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High Cecal Intubation Rates With a New Computer-Assisted Colonoscope: A Feasibility Study

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- OBJECTIVES:** The acceptability of colonoscopy as a screening test is limited by several factors including patient discomfort. A new self-propelled colonoscope, the Invendo SC20 (Invendo Medical GmbH), may be helpful in reducing sedation. It consists of a sheathed endoscope contained within an “inverted sleeve,” and having an instrument channel and an electrohydraulic bendable tip; it is steered using a handheld device and propelled by a motorized drive unit. This study assessed the safety and efficacy of this new endoscope in volunteers undergoing colorectal cancer (CRC) screening.
- METHODS:** Paid healthy volunteers aged 50–70 years and eligible for screening colonoscopy were included. Total colonoscopy using carbon dioxide insufflation or water instillation on demand was attempted, with all procedures being started without sedation. The main outcome parameters were safety and the cecal intubation rate.
- RESULTS:** A total of 61 volunteers participated (34 men and 27 women; mean age 57.5 years). The cecum was reached in 60 volunteers (cecal intubation rate of 98.4%). The median time to reach the cecum was 15 min (range 7–53.5). Sedation was given in three individuals (4.9%). On withdrawal (median time 15 min), the material for histological evaluation was obtained from 33 polyps (mean size 4.8 mm) in 23 people by biopsy forceps or snare. No device-related complications were encountered.
- CONCLUSIONS:** A new computer-assisted colonoscope, controlled using a handheld device, showed excellent cecal intubation rates during screening examinations, with sedation required in only ~5% of screenees. Further clinical and comparative studies are warranted.

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INTRODUCTION

Colonoscopy has been incorporated into colorectal cancer (CRC) screening programs in some countries (1–3). However, take-up of screening colonoscopy is limited owing to various factors that include fear of pain and the need for sedation.

The alternative platforms for endoscopic imaging of the colon that have recently been presented include diagnosis-only devices such as capsule colonoscopes (4,5) and the Aer-O-Scope (GI View Ltd, Ramat Gan, Israel) (6), and therapeutic colonoscopes with alternative propulsion mechanisms such as the NeoGuide (Neoguide Systems Inc, Los Gatos, CA) (7) and the Invendo SC20 (Invendo Medical GmbH, Kissing, Germany). The Invendo SC20 is a computer-assisted colonoscope, propelled by an “inverted sleeve” mechanism and steered by means of a reusable handheld device (8). The latest version of the Invendo SC20 is CE-marked. We report a prospective trial in volunteers eligible for and willing to undergo screening colonoscopy.

METHODS

Participants

The trial was conducted as a prospective single-arm study in November and December 2009 with the aim of including 60 participants. All the participants were people who were willing to undergo screening colonoscopy, who were at an average risk for CRC, and who were between 50 and 75 years of age. An honorarium of €350 (~\$440) was offered. The study was approved by the Ethical Committee of the Ärztekammer Hamburg (trial no. PV 3314).

The inclusion criteria were:

1. Screenee status, i.e., asymptomatic and willing to undergo screening colonoscopy, and at average risk for CRC.
2. Age between 50 and 75 years.
3. Provision of signed informed consent.

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The exclusion criteria were:

1. Family or personal history of colorectal neoplasia including familial adenomatous polyposis or hereditary nonpolyposis CRC.
2. Previous colonoscopy, within preceding 10 years.
3. Diagnosis of suspected inflammatory bowel disease, bowel obstruction, or acute diverticulitis, or known severe diverticulosis, or any known large-bowel disease.
4. Clinically significant cardiovascular or pulmonary disease.
5. Gastrointestinal tract-related symptoms, complaints, or diseases suggesting performance of a diagnostic colonoscopy (nonscreening cases).
6. Cancer or other life-threatening disease or significant chronic condition.
7. Blood-clotting disorders and/or anticoagulant therapy (anticoagulant therapy included aspirin within the previous 7 days).
8. Known pregnancy or positive pregnancy-screening test.
9. Previous abdominal surgery, except for uncomplicated cholecystectomy, appendectomy, or minor pelvic surgery (e.g., hernia repair, oöphorectomy).
10. Morbid obesity (body mass index > 40 kg/m²).
11. Clinically significant abnormal screening laboratory findings.
12. Clinically significant abnormal screening electrocardiographic findings.
13. Drug abuse or alcoholism.
14. Inability of the screenee to communicate adequately.
15. Being under custodial care.
16. Participation in a clinical study within the previous 30 days.

