

Functional evaluation of the Endotics System, a new disposable self-propelled robotic colonoscope: *in vitro* tests and clinical trial

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ABSTRACT: Objective: Currently, the best method for CRC screening is colonoscopy, which ideally (where possible) is performed under partial or deep sedation. This study aims to evaluate the efficacy of the Endotics System, a new robotic device composed of a workstation and a disposable probe, in performing accurate and well-tolerated colonoscopies. This new system could also be considered a precursor of other innovating vectors for atraumatic locomotion through natural orifices such as the bowel. The flexible probe adapts its shape to the complex contours of the colon, thereby exerting low strenuous forces during its movement. These novel characteristics allow for a painless and safe colonoscopy, thus eliminating all major associated risks such as infection, cardiopulmonary complications and colon perforation.

Methods: An experimental study was devised to investigate stress pattern differences between traditional and robotic colonoscopy, in which 40 enrolled patients underwent both robotic and standard colonoscopy within the same day.

Results: The stress pattern related to robotic colonoscopy was 90% lower than that of standard colonoscopy. Additionally, the robotic colonoscopy demonstrated a higher diagnostic accuracy, since, due to the lower insufflation rate, it was able to visualize small polyps and angiodysplasias not seen during the standard colonoscopy. All patients rated the robotic colonoscopy as virtually painless compared to the standard colonoscopy, ranking pain and discomfort as 0.9 and 1.1 respectively, on a scale of 0 to 10, versus 6.9 and 6.8 respectively for the standard device.

Conclusions: The new Endotics System demonstrates efficacy in the diagnosis of colonic pathologies using a procedure nearly completely devoid of pain. Therefore, this system can also be looked upon as the first step toward developing and implementing colonoscopy with atraumatic locomotion through the bowel while maintaining a high level of diagnostic accuracy. (*Int J Artif Organs* 2009; 32: 517-27)

KEY WORDS: Painless colonoscopy, CRC screening, Robotic colonoscope, Disposable colonoscope

INTRODUCTION

Colon cancer is a major cause of neoplastic mortality, second only to lung cancer in males and breast cancer in females (1). The slow growth and potential development from adenoma to adenocarcinoma of colon cancer makes it an excellent target for screening programs (2). In fact, early diagnosis and endoscopic treatment of lesions has been shown to strongly reduce colonic cancer mortality

(2). Among available screening procedures, conventional colonoscopy is currently considered the best existing method (3); however, risk factors associated with sedation can sometimes lead to the contraindication of standard colonoscopy in some patients (4, 5). Additionally, standard colonoscopy is associated with various procedural risks, ranging from cardiopulmonary complications (6, 7) to colon perforation (15-17). An additional serious complication is the transmission of infections (8-14), since many studies



Fig. 1 - Endotics System workstation.

report contamination of gastrointestinal endoscopes due to inefficient cleaning and disinfection procedures (24). Therefore, the use of a disposable and sterile colonoscope would be advantageous, by reducing the risk of infection. Overall, the incidence of complications in diagnostic colonoscopy has been estimated between 0.14% to 1.1% (18, 19).

Another complication for the use of conventional colonoscopy in colon cancer screening programs is the patient's fear and dislike of the uncomfortable procedure, which reduces the patient's willingness to participate in the currently available colorectal cancer screening programs (20-22). In fact, although colonoscopy is acknowledged to be an optimal screening tool in both healthy and asymptomatic patients, most people are unwilling to participate in a screen program due to the invasive and painful colonoscopy procedure. For these reasons, colonoscopy is currently used as a screening test only in first-level demonstrative studies and pilot projects. While participation in the first-level FOB (fecal occult blood) screening test is always above 50% (39), compliance to colonoscopy as primary screening ranges from 29% to 75% (40). Furthermore, compliance for second-level screening programs, which in principle should be high due to previously receiving a positive FOB test, range from only 30% to 60%, as



Fig. 2 - Endotics System single-use probe (E-Worm).

reported in a study by the AIGO - Oncology Group Study. Therefore, this data strongly implies that the ideal screening investigation should be as non-invasive as possible, safe, well accepted, and cost effective while maintaining a high diagnostic accuracy (23). In this study, the preliminary results demonstrate that the Endotics System is both safe and uses atraumatic locomotion through the bowel.

