic endoscope to address technological challenges in current colonoscopy procedure

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Abstract

Colorectal cancer is one of the most common types of cancer in the world. The main method used to detect colorectal cancer is an exploration of the colon through a colonoscopy, but enhancements in endoscopes are essential to improve this procedure. New diagnostic techniques are required to differentiate in situ hyperplastic and neoplastic polyps. With this purpose, a "focus group" with gastroenterologists has been developed to identify medical needs related to the limitations of endoscopic technology and the colonoscopy procedure, and to optimize the design and development of new technologies. The "focus group" was carried out with four gastroenterologists, following a semi-structured interview of 30 minutes. Analysis of comments of the clinicians shows several main topics to perform improvements: (a) equipment related to image quality and colon lighting; (b) problems in polyp detection and classification; (c) provide visual information; and (d) physical characteristics of the endoscope. The European PICCOLO project is addressing these technological needs, in which an innovative multiphotonic endoscope will be developed to enhance the diagnosis of colorectal cancer. This endoscope, based on Optical Coherence Tomography (OCT) and Multi-Photon Tomography (MPT) technologies, will allow performance of image-guided "optical biopsies" for in-vivo real-time diagnosis. It will provide high resolution OCT/MPT images, white light and fluorescence wide field images and a Computer Aided Diagnosis (CAD) software. With this technology, neoplastic and hyperplastic polyps would be better detected and classified in real time, especially flat polyps. This software will support decision-making in diagnosis by providing visual information of polyps' characteristics.

1. Introduction

Worldwide, colorectal cancer is the third most common cancer in men, behind lung and prostate cancer, and second in women, behind breast cancer. This cancer represents around 10% of all cancers, causing almost 700,000 annual deaths around the world, representing 8.5% of the total deaths associated with cancer, with the highest estimated mortality rates in Central and Eastern Europe [1]. Specifically, adenocarcinoma represents more than 95% of all these cases [2]. There is scientific evidence showing that early detection leads to a nearly complete cure of patients diagnosed in early stages of the disease, reaching cure rates up to 90% [3]. Moreover, the duration and costs of diagnosis and treatment will be reduced and a lower number of future reoperations will be achieved [4].

To achieve an early detection of the disease, it is highly recommended to get the risk population involved in colorectal cancer screening programmes, where the main method utilized is the colonoscopy. Up to 40% of patients [5] undergoing routine analysis colonoscopy present one or more polyps, which can be, in summary, hyperplastic (with no malignant potential) or neoplastic (with malignant potential). Specifically, 29-42% of these polyps are hyperplastic, whereas the rest are neoplastic [5]. Furthermore, greater than 40% of patients with colorectal polyps present with multiple polyps [6]. Additionally, almost 30% of these polyps are not detected [7]. In the current gold standard procedure (*Figure* 1), all polyps (both hyperplastic and neoplastic) are resected and sent to the histopathological analysis to get the diagnosis. This standard clinical procedure for diagnosis still depends on biopsy, a tissue sample preparation and an analysis taken by an expert pathologist including extraction, preparation, cutting, and staining with Hematoxilin-Eosine (H&E) to assess the morphological pattern. This procedure implies high diagnosis time and costs, and may unnecessarily expose patients to the risks associated with polypectomy, besides the high psychological impact that can cause on them. Adenomatous polyps have malignant potential, so they must be resected to protect against colorectal cancer. But hyperplastic polyps do not present malignant potential, so they can be left.
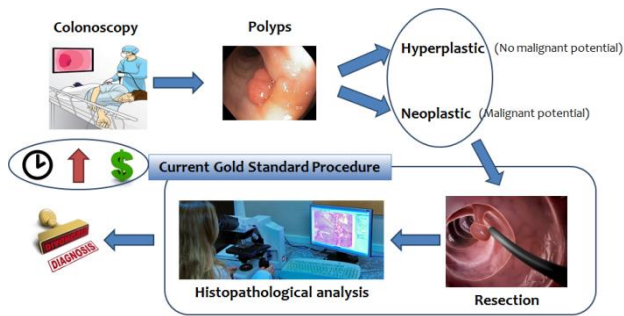
Figure 1. Current gold standard procedure

Therefore, improved diagnostic techniques are required to differentiate hyperplastic and neoplastic polyps, allowing in situ assessment, safe characterization and appropriate resection of lesions during clinical interventions. However, it is important to previously identify the medical needs related to the constraints in the context of endoscopic technology and the colonoscopy procedure currently used to improve the design and development of new technologies. With this purpose, semi-structured interviews with experienced gastroenterologists have been conducted..

2. Methods

This section details the protocol followed for the design of the interview, as well as the questions that compose it.