Colonoscopic examinations

Two centers and four investigators (S.G., N.H., D.K.R., and T.R.) were involved in the study. These investigators were experienced in colonoscopy (3,000–30,000 lifetime experience) and two of them had done > 100 colonoscopies with the SC20 colonoscope before the start of the study (N.H. and T.R.). The two other investigators received training with one (S.G.) or two (D.K.R.) procedures using the Koken Colonoscopy Training Model and reported proficiency regarding passage after two training procedures in humans (screenees). These two investigators performed nine procedures each with the Invendo SC20 before the start of the study.

The study was carried out at two sites in Germany, in Frankfurt and Hamburg. Following conventional colon lavage preparation using polyethylene glycol solution (MoviPrep, Norgine GmbH, Marburg, Germany, in split dosage), the colonoscopic examination was begun with the screenee in the left lateral position. An intravenous line was only placed if sedation or antispasmodic agents became necessary during the examination. Participants were reassured that they could receive sedation at any point during the examination if this was requested, and were repeatedly asked by the colonoscopist during the examination whether they were comfortable or wanted sedation. If sedation was requested, propofol was administered by a second endoscopist and the patient was monitored by pulse oximetry, and pulse and blood pressure measurement.

Position change and application of abdominal pressure were used at the discretion of the colonoscopist. CO₂ was used for insufflation in all cases. Water immersion, administered via a foot pump, was used during insertion at the discretion of the endoscopist.

The instrument was steered to the cecum; this was confirmed by images of the appendiceal orifice from a point proximal to the ileocecal valve and of the ileocecal valve from just distal to the valve. On introduction and especially on withdrawal (this was the main step of the examination for diagnostic activity), pathological findings such as polyps were documented and biopsied, or removed by forceps or snare if the endoscopist deemed that this was indicated and feasible. The quality of bowel preparation was rated by the investigator on a scale of 1 (excellent) to 6 (very poor) for the three segments of the colon (right colon up to mid-transverse, left colon including sigmoid, and rectum).

After the examination, participants were interviewed about their general impression of the examination and they rated pain and discomfort on a visual analog scale (1 = excellent to 6 = very poor, unbearable). If volunteers required sedation, a rating of 6 was automatically assumed for the record immediately after the procedure. Participants were contacted again at 24 h and 7 days.

Instrument description: the Invendo SC20

The Invendo SC20, a single-use colonoscope controlled using a handheld unit (Invendo Medical GmbH, Germany) that is not yet commercially available in the United States, has been previously described in detail (8). Briefly, the colonoscope has a working length of 210 cm; the endoscope *per se* is covered by a 10-mm inner sheath. The sheath is covered by double layers of an “inverted sleeve” that provides the propulsion mechanism. A propulsion (drive) connector allows a mechanical link to the inner layer of the sleeve. Before the examination, the drive connector is locked into the endoscope’s external driving unit; the examination is then started (**Figure 1**). Eight drive wheels in the driving unit grip the inner layer of the inverted sleeve and rotate, causing the inner layer of the inverted sleeve to drive forward. The “inverted sleeve” mechanism causes the colonoscope to “grow,” at a position just 10 cm below the distal end. Similarly, when the colonoscope is being driven backward, the drive wheels rotate in the opposite direction and the endoscope “shrinks.” It can be actively pulled out if needed (e.g., if a sedation emergency occurs); no direct manual maneuvers such as rotation are possible during introduction and withdrawal; this can be compensated in some way by 190° tip rotation in all four directions.

A handheld control unit is used to activate all the endoscopic and software functions. The endoscope tip can be flexed electrohydraulically 180° in any direction by moving a joystick on the handheld device. Otherwise, the design of the colonoscope is similar to conventional endoscopes, allowing for insufflation, rinsing, and suction. It also has a 3.1-mm working channel.

Study parameters

The main outcome parameters of the study were:

- Safety as measured by the frequency and severity of device-related adverse events.

