Comparison of adenoma detection and miss rates between a novel balloon colonoscope and standard colonoscopy: a randomized tandem study

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Background and study aims: Although colonoscopy is the "gold standard" for colorectal cancer screening, a significant number of adenomas are still missed during standard colonoscopy, often because they are hidden behind colonic folds and flexures. The aim of this study was to assess the ability of a novel balloon colonoscope (G-EYE endoscope; Smart Medical Systems, Ra'anana, Israel) to increase adenoma detection and reduce the miss rate compared with standard colonoscopy.

Patients and methods: This was a multicenter, randomized, prospective, controlled study in patients (age ≥ 40 years) undergoing colonoscopy for screening or diagnostic work-up (including surveillance). Patients underwent same-day, back-to-back tandem colonoscopy. Patients in Group A underwent standard colonoscopy followed by balloon colonoscopy, and patients in Group B underwent balloon colonoscopy followed by the standard technique. The adenoma detection and miss rates were compared between the two colonoscopy procedures.

Results: A total of 126 patients were enrolled and randomized into Group A (n = 60) or Group B (n = 66). The adenoma miss rate of balloon colonoscopy was significantly lower than that of standard colonoscopy (7.5 % vs. 44.7 %; $P = 0.0002$). The detection of additional adenomas by balloon colonoscopy was significant (81.0 %; P = 0.0002), in particular, the relative amount of adenomas detected in the ascending colon by balloon colonoscopy was 41 % versus 14 % for standard colonoscopy.

Conclusions: A novel balloon colonoscopy technique detected significantly more adenomas than standard colonoscopy, and missed fewer adenomas. Balloon colonoscopy has the potential to increase the effectiveness of colorectal cancer screening and surveillance colonoscopy.

Introduction

Adenomatous polyp is the most common neoplasm found during screening for colorectal cancer (CRC). Removal of such adenomas during colonoscopy is known to prevent CRC, and is the standard of care in CRC prevention and early detection [1,2]. However, a significant number of polyps and adenomas (typically 20 %–30 %) are missed during routine colonoscopy [3–5]. Reasons for missing polyps during colonoscopy include the location of polyps on the proximal aspect of colonic folds and flexures [6,7], and insufficient endoscopic technique [8,9]. This high number of missed polyps could explain the high incidence of interval cancer [10, 11], and motivates both gastroenterologists and the device industry to seek better colonoscopy clinical outcomes for the benefit of patients and the screened population.

One approach being pursued is the improvement of colonoscopy techniques and practice, while continuing to utilize existing equipment. Such practices include increasing the inspection time during withdrawal [12], and adding retroflexed endoscope withdrawal in the ascending colon in order to examine behind the haustral folds [13]. Utilization of high definition optics has also demonstrated a lower miss rate [14]. Occasional mechanical stretching of colonic folds during endoscope withdrawal by a plastic cap mounted onto the tip of a standard colonoscope has shown mixed results in the improvement of polyp detection [15,16]. Another novel approach being explored is the use of rearward viewing capability that enables inspection of the proximal aspect of folds and flexures. The Third-Eye Retroscope (Avantis Medical Systems, Sunnyvale, California, USA) employs a retroflexed optical catheter introduced through the colonoscope instrument chan-

nel [17], whereas the full spectrum endoscopy system (FUSE; EndoChoice, Inc., Alpharetta, Georgia, USA) employs a stand-alone colonoscope utilizing three cameras. One camera provides the forward view on a central screen, while the other two cameras provide a side-view on two additional screens [18].

A particular interest is drawn to polyps and adenomas missed in the right colon and, more specifically, in the ascending colon. Studies have shown that a large number of adenomas are missed in the right colon [11,19,20], and that while 15%–19% of the adenomas and polyps are detected in the ascending colon, up to 55% of the missed CRC incidents are located in the ascending colon [19,21–23]. An essential qualification criterion for a new colonoscopy technique or technology would thus be its ability to increase the detection of adenomas in the right colon.

A novel device has been introduced (G-EYE endoscope; Smart Medical Systems, Ra'anana, Israel), which aims to enhance detection capabilities during colonoscopy. The device consists of a conventional colonoscope onto which a unique balloon has been permanently integrated. Withdrawal of the colonoscope with the balloon partially inflated centralizes the optical image and flattens colonic folds, thereby providing enhanced visualization of the colon.