METHODS

The aim of this paper is to evaluate the diagnostic effectiveness and pain reducing capabilities of the novel colonoscopic procedure performed by the Endotics System (ERA Endoscopy S.r.l., Peccioli (Pisa), Italy) a newly conceived endoscope. The device includes a flexible probe allowing for painless locomotion through the colon since it easily adapts to the complex geometries of the human intestine. The unique working principle behind this device is inspired by inchworm locomotion, resulting in a self-propelled device that exerts low forces during its movements. This characteristic, together with its extreme flexibility, drastically reduces the risk of colon perforation. In the following sections, both in vitro tests and the results of a clinical trial will be discussed. The in vitro tests were used to measure the forces exerted during colonoscopy performed either by means of the Endotics System or by using conventional instrumentation. The clinical trial had the objective of both

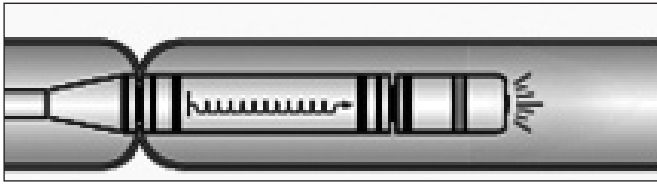


Fig. 3 - Adhesion of proximal clasper.

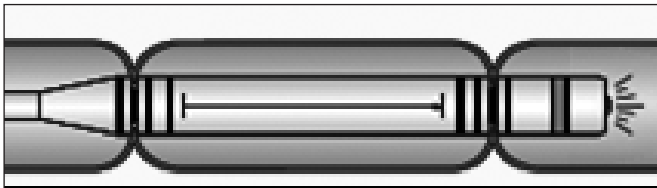


Fig. 4 - Elongation and adhesion of distal clasper.

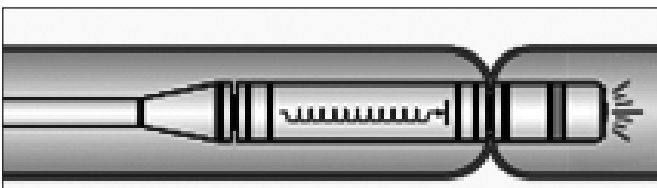


Fig. 5 - Release of proximal clasper and E-Worm shortening.

assessing the diagnostic quality of the device versus the standard colonoscope, and confirming the *in vitro* results related to issues of pain and discomfort.

The Endotics System

The Endotics System is a new CE-marked medical device for diagnostic colonoscopy, the result of academic research in the field of robotic biomimetics (see Figs. 1 and 2) and manufactured by ERA Endoscopy S.r.l. (Peccioli (Pisa), Italy). This new discipline is the application of biological methods and systems found in nature to the study and the design of robotic systems.

The Endotics System is composed of a sterile, disposable probe (E-Worm) and a workstation. The probe has a head, a steerable tip, a flexible body, a thin tail (7.5 mm in diameter) and a special tank with an electro-pneumatic connector. The head hosts both a vision system, including camera (110° vision angle), LED light sources and channels for water jet and air in order to provide rinsing and suction/insufflation, respectively. The workstation allows the endoscopist to fully control the disposable probe by means of a hand-held console and to visualize real-time images on a screen. The operator can steer the head of the

robotic colonoscope of 180° in every direction, elongate the body of the probe in order to move it forward following the shape of the intestine, and can control rinsing, insufflation and suction. During the suction phase, the operator can remove liquid fluid from the bowel that will be conveyed to the special tank positioned at the end of the thin tail. The insufflation action, controlled by the operator, is also useful to unfold the bowel tissue in order to improve diagnosis. Moreover, a semiautomatic sequence of actions is implemented to move the probe like an inchworm. This kind of locomotion, which is particularly suited to an unstructured environment like the intestine, is possible due to two claspers specially designed for this purpose that are located in the proximal and distal part of the probe. They adhere to the intestinal mucous membrane by means of a vacuum technique and a mechanical grasping action. In accordance with the intended use of the Endotics device, it is not approved for use in pediatrics and its contraindications are the same as those for conventional colonoscopy.

The locomotion phases can be described as follows (see Figs. 3, 4, 5):

- the proximal clasper adheres to the mucosa (automatic phase);
- the central part of the body is elongated under control of the medical doctor, who steers the probe (manual phase);
- the distal clasper adheres to the mucosa (automatic phase);
- the proximal clasper is released (automatic phase);
- the central part of the body is contracted (automatic phase);
- the proximal clasper adheres to the mucosa (automatic phase);
- the distal clamp is released (automatic phase);
- the sequences begin again.

Automatic phases are used only to recover the initial position of the probe, while the operator provides instruction for movements of elongation and steering of the probe head.