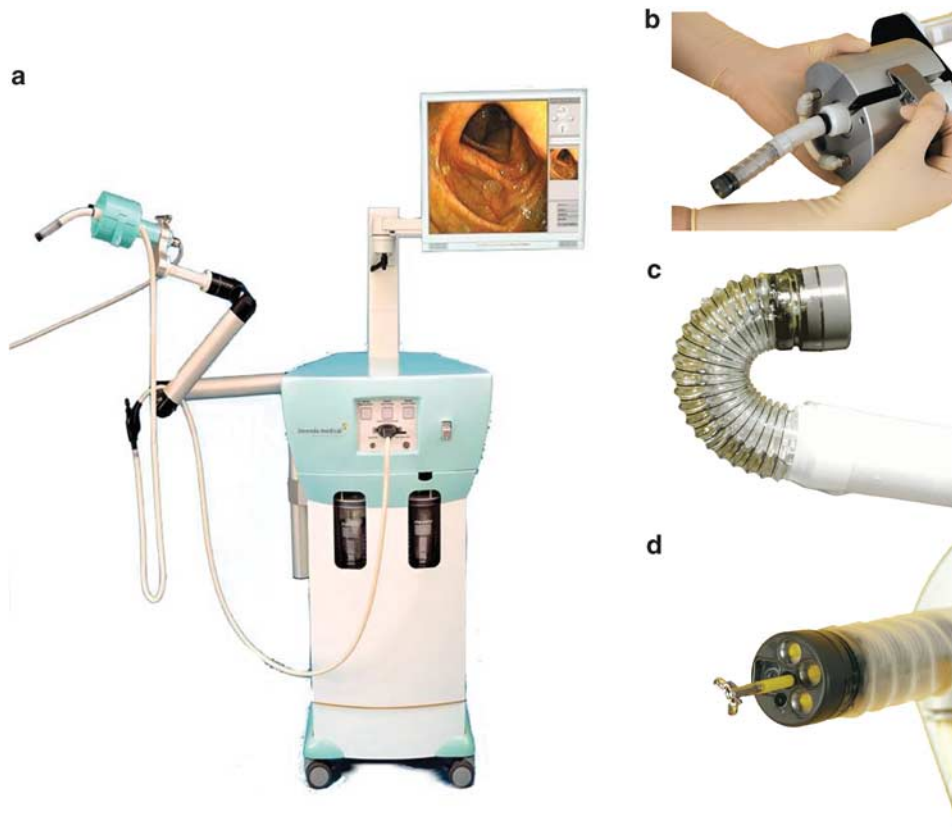


Figure 1. The SC20 colonoscope shown in the newest version. (a) The complete device with the instrument, driving unit, and processor; (b) the tip is introduced through the driving motor; (c) tip in full flexion; (d) tip with a biopsy forceps introduced through the working channel.

- Device effectiveness as shown by cecal intubation rate.
- The secondary outcome parameters were:*
- Utility of the device in the documentation and biopsy of pathological findings.
 - Pathological findings such as polyps, inflammatory changes, and so on. These were to be biopsied and/or polypectomies carried out according to the decision of the investigator. All findings were documented with respect to type, size, and location. The histological findings from polyps and the percentage of polyps that were biopsied or removed were also to be recorded. Sedation was recorded as an observation. Screenees started colonoscopy without sedation and analgesia but had the freedom to choose sedation and/or analgesia at any point during the examination. The need for sedation was recorded as a percentage of all examinations.

The following additional parameters were also recorded:

- Baseline characteristics: age, gender, height, weight, body mass index, and medical history.
- Vital signs before and after the procedure.
- Duration of introduction and withdrawal of the colonoscope.
- The volunteer's perception of the procedure with respect to pain/discomfort, and their general impression, as described above (1 = excellent, no pain; 6 = unbearable, procedure had to be stopped due to pain, on the visual analog scale). A rating

of 6 was automatically given immediately after the procedure in cases where sedation was used. Screenees were asked by examiner and/or study personnel after study completion.

- Quality of bowel preparation as judged on a scale of 1 (excellent) to 6 (very poor).

Statistical analysis

The main outcome was evaluated as the proportion of patients with successful examinations, with a 95% confidence interval. The sample size of 60 was chosen in line with the expectation of a $\geq 90\%$ true success rate. Intubation time and the patients' evaluations of the procedures are presented as means and medians. Further presentation of the results is primarily descriptive; therefore, no power calculation was done.

RESULTS

Between 25 November 2009 and 19 December 2009, 61 volunteers were included; these were 34 men and 27 women, with a mean age of 57.5 years (range 50–70) and a mean body mass index of 26.3 kg/m^2 (19.5–36.8). Of the screenees, 15 (24.6%) had previously undergone minor abdominal surgery. Thirty-four procedures were carried out in Frankfurt and 27 procedures in Hamburg. There were no drop-outs and no nonevaluable participants; the follow-up rate was 100%.

The cecum was reached in 60/61 of participants (98.4, 95% confidence interval 91.2–99.9%). The rate was significantly higher than 90% (exact binomial test; one-sided *P* value 0.013). In the one case where the cecum was not intubated, the deepest point of advancement was the ascending colon. Water instillation was used in 29 cases. Abdominal compression and/or position change was used in approximately two-thirds of the patients that helped in further advancing the scope; in the case of failed cecal intubation, these measures did not help and a longer scope might have been necessary to reach the cecum. Systematic retroflexion (e.g., in the rectum) was not part of the study protocol; we nevertheless felt that retroflexion, which can happen inadvertently, is safe and can be easily achieved, e.g., in rectum, at flexures, and in the cecum if aimed at (examples of colon views and findings are shown in Figures 2 and 3).