The aim of this study was to compare the adenoma detection and miss rates between the new balloon colonoscope and a standard colonoscope.

Patients and methods

Study design

The study was designed as a multicenter study, where patients were randomized to one of two groups, and underwent same-day, back-to-back tandem colonoscopy (i.e. colonoscopy was followed immediately by the other procedure, performed by the same endoscopist during the same session). Patients randomized to Group A underwent standard colonoscopy followed by balloon colonoscopy, and patients randomized to Group B underwent balloon colonoscopy followed by the standard procedure. In this design, each patient serves as their own reference for determining adenoma detection but the two groups are independent of each other. Reversing the order in Group B allowed detection rates with standard colonoscopy to eliminate the second-pass effect, which is often observed in tandem colonoscopy studies. The balloon colonoscope and standard colonoscope used were the same models respectively for all procedures in order to eliminate endoscope-related or optics-related distortion of results.

During the procedures, detected polyps were measured by comparing them against open biopsy forceps of a known width. All polyps of size ≥2 mm were recorded, biopsied, removed, and sent for histological evaluation. Adenomas were classified by size, as "diminutive" (2–5 mm), "small" (6–9 mm), or "large" (≥10 mm). Histology results were reported back to the colonoscopist. For the purpose of the study, polyps classified as advanced adenoma, nonadvanced adenoma, and serrated polyps (including sessile serrated adenoma/polyp, traditional sessile adenoma, and hyperplastic polyp) were analyzed. An advanced adenoma was defined as an adenoma of size ≥10 mm, adenomas incorporating a villous component, or those with high grade dysplasia. Polyp location was also noted according to colonic segment. During the procedure, insertion time and total withdrawal time were measured and recorded.

Fig. 1 The G-EYE Balloon Colonoscope (Smart Medical Systems, Ra'anana, Israel).

Fig. 2 The NaviAid SPARK²C inflation system (Smart Medical Systems, Ra'anana, Israel).

Bowel preparation was performed according to standard guidelines for the medical center, and was graded according to the Ottawa Bowel Preparation Quality Scale Score [24]. Patients with a score ≥7 were excluded from the study. Conscious sedation was used for colonoscopy examinations, and included midazolam, fentanyl, propofol, or a combination thereof.

The study received institutional review board approval (G-EYE 15501). All patients signed an informed consent form prior to participating in the study. The study was registered at ClinicalTrials.gov (NCT01552200, March 2012).

Patients

Patients aged ≥40 years undergoing colonoscopy for screening or diagnostic work-up (including surveillance) were recruited for the study. Exclusion criteria included previous colonic resection, known inflammatory bowel disease, polyposis, suspected colonic stricture, diverticulitis or toxic megacolon, history of radiation therapy to abdomen or pelvis, pregnant or lactating women, those currently enrolled in another clinical study, routine Coumadin use, and recent (3 months) coronary ischemia or cerebrovascular accident.

The G-EYE balloon colonoscope

The G-EYE balloon colonoscope consists of a conventional colonoscope of any brand and model onto which a unique reusable balloon has been permanently integrated (**Fig. 1**). Three Pentax colonoscope models were used in the current study (EC-3890Li, EC-3890Fi2, EC-380LKP; Pentax Medical, Tokyo, Japan). The diameter of the balloon colonoscope, while the balloon is deflated, is only 0.1 mm larger than the conventional colonoscope. The resulting balloon colonoscope is used in the conventional manner, including standard interface with the standard video processor and reprocessing protocol. The balloon is inflated by a dedicated inflation system (NaviAid SPARK²C; Smart Medical Systems), which provides, beyond anchoring pressure, three levels of lower nonanchoring partial pressure (**Fig. 2**).

During balloon colonoscopy, the colonoscope is inserted with the balloon deflated, until the cecum is reached. Once the cecum has been reached and inspected, the balloon is inflated to partial pressure selected by the colonoscopist, typically level three,

which is the highest partial pressure level provided. The partial pressure level can be modified during withdrawal to accommodate specific anatomical characteristics, such as narrowing in flexures.

Withdrawal of the balloon colonoscope with the balloon partially inflated flattens colonic folds, centralizes the optical image, and reduces bowel slippage during withdrawal, thereby providing enhanced visualization of the colon. The fold-flattening action of the colonoscope during withdrawal brings the mucosal surface normally located behind haustral folds into the field of view of its forward-viewing optics. Therefore, polyp removal upon detection is immediate and straightforward. In addition, during polypectomy (or other interventional procedures), the balloon can be inflated to anchoring pressure, thereby stabilizing the colonoscope and expediting the interventional session.