In vitro experimental tests

The aim of the *in vitro* experimental tests was to measure the forces exerted on mesenteries during colonoscopy either by the Endotics System or standard colonoscopy. Mesenteric stretching is the main cause of pain and discomfort related to the colonoscopic procedure, thus this *in vitro* comparison represents an initial key assessment of the pain-related characteristics of this new device. For the

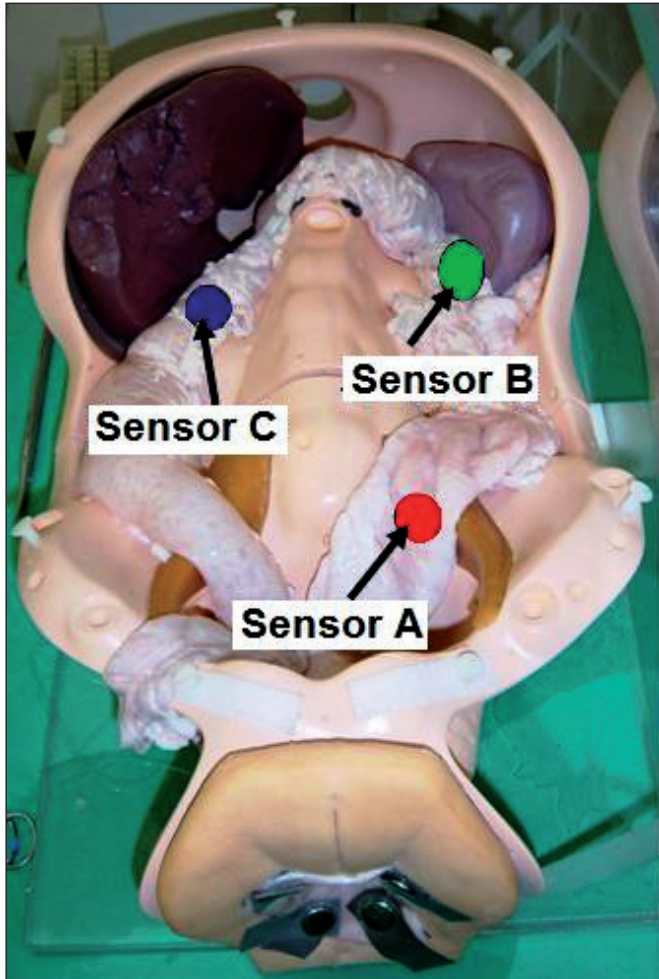


Fig. 6 - The positions of the three load cells in the bodyform.

test-bench, a plastic model of a human adult abdomen was used as a phantom (see Fig. 6). A porcine bowel was fixed to the phantom through nylon threads, positioned so that the geometry of the human colon was reproduced. Three load cells (Model 11; Honeywell Sensotec Inc. Columbus, OH, USA) were positioned in points where maximum stress levels commonly affect mesenteries during conventional colonoscopy (sigma, splenic flexure and hepatic flexure). The sensors were connected from one side to the bowel by means of semi-elastic wires, and from the other side to the phantom. The electronic signals from the load cells were acquired through an AT-Mio-16 I/O card connected to a PC using Lab View 7.0 software (all National Instruments, Austin, TX, USA). An experienced physician carried out two endoscopic procedures, first using the conventional colonoscope and then the Endotics colonoscope.

An additional study using an animal model was performed in order to demonstrate the safety of the clamping mechanism (data not shown).

Clinical trial

A prospective, open labeled, multi-center clinical study was carried out to evaluate the Endotics System colonoscopy in comparison with "standard colonoscopy" in terms of diagnostic capabilities and patient acceptance.

Primary end points of the procedure were:

- To demonstrate that robotic colonoscopy performed by the Endotics System and the standard colonoscopy have the same diagnostic accuracy.
- To evaluate the patient acceptance of the Endotics System, in terms of the pain level experienced by the patient.

Secondary end points were:

- The percentage of Ileo-Cecal valves reached.
- The Cecum Reaching Time (CRT).

Inclusion criteria of the present study were the following:

- Patients between 18 and 75 year old, including both males and females
- Patients over 40 years old with at least a first-grade relative with a previous history of CRC or adenomas before 60 years old.
- Follow-up in patients already treated with endoscopic polypectomy.
- Patients positive at FOB during screening tests.

Two Italian medical centers were involved in this study. The study was approved by the Ethics Committee at the Pisana University Hospital, Pisa (2426/2007), and by the Ethics Committee at the San Paolo Hospital, Milan (989/2007). Informed consent was obtained from each patient. Two endoscopists per center were trained in vitro with an animal bowel body form for the Endotics System. It is important to note, therefore, that while these endoscopists possessed extensive experience with the standard colonoscope, this trial included their first 20 procedures using the Endotics System. This number is ten times lower than the 200+ procedures requested for the colonoscopy training program (24).