The median time to reach the cecum was 15 min (range 7–53.5, mean 16.4). The median withdrawal time was also 15 min (range 3.5–51, mean 16.4); for the cases in whom polyp removal was performed it was a mean of 21.2 min (range 6.5–51), and for patients without findings it was a mean of 13.6 min (range 3.5–27.5). There was a nonsignificant trend for shorter times, by 2 to 3 min, with the investigators with more experience with the device (13–14 vs. 16–17 min). The mean value for quality of bowel cleansing in all participants, as subjectively assessed by the examiners, was 1.8 (range 1–5); each individual had a mean value derived from the values in the three colonic segments as described above.

In two cases, a second Invendo SC20 had to be used in the same volunteer because of endoscope malfunction. In one case, there was a malfunction of the tip flexion, probably caused by the introduction of a rough-running forceps. In the other case, the working channel had been completely blocked by aspirated bowel content.

Sedation was used in three participants (4.9%); the propofol doses used were 120, 130, and 180 mg. The mean ratings from the screenees, immediately after colonoscopy, for overall assessment and pain/discomfort were 1.6 (range 1–3) and 2.3 (range 1–6). Follow-up at 24 h and 7 days was complete for all the study participants. The mean overall ratings at 24 h and at 7 days were 1.4 and 1.3 (range 1–5). The mean pain/discomfort ratings at 24 h and at 7 days were 1.5 and 1.3 (range 1–6). Only three screenees had previous colonoscopy, 12, 17, and 35 years before, with little memory of these procedures.

A total of 36 polyps were detected in 23 participants, ranging in size from 2 to 18 mm (mean 4.8 mm). Of these, 32 polyps were removed by either forceps (*n* = 22) or snare (*n* = 10) (Figure 4); one additional polyp, a 12-mm flat lesion, was referred for polypectomy using conventional colonoscopy. Histological investigation showed 11 low-grade adenomas (including the polyp removed conventionally), hyperplastic tissue in 12 cases, and normal colonic mucosa in 10. In two screenees, three small polyps detected on scope introduction could not be found again on withdrawal.

There were no device-related adverse events. One occurrence of minor bleeding, after snare polypectomy of a 15-mm polyp in the sigmoid colon and insufficient high frequency current delivery during intervention, was observed (considered to be a minor adverse event, and not device related). The investigator decided

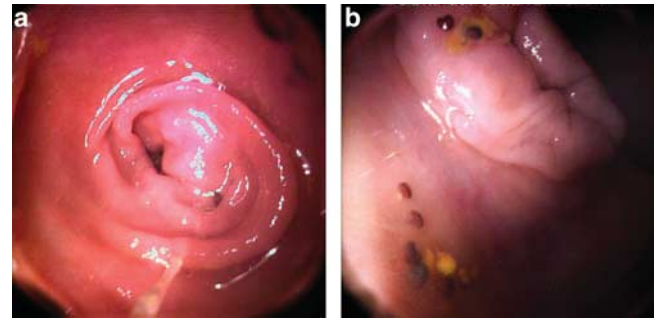


Figure 2. Endoscopic images of the cecal floor. (a) A rather large appendiceal orifice; (b) the cecal valve.

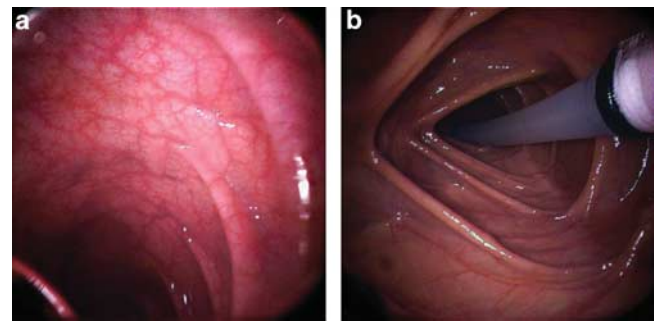


Figure 3. Image quality of the Invendo SC20. (a) Endoscopic image of the colonic mucosa; (b) full lumen view on retroflexion.

to check the resection site and treat possible bleeding via conventional colonoscopy; minor postpolypectomy bleeding was successfully treated using hemoclips. There was no other in-procedure adverse event. At follow-up at 24 h and 7 days, no adverse events were detected.