A semi-structured interview has been used, which is a technique that allows respondents the freedom to express their points of view in their own terms. Interviewer use a paper-based interview guide (a list of questions usually in a particular order) that is needed to be covered during the conversation. Since this kind of interviews contains open-end questions, it is best to tape-record and later transcript these recordings for analysis, although also interviewers can write notes. The interview have questions from generic to concrete, should last approximate 30 minutes, and is in English and Spanish, depending on the language of the clinicians. It is divided in 4 blocks, each one with several questions. The number of interviews needed has been set by applying the theoretical saturation, that is the phase of qualitative data analysis in which the researcher has continued sampling and analyzing data until no new data appear and all concepts are well-developed. It is necessary to select proper profile of respondents. In our case, the most adequate profiles are gastroenterologists.

The design of the interview is as follows:

Block 1. Presentation (1-2 minutes)

1. Dear [Respondent], I would like to thank your participation in this study. I am [Interviewer], from [Interviewer's institution], a partner belonging to the consortium of the PICCOLO project, a European research project that aims to develop an endoscope based on photonic technologies for improving colorectal cancer diagnosis providing in-vivo image-guided biopsy capabilities. With this study we aim to advance the current state of the art for procedures and technologies used for the diagnosis of colon cancer and to understand the needs for the development of new systems that allow the procedure to be improved. The methodology to be followed will consist of an interview of 30 minutes approximately, comprising three blocks of questions: (1) review of your demographic data in 5 minutes, (2) 10 minutes with questions about current procedure and technologies for colonoscopy and colorectal cancer diagnosis, and finally, (3) 15 minutes to ask you about challenges you think should be addressed to improve the current procedure and technologies. Your interview will be recorded to be later analysed. Your participation is voluntary and you can withdraw from the interview at any time you wish. However, we would appreciate you completing the entire interview to obtain higher quality data.

Block 2. Demography (up to 5 minutes)

1. Let's start the interview with a brief description of your demographic data, such as name, age, academic training, number of colonoscopies performed, where you are working or have worked, in what position, etc.

Block 3. Current procedure for colonoscopy and colorectal cancer diagnosis (10 minutes)

1. What is the current screening procedure for the diagnosis of colorectal cancer?

2. But more specifically, and more related to your field of work, what is the current colonoscopy procedure?

3. What problems you encounter while performing such procedure? And related to the technology used?

Block 4. Challenges (15 minutes)

1. What improvements would you like to see in the colonoscopy procedure? And related to current technology and equipment (expected innovations)?

2. What is your opinion and personal experience of the use of advanced imaging techniques (including dye-spray, virtual chromoendoscopy, photonics techniques) for the diagnosis of polyps and colorectal cancer?

3. If you could have at your disposal an ideal device for supporting your decision-making in the assessment of polyps or colorectal cancer, what additional information would you like to be provided with? (Detection, classification, visual information, auditory information…)

3. Results

Four gastroenterologists from "Hospital San Pedro de Alcántara" in Cáceres were interviewed. Due to the availability of time of the clinicians, there have been no individual interviews, but a joint "focus group" interview. In this kind of interview, a group of people assemble to participate in a discussion about some topics to provide feedback. Furthermore, "focus group" method has the advantage of having a characteristic group interaction and non-verbal communication that reveals beliefs, attitudes and feelings about the discussed topic [8].

A team of two researchers conducted and moderated the interview. The "focus group" was audiotaped and transcribed verbatim for accuracy.

The more relevant results are the ones shown below:

One of the clinician described the need to improve the image quality to develop a more precise work:

"…regarding the image quality, we have 4K TVs in our homes, and here we are waiting to reach high definition.

I suppose it could be a problem with miniaturization of the chips or whatever, but the reality is that imaging technology is much more advanced in home consumption material. I think that the more definition, the more you can get."

And also indicates some areas for improvement:

"...both the image capture and the illumination of the interior of the colon are the fields in which we can move forward."

Other clinician complains about some types of polyps:

"...flat polyps are the hardest to see..."

indicating that the shape is not important for diagnosis:

"The shape I don't know if contributes because malignant or benign polyps have all the shapes... from the flat polyp, that is almost only a change of color in the mucosa, to a polyp that is like a pedicled polyp that is a small tree with its leaves... the shape really does not matter, you just have to know how to identify... "

But it is important to delimit the edge of the polyp:

"I think that the polyps highlightedfrom the rest of the mucosa would be important, because there are times that you do not see very well what the edge of the polyp is. So then to delimit better the polyps would help at the time of doing the resection."

Another aspect to improve is the possibility of measuring the size of the polyp:

"The size, because the measurements that are made now are estimated... there are differences between measurements performed by one and other clinician... if you could quantify it..."