In this study, 40 consecutive patients fulfilling inclusion criteria, 27 males and 13 females, were enrolled and underwent both the Endotics System procedure and standard colonoscopy. Physicians were randomly selected for the two procedures: the operator who performed the robotic colonoscopy did not attend the procedure with the standard device, and whoever performed standard colonoscopy was blinded to the findings of the first procedure. All patients, after standard colon preparation with several liters of polyethylene glycol (PEG) lavage solution (until evacuation of clear yellowish fluid) were submitted first to

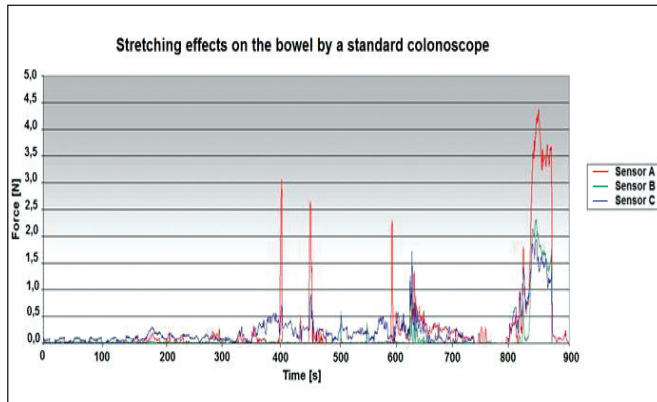


Fig. 7 - Stretching effects on the bowel by conventional colonoscopy.

the robotic colonoscopy and immediately after to conventional colonoscopy. This sequence was decided in order to find the physiological condition of the colon during the Endotics System procedure, and also to perform a polypectomy or biopsy if required. According to the protocol of the clinical trial for both procedures, no sedation was provided unless the patient specifically requested it. All records were registered and compared.

RESULTS

In vitro experimental tests

The comparison between the stretching effects of the bowel by the Endotics System versus conventional colonoscopy was performed *in vitro* using a plastic abdominal model. In Figures 7 and 8 the different colors indicate the output signal of the three sensors positioned in the sigma, splenic flexure and hepatic flexure of the model.

Impressively, the forces exerted by the E-worm robot were 90% lower than that of the conventional colonoscopy values. Moreover, when considering the behavior of the signal acquired by Sensor A, it is important to underline that during the conventional endoscopy, the sensor was intensively stressed throughout the entire procedure, i.e., even when the colonoscope had already passed beyond the Sensor A position. Conversely, analysis of the stretching effects of the Endotics System showed that Sensor A was stressed only during locomotion in its proximity. This significant result, due to the fact that the E-worm advances by means of self-locomotion rather than by pushing, was a clear indication that a painless procedure could be performed with the Endotics System.

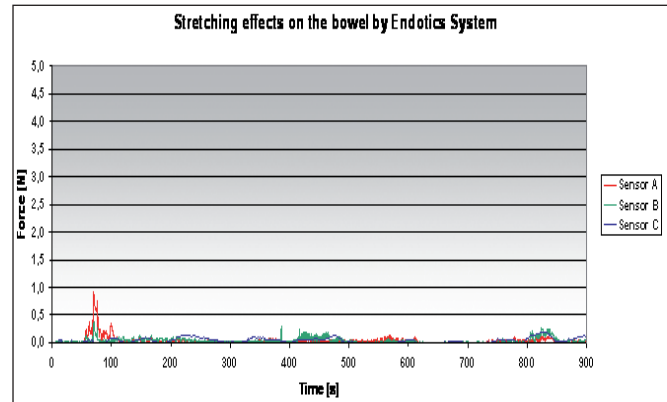


Fig. 8 - Stretching effects on the bowel by Endotics System.

In vivo experimental tests

The study demonstrated that the Endotics System is not harmful to the colon wall. The clamping mechanism does not create lesions in the bowel wall, such as mucosal lacerations. No bleeding was found as a result of the interaction of the clamping mechanism with the colonic wall, even in the case of prolonged clamping. A colonoscopy procedure was performed after a follow-up period of 7 days and no remarks were noted. The clamping system of the device can thus be considered safe.