DISCUSSION

We demonstrated that a computer-assisted therapeutic colonoscope controlled by means of a handheld unit could be advanced to the cecum in a high percentage of cases (>98%) with very few of the paid volunteers (<5%) requiring sedation. Furthermore, experienced colonoscopists could successfully and safely use the device in screenees after minimal bench training. Finally, there were no complications in this small number of patients. Thus, the device appears promising as a means of providing unsedated screening colonoscopy. The extreme flexibility of the device suggests a low-risk profile, and the easy operation by joystick suggests that nonspecialists could learn to operate the device, although safety profile and operation with nonspecialists remain to be demonstrated. The device is disposable that confers an advantage in situations where reprocessing methods are suboptimal and/or in countries where there are principal objections to endoscope reprocessing (9,10).

Compared with the times reported from expert centers in conventional colonoscopy, the Invendo SC20 takes longer to reach the cecum, withdrawal is slower, and interventions such as



Figure 4. Polypectomy performed with the Invendo SC20.

polypectomy (from our anecdotal impression) take longer to perform. Future versions of the device should improve performance in these respects. Indeed, insertion times decreased from 24 min in the first study of the device (8) to 15 min in this study. In addition, experience appears to improve performance, as the endoscopists with greater experience tended to have shorter insertion times. Experience may also improve the speed for performing polypectomy, as none of the examiners has yet carried out large numbers of polypectomies. The marked flexibility of this device allows for passing of the endoscope keeping the natural anatomical shape of the large bowel without straightening of the endoscope and the colon. In situations where the bowel shape is grossly modified or the colon is rigid (excessive scarring after previous surgery, diverticular disease, and so on) we do not have enough experience with the Invendo SC20. On the other hand, such a situation may also require use of thinner or more flexible endoscopes in the conventional setting. Almost 25% of our screenees had previous pelvic surgery without any difficulties in passage.

The low proportion of screenees in our study that required sedation could reflect that they were paid volunteers, although they were told they could get sedated if required. To prove a reduced sedation rate in comparison with conventional colonoscopy would require a truly comparative, preferentially randomized, and blinded study; the results of this pilot study may be used as hypothesis generating for such a study. Use of water instillation in about half of the cases and CO₂ in all cases may also have made colonoscopy easier (11–13). In addition, the use of sedation for endoscopic procedures varies widely by country (14,15). In countries such as the United States, where nearly all those undergoing colonoscopy are sedated, the initial evaluation of the Invendo SC20 might best be performed in people who are better candidates for scheduled, unsedated conventional colonoscopy. These individuals are typically older, male, highly educated, have no abdominal pain, and have low anxiety levels (16).

The optics of the current device utilize a complementary metal-oxide-semiconductor (CMOS) chip, and although the image resolution allowed recognition of a number of polyps that was in line with expectations, the performance of the device compared with colonoscopes with high resolution or high definition optics (17,18) has not been evaluated. In general, several factors may have contributed to the fact the adenoma rate was slightly lower

than known from the German screening colonoscopy registry (~20–25%) (http://www.zi-berlin.de/cms/fileadmin/images/content/PDFs_all/Darmkrebsfrueherk_Bericht.pdf). However, it is our impression that there is no principal limitation of the Invendo SC20 with regard to adenoma detection. Furthermore, the low case number and the fact that adenoma detection was not an explicit study aim make conclusions about the diagnostic capability of the new scope impossible.

In summary, we demonstrated that a computer-assisted colonoscope controlled with a handheld unit could be advanced to the cecum in a high percentage of cases. Very few patients needed sedation. The device warrants additional investigation as a means of providing screening colonoscopy.

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CONFLICT OF INTEREST

Guarantor of the article: Thomas Rösch, MD.

Specific author contributions: All four authors performed and documented the examinations; S.G. and N.H. collected and analyzed data, and paper writing was by T.R. and D.K.R.

Financial support: Invendo Medical supported study performance by providing instruments and all technical support as well as covering costs for study registration at Ethics Committee as well as honoraria to volunteers and statistician. Data collection after each colonoscopy by company representatives was counterchecked by examiners. All colonoscopy and histopathology reports were reviewed by authors (S.G. and N.H.).

Potential competing interests: The investigators hold consultant contracts with Invendo Medical, the manufacturer of the SC20 colonoscope, the device under investigation in this study.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Colonoscopy has been incorporated into colorectal cancer screening.
- ✓ Take-up of screening colonoscopy is limited in population.

WHAT IS NEW HERE

- ✓ Colonoscope with “inverted sleeve” propulsion mechanism.
- ✓ Electrohydraulic bendable tip controlled with handheld control.
- ✓ Reducing the need for sedation.
- ✓ Single-use colonoscope.

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