Study end points

The study included a single primary end point of adenoma detection rate, on a per-lesion analysis, of the balloon colonoscope relative to that of standard colonoscopy; the unit of measurement was a lesion rather than a patient. The size distribution of polyps or adenomas and their location in the colon were also recorded. In addition, though not statistically powered in the present study, per-patient data, such as ADR (percentage of patients with at least one adenoma detected), insertion time, total withdrawal time, and bowel preparation score, were also recorded.

The per-lesion adenoma detection rate of balloon colonoscopy was calculated from the second-pass procedure in Group A (i.e. the number of additional adenomas detected over and above those detected by standard colonoscopy during the first-pass procedure). The adenoma miss rate of balloon colonoscopy was calculated following the second-pass procedure of standard colonoscopy over the balloon technique in Group B. It is well known that back-to-back colonoscopies performed using a standard colonoscope (same colonoscopist, same day) demonstrate additional adenoma detection in the second pass of up to 24%, even though the same technology is used in both examinations [3]. The randomization into two groups in which the standard and balloon procedures are performed in opposite order, allows elimination of the "same technology additional detection" effect in the second procedure, thus allowing the comparison of the additional adenoma detection of balloon colonoscopy in the second pass to its adenoma miss rate in the first pass. The ratio of balloon colonoscopy additional adenoma detection to the standard colonoscopy miss rate is a measure of the adenoma detection enhancement power of the novel technology, and can be used to compare results of different adenoma detection enhancement technologies in different studies on a common basis.

Randomization and blinding

Patients were randomized to "Group A" or "Group B," with 1:1 allocation and stratified by center (with a block size of 6), via a computer-generated randomization scheme created by SAS version 9.3 statistical software (SAS Institute, Cary, North Carolina, USA). Patients were enrolled by the study investigators and allocated to one of the study groups by opening one of the sequentially numbered, sealed envelopes. The colonoscopist was blinded to the allocation group until the patient entered the procedure room.

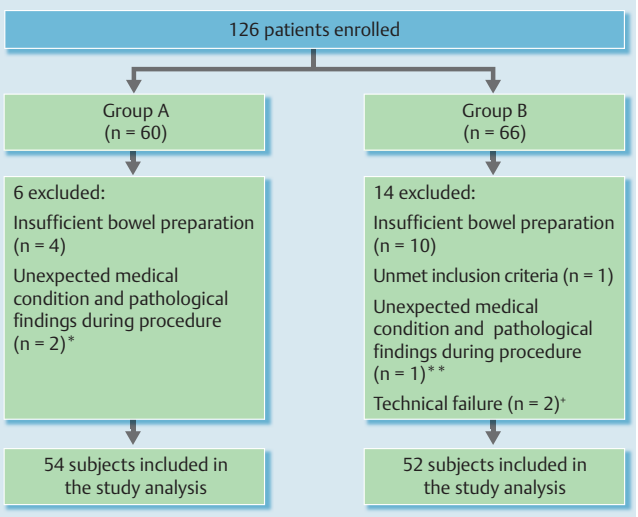

Fig. 3 Study outline. *Includes polyposis, and diverticulosis ,**includes stenosis, + In one procedure, the intermediate pressure level was not operated properly, and in another, the endoscope × 1.5 zoom was mistakenly activated during the procedure.

Statistical methods

The primary outcome measure of the study was the adenoma detection rate of balloon colonoscopy vs. standard colonoscopy, calculated as the number of additional adenomas detected during the second procedures for each group (this also gives an indication of first-procedure miss rates). Based on previous studies [15], a 30% adenoma miss rate was assumed for standard colonoscopy. In order to demonstrate a 10% adenoma miss rate when performing the balloon colonoscopy, a sample size of 63 adenomas per group were required to provide 80% power at a two-sided 5% level of significance. The null hypothesis of equal detection rates was tested using the chi-squared test. Assuming an average of 1 adenoma per patient, a total of 126 patients were required to ensure an adequate number of adenomas in the study.

Continuous variables were summarized by the mean and SD, and were compared using a two-sample *t* test (age) or a paired *t* test (for time comparisons). Categorical data were summarized by a count and percentage, and were compared using chi-squared tests or Fisher's exact test where applicable.