Primary end points

Diagnostic accuracy

In the clinical study, considering the tract of colon investigated with both systems, the diagnostic accuracy was found to be higher with the robotic colonoscopy compared to the standard instrumentation. Indeed, the Endotics System was able to visualize two small polyps not seen using standard colonoscopy, in two different cases, possibly due to over-stretching caused by greater air insufflations of the intestine. With regard to this effect, angiodysplasias were also noted in two cases during the Endotics procedure but were not seen with standard colonoscopy; however, this was not included as an end point in the protocol. Table I shows the size and the distribution of polyps detected during the study.

In comparison to standard colonoscopy, the Endotics System requires minimal air insufflations and provides a more accurate insufflation-suction balance, allowing the bowel to keep its natural physiological shape. In the Endotics System, air insufflation is only required in the im-

TABLE I - SIZE AND DISTRIBUTION OF POLYPS DETECTED DURING THE STUDY

N	Polyp size (mm)	Location	ENDOTICS	STANDARD COLONOSCOPY	Histological results
1	10	Sigma	X	X	Tubulovillous adenoma - High-grade dysplasia
	15	Sigmo-rectal	X	X	Tubulovillous adenoma - High-grade dysplasia
2	5	Sigma	X		
3	8	Sigma *	X		
4	5	Rectum	X	X	Hyperplastic
	5	Descending	X	X	Tubular adenoma - Medium-grade dysplasia
5	15	Descending	X	X	Tubular adenoma - Medium-grade dysplasia
6	9	Sigma	X	X	Tubulovillous adenoma - without dysplasia
	4	Sigma	X	X	Hyperplastic
7	6	Sigma	X	X	Hyperplastic
8	3	Rectum	X	X	Hyperplastic
9	4	Rectum	X	X	Hyperplastic
10	4	Sigma	X		

* The polyp was not seen in this case because the traditional procedure was stopped due to pain before reaching its location; for this reason it has not been included in the accuracy comparison.

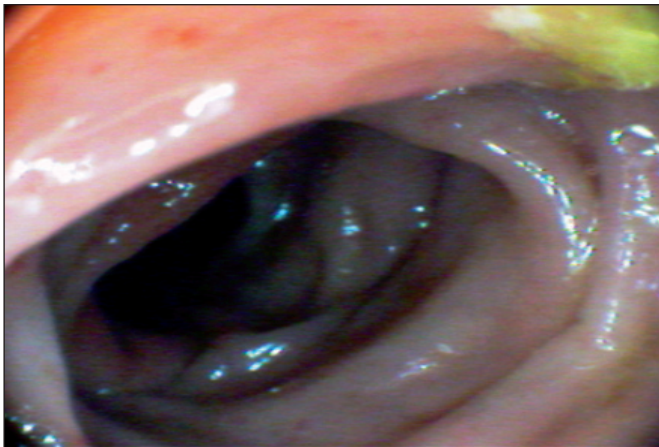


Fig. 9 - Colon visualization with Endotics System.

mediate proximity of the head lens to increase the portion of bowel visualized. A representative picture of the colon during the Endotics System procedure is shown in Figure 9.

Clinical acceptance

All patients considered the new robotic colonoscopy more tolerable than conventional colonoscopy:

using a scale from 0 to 10 for pain and discomfort, the Endotics System scored on average 0.9 and 1.1, respectively (mode 0 for both), compared to 6.9 and 6.8, respectively (mode 9 and 8), for standard colonoscopy.

More specifically, with the standard procedure, about 50% of patients assigned a pain value greater than 8, while with the Endotics System 50% of patients set a value a pain value equal to 0. Moreover, for the Endotics System about 70% of patients choose a pain value of less than 1.

Additional considerations regarding pain and discomfort can be observed by comparing clinical results to those of the in vitro tests. The in vitro experimental test with the traditional endoscope showed that sensors A and B were much more stressed than sensor C. Sensors A and B referred to the “Left Colon”, whereas Sensor C referred to the “Right Colon”.

Dividing patients in two categories, namely, those who received only a partial examination (left colon) or those who received a complete examination (right colon), results of pain and discomfort confirmed that of the in vitro experimental data (Tab. II).

The results of the patients’ evaluation are plotted in the following Figures 10 and 11.

TABLE II - PATIENT PAIN AND DISCOMFORT SCORES UPON REACHING THE LEFT OR RIGHT COLON

	ENDOTICS SYSTEM			STANDARD COLONOSCOPY		
	Right Colon (N=29)	Left Colon (N=11)	Average	Right Colon (N=34)	Left Colon (N=6)	Average
Pain	0.7	1.5	0.9	7.0	6.7	6.9
Discomfort	0.7	2.1	1.1	6.8	6.8	6.8

All patients ranked pain and discomfort using a range from 0 to 10.