For one of the clinicians, the best technology would be:

"The best technology would be one that detects the polyp and tells you this is a polyp and is adenomatous, or this polyp has an area that looks like a tumor, or this polyp is hyperplastic and you do not have to do anything. All those things or the location more precise of polyps in the colon."

And in the same way, another of the clinicians says the following:

"...you are performing an endoscopy and besides what you see, there is the possibility of a system that tells you that here there is a thing... it measures X millimeters and is hyperplastic. And then I can say in the report, at such a distance, there is an injury of X millimeters, and has hyperplasic characteristics."

Also, they highlight the need for all additional information to be displayed on the screen:

"Visual will always be better."

And the automation of the report elaboration:

"That the system itself generates a report including the best of those images that have been seen, automatically."

Regarding the endoscopic devices in the market, a clinician admits:

"...in size I think they are... long enough..."

And another one also thinks that devices are well designed:

"Colonoscopes of 160 cm are used here in Spain, however colonoscopes used in Europe are 130 cm long... They are trying more flexible tips, variable stiffness... They are quite accomplished devices, and you can reach your goal more than 95% of the time..."

However, if in the future it is physically possible to make the tip more flexible, the work would be easier:

"But if you can turn the tip more in some polyps... you could work better."

4. Conclusions and future work

Findings of this study provide new information from gastroenterologists' comments about the main drawbacks in the context of endoscopic technology and the colonoscopy procedure currently used for the diagnostic of colorectal cancer. Qualitative analysis performed reveals the following main themes: (a) Equipment limitations related to image quality and colon lighting; (b) problems in polyp detection and classification, especially flats polyps, and their location and size more precisely; (c) provide visual information; and (d) physical characteristics of the endoscope, such as size or tip stiffness.

Colorectal polyps currently detected with white light colonoscopy can be improved by means of fluorescence [9,10]. This approach offers the possibility of improving diagnostic capability without using exogenous agents, as demonstrated by various studies employing both visible [11] and near-infrared light [12].

The emerging optical imaging technologies (i.e: Confocal fluorescence microscopy, Optical Coherence Tomography, Raman spectroscopy, Hyperspectral spectroscopy, Multi-Photon Tomography and subsequent variations) show great potential for assisting clinicians in the early detection of cancerous diseases [13]. Among these technologies, Optical Coherence Tomography (OCT) and Multi-Photon Tomography (MPT) combination is a promising approach that can offer high sensitivity and specificity for diagnosis [14], representing an unprecedented powerful clinical tool to be used for both early diagnosis and follow-up of colorectal cancer. These images modalities provide microscopical structural and functional information,

In the European PICCOLO project [15] we aim to solve some of the abovementioned drawbacks developing a new technology for improving diagnostic identification of polyps at the time of colonoscopy. In this project, it is intended to provide an innovative minimally invasive endoscope based on OCT and MPT photonics that will allow performance of image-guided optical biopsies for in-vivo diagnosis of hyperplastic and neoplastic polyps that will increase detection rates, especially of flat polyps.

Also, the PICCOLO endoscope will be equipped with advanced image processing methods that will facilitate the detection, analysis and diagnosis of polyps on real time through a Computer Aided Design (CAD) system. This software will provide clinicians "Optical Biopsy" capabilities from OCT/MPT images. Visual aids for polyps delimitation, diagnosis suggestion and histopathological

characteristics will be automatically extracted from the images and presented to the user..

In this way, this innovative multiphotonic endoscope and its CAD system will address the current technological needs in colonoscopy procedure mentioned by gastroenterologists. The high resolution of the MPT/OCT images, and the jointly use of white light and fluorescence, would enhance the image quality and reduce the problems of colon lighting through a better detection of polyps. With the photonic technologies and the CAD software, neoplastic and hyperplastic polyps would be better detected and classified in real time, especially flat polyps, and visual information of diagnostic would be provided to gastroenterologists by the CAD software, as well as the location and size of the polyps, among other relevant metadata. Regarding the physical characteristics of the endoscope, it will be similar to the current ones regarding the size and tip stiffness, so it should be addressed in future improvements.

The results of this study with the focus group serve as a basis for establishing the functional and non-functional requirements necessary for the design of the PICCOLO endoscope. In addition, they are taken into account also for the design of CAD software, both the Graphical User Interface (GUI) that will allow the acquisition of data and the GUI for the control and display of the results to gastroenterologists.

Currently, more interviews are being performed to gastroenterologists from other regions of Spain, and even from other countries in Europe, so as the results could be generalized/extrapolated at a national or European level. As future work, these interviews will be analysed to improve the identification of medical needs. Additionally, questionnaires should be designed based on results from interviews to obtain information from a wider sample of gastroenterologists, not only from Spain, but also from other European countries.

Acknowledgements

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