Statistical analyses were performed using SAS version 9.3 (SAS Institute). A *P* value of 0.05 or lower was considered to be statistically significant.

Results

A total of 126 patients were enrolled and randomized in the study between 31 July 2012 and 5 June 2013, of whom 20 were excluded from the study, mostly as a result of insufficient bowel preparation. Patients were recruited by four centers, three in Israel (Laniado Hospital, Netanya; Hadassah Medical Center, Jerusalem; Tel Aviv Sourasky Medical Center, Tel-Aviv), and one center in Germany (Marienkrankenhaus Frankfurt, Frankfurt).

The study outline, including details of dropouts, is provided in **Fig. 3**. In total, 106 patients completed the study, 54 in Group A and 52 in Group B. Screening was the main reason for undergoing colonoscopy (Group A 85.2%, Group B 94%). Baseline characteris-

Table 1 Baseline characteristics and reason for undergoing colonoscopy.

	Group A[1] (n = 54)	Group B[2] (n = 52)
Baseline characteristics		
Sex, n (%), females	29 (53.7)	31 (59.6)
Age, mean ± SD, years	55.4 ± 7.9	57.9 ± 7.8
Indication for colonoscopy, n (%)		
Screening[3]	46 (85.2)	49 (94.2)
Surveillance[4]	1 (1.8)	2 (3.9)
Diagnostic work-up	7 (13.0)	1 (1.9)

[1] Group A: standard colonoscopy followed by balloon colonoscopy.
[2] Group B: balloon colonoscopy followed by standard colonoscopy.
[3] Positive fecal occult blood test was included within the screening patients and accounts for one patient in each group. Of the screening patients, a family history of colorectal cancer (CRC) was present in one patient in Group A and two patients in Group B.
[4] All surveillance patients had past CRC.

Table 3 Histology results.

Histology result	Group A[1] (n = 54)		Group B[2] (n = 52)	
	1st pass	2nd pass	1st pass	2nd pass
Advanced adenoma	3	1	10	0
Nonadvanced adenoma	17	15	26	3
Serrated polyps				
SSA/P	1	1	1	0
Hyperplastic polyp	6	8	10	0
TSA	0	0	0	0

SSA/P, sessile serrated adenoma/polyp.
TSA, traditional sessile adenoma.
[1] Group A: standard colonoscopy followed by balloon colonoscopy.
[2] Group B: balloon colonoscopy followed by standard colonoscopy.

tics and indications for colonoscopy are presented in **Table 1**. No statistically significant differences were found between the groups with respect to age ($P = 0.1116$) or sex ($P = 0.5393$).

Per-lesion adenoma detection and miss rates

In Group A (standard colonoscopy followed by balloon colonoscopy), 21 adenomas were detected by standard colonoscopy and 17 additional adenomas were detected by subsequent balloon colonoscopy. This result represents an 81.0% additional adenoma detection (17/21) by balloon colonoscopy over and above the standard procedure. The adenoma miss rate of standard colonoscopy was therefore 44.7% (17/38) (**Table 2**).

In Group B (balloon colonoscopy followed by standard colonoscopy), 37 adenomas were detected by balloon colonoscopy and 3 additional adenomas were detected by the subsequent standard technique. This result represents an adenoma miss rate of 7.5% (3/40) for balloon colonoscopy (**Table 2**).

The balloon colonoscopy adenoma miss rate was significantly lower than that of standard colonoscopy (sixfold lower; $P = 0.0002$) (**Table 2**). The ratio balloon colonoscopy additional adenoma detection to the standard colonoscopy miss rate was 10.8 (81%/7.5%).

Adenoma size

In Group A, the additional adenomas detected by balloon colonoscopy stratified by size were 92.3% (12/13) for diminutive adenomas, and 66.7% (4/6) and 50% (1/2) for small and large adenomas, respectively. In Group B, standard colonoscopy detected 14.3% (3/21) additional diminutive adenomas, and no additional small or large adenomas. These results translate into a balloon colonoscopy miss rate of 12.5% for diminutive adenomas, and 0% for small and large size adenomas (**Table 2**).

Histology results

Histology results are provided in **Table 3**. Of the 17 adenomas missed by standard colonoscopy in the first pass, one was an advanced adenoma. The balloon colonoscope detected 10 advanced adenomas in its first pass, accounting for 27.0% (10/37) of the total adenomas detected by balloon colonoscopy in Group B. No advanced adenomas were missed by the balloon colonoscope. All adenomas detected in the study were of low grade dysplasia.