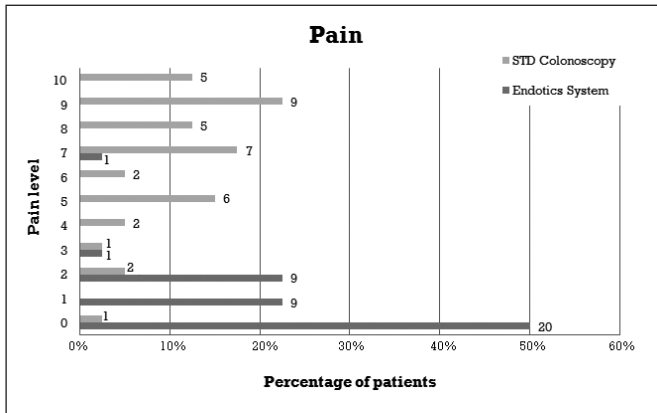


Fig. 10 - Pain levels with Endotics System and with conventional colonoscope.

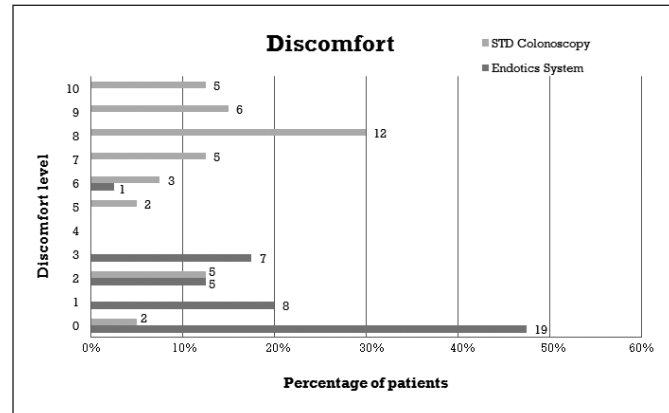


Fig. 11 - Discomfort levels with Endotics System and with conventional colonoscope.

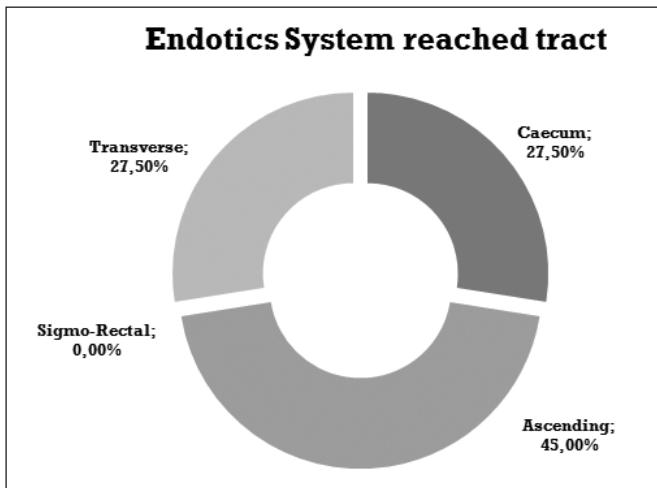


Fig. 12 - Tract reached with Endotics System.

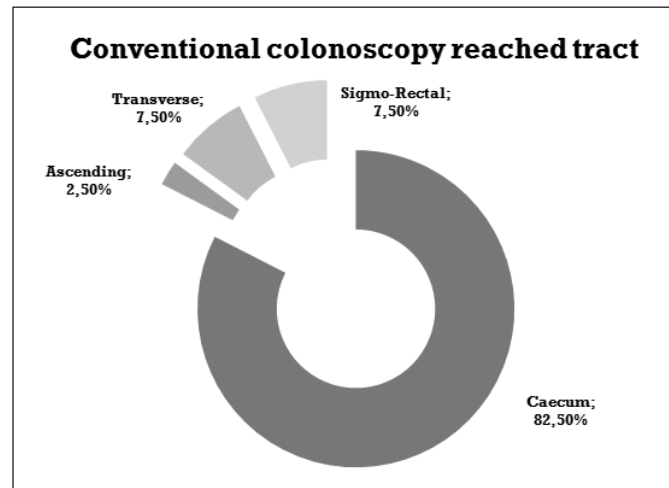


Fig. 13 - Tract reached with conventional colonoscope.

Secondary end points

Cecal intubation rate

During this study, intubation rates with the Endotics System was 27% for cecal intubations, due to 11 successful intubations and 45% for right colon intubations, representing 18 successful procedures. In comparison, using the standard colonoscopy technique there were 34 (85%) successful right colon intubations and 33 (82%) successful cecal intubations (Figs. 12 and 13).