Adenomas in the ascending colon

Adenomas were allocated according to colon segments (**Table 4**). In Group A, of the 17 additional adenomas detected by the balloon colonoscope in its second pass, 35.3% were found in the ascending colon, adding 6 adenomas to the 3 adenomas originally detected in the ascending colon by the standard colonoscopy first-pass procedures. In Group B, 37 first-pass adenomas were detected by the balloon colonoscopy. The second-pass standard procedure found two additional adenomas in the ascending (right) colon and one adenoma in the descending (left) colon. Furthermore, the balloon colonoscope detected 40.5% (15/37) of its first-pass adenomas in the ascending colon. When considering the common classification of "right colon adenomas" as adenomas located proximal to the splenic flexure [25], the second-

Table 2 Per-lesion analysis.

Findings	Group A[1]				Group B[2]			
	Standard (1st pass)	Balloon (2nd pass)	Balloon additional detection, %	Standard miss rate, %	Balloon (1st pass)	Standard (2nd pass)	Standard additional detection, %	Balloon miss rate, %
All adenomas	21	17	81.0[3]	44.7[3]	37	3	8.1[3]	7.5[3]
Diminutive (2 – 5 mm)	13	12	92.3	48.0	21	3	14.3	12.5
Small (6 – 9 mm)	6	4	66.7	40.0	6	0	0	0
Large (≥ 10 mm)	2	1	50.0	33.3	10	0	0	0

[1] Group A: standard colonoscopy followed by balloon colonoscopy.
[2] Group B: balloon colonoscopy followed by standard colonoscopy.
[3] $P = 0.0002$.

Table 4 Adenomas by location.

Colon segment	Group A[1]		Group B[2]	
	1st pass	2nd pass	1st pass	2nd pass
Cecum	2	1	0	0
Ascending colon	3	6	15	2
Hepatic flexure	1	2	4	0
Transverse colon	6	0	2	0
Splenic flexure	0	0	1	0
Descending colon	1	3	1	1
Sigmoid colon	3	2	11	0
Rectum	5	3	3	0
Total	21	17	37	3

[1] Group A: standard colonoscopy followed by balloon colonoscopy.
[2] Group B: balloon colonoscopy followed by standard colonoscopy.

Table 5 Colonoscopy quality parameters.

Quality indicators	Standard	Balloon	*P* value
Cecal intubation, %	100	100	N/A
Bowel preparation, mean ± SD[1]	3.17 ± 1.80	3.38 ± 1.71	0.5538[2]
ADR, %[3]	25.9	40.4	0.1153[4]
Total withdrawal time, mean ± SD, minutes	6.3 ± 2.6	8.3 ± 3.4	<0.0001[5]
Serious adverse events	None	None	N/A

N/A, not applicable.
[1] Bowel preparation according to the Ottawa Bowel Preparation Quality Scale [24].
[2] Chi-squared test.
[3] ADR was calculated based on the first pass per technology.
[4] Two-sample *t* test.
[5] Paired *t* test.

Table 6 Tandem colonoscopy studies.

Reference	2nd-pass device, company	Standard colonoscopy miss rate, %
Rex et al., 1997 [3]	Standard colonoscope	24
Hewett & Rex, 2010 [15]	Cap-fitted colonoscope (Olympus)	33
Leufkens et al., 2011 [17]	Third Eye Retroscope (Avantis Medical Systems)	31.4
Gralnek et al., 2014 [26]	FUSE Colonoscope (EndoChoice)	41
Halpern et al., 2014 [current study]	G-EYE Endoscope (SMART Medical Systems Ltd.)	44.7

pass additional right-colon adenomas detected by the balloon colonoscope totalled 52.9% (9/17) of all additional adenomas. Furthermore, according to this classification, the balloon colonoscope first-pass right-colon adenomas constituted 56.8% (21/37) of all first-pass adenomas in Group B.

Per-patient ADR

In the first-pass procedure in Group A, standard colonoscopy detected adenomas in 14 of the 54 patients, giving an ADR of 25.9% (14/54). The second-pass balloon colonoscopy procedures detected additional adenomas in 10 patients, 3 of whom had no adenomas detected by the previous standard procedure. In the first-pass procedures in Group B, the balloon colonoscope detected adenomas in 21 of the 52 patients, giving an ADR of 40.4% (21/52). The second-pass standard procedure detected additional adenomas in two patients, both of whom had other adenomas found by the previous balloon colonoscopy. The ADR of balloon colonoscopy was considerably higher than that of standard colonoscopy (40.4% vs. 25.9%; $P=0.115$), exhibiting a 56.0% increase in ADR over standard colonoscopy.

Additional results

Time to cecal intubation was similar using the balloon colonoscopy vs. the standard procedure (5.2 ± 2.9 vs. 5.3 ± 3.1 minutes; $P=0.8205$). However, total withdrawal time was longer for balloon colonoscopy (8.3 ± 3.4 vs. 6.3 ± 2.6 minutes; $P<0.0001$). Not counting the one Group B patient who was excluded for medical reasons (stenosis), cecal intubation was 100% for both groups. No serious or moderate adverse events occurred in any of the procedures. One case of minor abdominal pain was reported in Group B.

Split dosing was used for bowel preparation in all patients.

Colonoscopy quality parameters including cecal intubation, bowel preparation, ADR, total withdrawal time, and serious adverse events are shown in **Table 5**.

Discussion

The G-EYE balloon colonoscope employs a new concept for increasing detection yield and reducing the miss rate in colonoscopy. Published literature reports substantial polyp and adenoma miss rates with standard colonoscopy. In particular, a randomized, tandem study presenting two consecutive same-day standard colonoscopies performed by different endoscopists exhibited an adenoma miss rate of 24% [3]. It has been suggested that the actual miss rate might be even higher than reported in tandem studies, as the same technology was used in both the first and second colonoscopies, and lesions behind folds or flexures could be missed during both procedures [3,6,26]. In another same-day, tandem study, comparing standard colonoscopy with cap-fitted colonoscopy, a standard colonoscopy adenoma miss rate of 31.4% was demonstrated [13]. A multicenter, randomized tandem study comparing standard colonoscopy with combined forward and rearward viewing Third-Eye Retroscope colonoscopy, demonstrated a 33% adenoma miss rate for standard colonoscopy [17]. A recently published study of the FUSE colonoscope reported an adenoma miss rate of 41% for standard colonoscopy [26]. In the current randomized, multicenter, tandem colonoscopy study, a standard colonoscopy adenoma miss rate of 44.7% was recorded, which is comparable with results found in the FUSE study. **Table 6** presents a summary of tandem studies of the various technologies described herein, including the miss rates for standard colonoscopy in these studies.

It is known that there is a correlation between colonoscope withdrawal times and rates of neoplasia detection. Colonoscopy withdrawal times of >6 minutes are associated with a significantly higher ADR compared with withdrawal times of <6 minutes [27]. Therefore, it may be hypothesized that the shorter withdrawal time of standard colonoscopy compared with balloon colonoscopy may have had an influence on the miss rate of the standard procedure. Results from published tandem studies indicate that diminutive polyps (<5 mm) are more commonly missed than small or large polyps [3,15,26]. It is also notable in these studies that the miss rate of diminutive polyps is higher than

the total miss rate, and the miss rate of standard colonoscopy in the current study is aligned with these results. As the miss rate of standard colonoscopy was relatively high in the current study compared with other technologies, the miss rate for the various adenoma sizes is also regarded as relatively high compared with current technologies. The study also exhibited sizable additional adenoma detection (81.0%) and a significantly lower adenoma miss rate (7.5%) of balloon colonoscopy compared with the standard procedure. When stratifying findings according to adenoma size, the balloon endoscope in its second-pass examination detected small and large adenomas that had been missed by the first-pass standard procedure, whereas it missed only diminutive adenomas in its first pass. The rate of additional adenomas detected by the balloon colonoscope was 92.3% for diminutive adenomas (2–5 mm) vs. 66.7% for small adenomas (6–9 mm) and 50.0% for large adenomas (≥10 mm). These results are aligned with comparable data for adenoma detection enhancement technologies [15,26]. A larger sample size is required in order to provide statistical significance for the additional detection rate relative to adenoma size distribution. In any case, according to the United States guidelines for colonoscopy surveillance, detection of diminutive and small adenomas (<10 mm) has an impact on the surveillance interval [1], which demonstrates the clinical impact of increased detection by balloon colonoscopy.