To confirm cecal intubation, a second experienced endoscopist assisted in the withdrawal of the probe. In the literature, the percentage of cecal intubation during standard colonoscopy without sedation is in the range of 81% (25). During this study two patients (2.5%) requested the procedure

to be stopped during conventional colonoscopy due to high levels of pain, since sedation had been refused. In two cases when traditional colonoscopy did not reach the cecal valve, the Endotics System had visualized a longer intestinal tract. In the remaining cases, the two procedures reached the same colon tract. Moreover, it should be taken into account that the medical doctors involved in the study were experienced operators of the standard colonoscope, having executed more than 10,000 examinations, while their experience with the Endotics System was limited to only 20 procedures.

Cecum Reaching Time (CRT)

Analysis of the time required to perform the Endotics System procedure results in a mean value of 57 minutes.

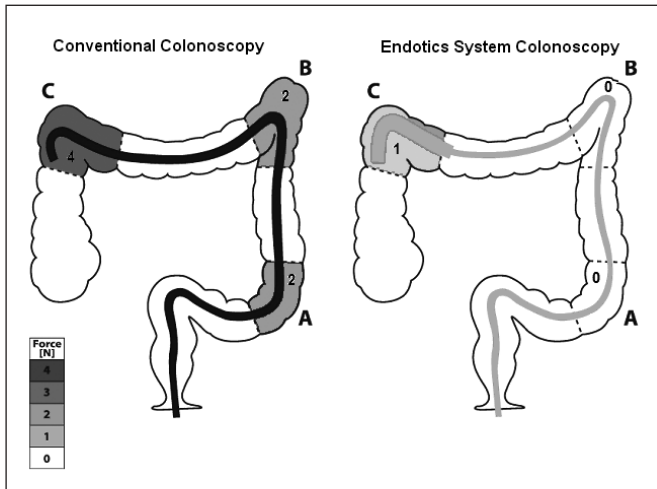


Fig. 14 - Stretching force comparison between Endotics System and conventional colonoscopy.

Several studies in the literature report that for standard colonoscopy the median duration time is 20 minutes (26). Importantly, in 4 cases the Endotic System procedure was interrupted due to malfunction of the robotic colonoscope; however, in one of these cases once the device was changed, cecal intubation was obtained.

DISCUSSION

Besides operator expertise, colonoscopy success strongly depends on the geometrical and mechanical characteristics of the patient's individual bowel. Due to the high invasiveness of the colonoscopic procedure, the patients enrolled for the study had been strongly advised to undergo colonoscopy. In most cases, they had experienced significant pain during their previous examinations, and were thus looking for a painless procedure. Although this functional evaluation used a blinded protocol, many patients presented particular conditions of the bowel: 4 patients (10%) had a long colon, 10 patients (25%) polypsis, 5 patients (12.5%) diverticulosis, and 1 patient (2.5%) Crohn's disease. Displayed (see Fig. 14) are pictograms (Fig. 15) describing the areas of deformations during either the standard colonoscopy procedure or the Endotics System. Furthermore, the diagnostic accuracy of the Endotics System is observed to be higher than that of standard colonoscopy, probably because lower insufflations provided better vision of small lesions. The virtually complete lack of pain using the robotic procedure was confirmed by these first 40 clinical cases.

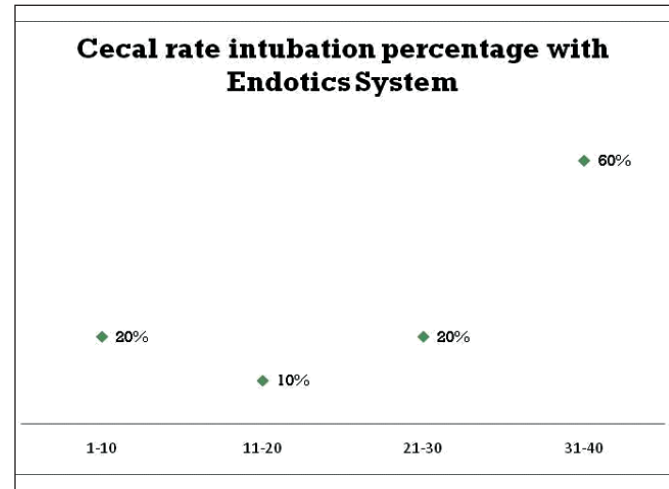


Fig. 15 - Cecal intubation rate using the Endotics System divided by enrolment quartiles.