Of particular interest was the enhanced detection of adenomas in the ascending colon by balloon colonoscopy. The balloon colonoscope detected 35.3% of its second-pass and 40.5% of its first-pass adenomas in the ascending colon. Studies have shown that the distribution of detected adenomas in the ascending colon is 15%–19%, and that 42.4%–55% of missed CRC incidents develop in the ascending colon [19,21–23]. It is known that interval cancer occurs more often in the right colon, and more specifically in the ascending colon [19,21]. Furthermore, right-colon adenomas are more likely to rapidly develop into cancer than left-colon adenomas [19,20,28,29], and in recent years there has been an increase in right-colon cancer and a decrease in left-colon cancer [20,30]. Taken together, these studies express the importance of increasing adenoma detection in the ascending colon, a location in which standard colonoscopy appears to miss a relatively high percentage, probably as a result of the anatomical structure of the right colon, which includes prominent folds [22]. The current study suggests particularly high adenoma detection by the balloon colonoscope in the ascending colon, and this warrants further investigation. The high adenoma detection yield of balloon colonoscopy in the ascending colon may also serve as validation of the fold-flattening capability of this technique.

The study was statistically designed to perform a per-lesion analysis. However, results also suggest per-patient enhanced performance of balloon colonoscopy (56% increase in per-patient ADR over standard colonoscopy), which needs to be investigated further, as the current study was not powered to establish statistical significance on a per-patient basis.

Colon intubation by the balloon colonoscope showed insertion times similar to the standard procedure, with 100% cecal intubation, and full capability to perform ileal intubation and rectal retroflexing when needed. The longer total withdrawal time with balloon colonoscopy (2 minutes longer on average), is not likely to be considered significant for the endoscopy room workflow and day-to-day endoscopy practice, especially given that approximately twice the number of polypectomies would be performed compared with standard colonoscopy.

Unlike the optically based retro-viewing Third-Eye Retroscope [17] and FUSE Colonoscope [18], the G-EYE system employs a mechanical fold-straightening technique for increasing colonoscopy detection and reducing the adenoma miss rate. In contrast to mechanical fold-straightening accessories such as in cap-fitted colonoscopy [15,16], where the fold straightening is associated with the tip of the colonoscope carrying an add-on accessory, the balloon colonoscope flattens the colon folds in a continuous and systematic manner throughout the entire colon, while centralizing the endoscopic image and preventing bowel slippage during withdrawal and interventions.

Potential limitations of the study should be addressed. First, the patient population was not large enough to establish per-patient clinical outcomes with statistical significance. Although the results appeared promising, per-patient parameters such as ADR and false-negative colonoscopy rates should be investigated further. Second, the two colonoscopies were performed by the same colonoscopist who was not blinded to the technology being used, and this may induce an unintentional bias towards one of the two technologies; it is possible that one or more of the study colonoscopists may have favored the balloon technology and may not have made equal effort to detect polyps during both procedures. Third, total withdrawal time of the balloon colonoscope was approximately 2 minutes longer compared with the standard procedure. The longer withdrawal time is attributed to the additional polypectomies performed during the balloon colonoscopy procedures. Therefore, there are no major differences between the actual withdrawal times of the two procedures. Fourth, 20 patients dropped out from the study analysis, mostly because of insufficient bowel preparation. This may be attributed to the requirement for high quality bowel preparation in the study. It should be noted that patients were randomly assigned to each group, therefore eliminating potential bias. Fifth, a high percentage of screening procedures and the relatively young age of patients resulted in a cohort profile that is different from those presented in other colonoscopy studies, which may render a comparison of the studies difficult.

In conclusion, this prospective, multicenter, randomized, controlled, tandem study, found that balloon colonoscopy was significantly superior to standard colonoscopy in terms of adenoma detection. The mechanical fold-flattening approach employed by the device enabled substantial enhancement in the clinical outcome of colonoscopy, while still using standard and familiar forward-viewing equipment and endoscopic technique. This solution for increasing colonoscopy detection yield has the potential to fit into the daily practice of endoscopy centers.

Study registered at ClinicalTrials.gov (NCT01552200).

Competing interests: Professor Halpern is a consultant for Smart Medical Systems Ltd. (Ra'anana, Israel). The study was supported by Smart Medical Systems Ltd.

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Endoscopy 2014-11161 "140", 11.2.15, seitenweise