Overall, the cecal intubation rate with Endotics System procedure was observed to be low in this study compared to traditional colonoscopy (22, 27). Nevertheless, the cecal intubation rate increased significantly over the course of the study (Fig. 15), thereby suggesting that the Endotics System technique requires a very short learning period. Moreover, it should be taken into account that the medical doctors involved in the study were experienced operators of the standard colonoscope, having executed more than 10,000 examinations, while their experience with the Endotics System was limited to only 20 procedures.

Previous studies have described the learning curve of standard colonoscopy to be approximately two years. Some studies have reported that to reach acceptable performance levels (determined by a cecal reaching rate of 66%) a physician is required to complete at least 100 colonoscopies. Furthermore, to reach the cecum in 75% of cases, the number of procedures needed increases to 200 (28). Additionally, it has been estimated that to maintain a proper performance level for standard colonoscopy, a medical doctor should perform a minimum of 200 procedures per year (29, 30). Conversely, the present study showed that the learning curve of the Endotics System is significantly reduced to just a few weeks. Furthermore, by adapting its shape to the bends of the colon, the Endotics colonoscope eliminates the need for physicians to perform complex torsion and push/pulling maneuvers, allowing their full attention to be focused towards directing the probe through the lumen.

The time required to perform the Endotics System procedure was observed to be longer than the median dura-

tion of 20 minutes for standard colonoscopy; however, it is believed that this result may also be partially attributed to the initial phase of the learning curve.

Compared with other techniques such as virtual colonoscopy and pill-cam endoscopy, polyp size for this device is evidently not a limitation since very small lesions were visible (31, 32). Studies on other non-traditional colonoscopy techniques, such as the Neoguide colonoscope (33), the In-vendo (34), the Aer-O-Scope (35-37), and the GI View vision system assessment (38), have focused on the description and performance of the individual devices, not including a comparison with standard colonoscopy (gold standard) or evaluating their accuracy in detecting polyps. In contrast, the current trial was specifically designed to carry out painless colonoscopy while providing a high accuracy of diagnosis compared with the gold standard procedure.

Based on a comparison between the robotic endoscope and the conventional colonoscope in detecting colorectal lesions and in performing painless procedures, this study shows the suitability of the Endotics System for colonoscopy. This innovative robotic system provides good quality images of the colon and accurately detects small polypoid lesions. This is further confirmed by the fact that in two cases the Endotics System visualized small polyps not seen at standard colonoscopy. This is believed to result from the lower amount of insufflations required with the Endotics System. Furthermore, this new equipment could additionally allow for continuous monitoring of pressure throughout the procedure. Moreover, the negligible stress on mesenteries induced during the procedure using the Endotics robotic system allows it to be virtually painless, thereby eliminating the need for sedation and allowing the procedure to be well accepted by patients. A painless colonoscopy, besides being a remarkable achievement for patients and eliminating any sedation-related risks, has major implications in terms of prevention. Another advantage of the Endotics System is that it includes a sterile, disposable probe.

Very few, non-serious adverse events occurred during this study, indicating that colonoscopy with the Endotics System is a feasible and safe procedure. However, the small sample size may have impaired the ability to observe rare but significant adverse effects. In addition to the results presented in this paper, further technical work has recently been conducted to improve the performance of the Endotics system with respect to the secondary end points. Initial results from these modifications show improvement in both the cecal intubation rate and required duration of the procedure.

The main goal of future work will be to further assess the performance of the system, thereby allowing it to be employed for safe, painless and widespread screening pro-

grams. The economic impact of this new technology should be evaluated based on the use of a disposable probe, thereby saving in reprocessing endoscopes and reducing the risks of cross-contamination. The introduction of this diagnostic instrument into clinical practice could facilitate the adoption of colonoscopy as first-level screening, with a further reduction in the incidence of the colon cancer-induced mortality, estimated in the order of 76% to 90% (41, 20).

CONCLUSIONS

In conclusion, the primary end points of this study were satisfied with results exceeding anticipated expectations, since high diagnostic accuracy was found in the absence of pain, rendering the Endotics System superior to conventional colonoscopy. If further studies confirm preliminary results regarding the improvement of the secondary end points, the Endotics System could play an important role in the future detection of colorectal cancer diseases and surveillance in both routine and screening settings. Further studies are needed to assess the optimal bowel preparation for the Endotics procedure. Moreover, a new prototype equipped with a tool channel aimed at improving the performance of the system in terms of fluid suction, forced washing and surgical capabilities will be available in the near future. Hence, minimally invasive medical robots will be used for diagnosis and interventions and while the Endotics System could be considered the precursor specifically for the natural orifice of the colon, further development of special probes may allow the use of this technology to be applied to other natural orifices.

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