



Missed adenomas with behind-folds visualizing colonoscopy technologies compared with standard colonoscopy: a pooled analysis of 3 randomized back-to-back tandem colonoscopy studies

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Background and Aims: The Third Eye Retroscope, Full Spectrum Endoscope (FUSE), and EndoRings devices have been shown to reduce overall adenoma miss rates. We evaluated the characteristics of adenomas and patient subgroups for which these behind-folds visualizing technologies mostly reduce adenoma miss rates.

Methods: Data of 3 multicenter randomized trials (NCT01044732, NCT01549535, NCT01955122) were combined. Patients underwent same-day, back-to-back tandem examinations with standard colonoscopy and Third Eye Retroscope, FUSE, or EndoRings colonoscopy, respectively. Adenoma miss rates were stratified by adenoma characteristics and patient subgroups.

Results: A total of 650 patients (60% male, mean age 57.5 years, standard deviation 9.7 years) were included; 330 patients underwent behind-folds visualizing colonoscopy first, and 320 patients underwent standard colonoscopy first. Regarding adenoma characteristics, adenoma miss rates were significantly ($P < .001$) lower with behind-folds visualizing technologies compared with standard colonoscopy for proximal (14% vs 38%) and distal (15% vs 35%), ≤ 5 mm (17% vs 38%), 6 to 9 mm (8% vs 44%), sessile (16% vs 37%), flat (9% vs 52%; $P = .014$), and tubular (15% vs 38%) adenomas and sessile serrated polyps (7% vs 50%; $P = .039$) but were not statistically significantly ($P > .05$) different for ≥ 10 mm, pedunculated, (tubulo-)villous, and advanced adenomas. Regarding patient subgroups, adenoma miss rates were significantly ($P \leq .020$) lower with behind-folds visualizing technologies for patients ≥ 50 years, both sexes, and all indications.

Conclusions: Behind-folds visualizing colonoscopy reduces miss rates for 1 to 9 mm adenomas in the entire colon, whereas no advantage was found for ≥ 10 mm and advanced adenomas. Whether increased detection and removal of < 10 mm adenomas also reduces colorectal cancer incidence and mortality remains to be determined. Future research is needed to determine which colonoscopy technology would be most beneficial for which patient or endoscopist. (Gastrointest Endosc 2017;86:376-85.)

(footnotes appear on last page of article)

Colonoscopy is the criterion standard for the detection and removal of polyps and adenomas in the colorectum.¹⁻⁴ However, a significant number of polyps and adenomas are missed when standard colonoscopy is used,⁵⁻⁸ with an estimated overall adenoma miss rate of 20% to 25% according to tandem colonoscopy studies with standard

colonoscopes.⁸ Because missed adenomas might result in interval colorectal cancer (CRC),⁹ reducing adenoma miss rates may ultimately reduce CRC-related mortality.¹⁰

Several factors are associated with adenoma miss rates, including difficulty to visualize adenomas behind colonic folds and in inner curves of flexures,^{11,12} flat lesions,⁵ lesions located in the proximal colon,^{13,14} and some others.¹⁵ Various endoscopic technologies have been developed to increase the detection rate of adenomas and early cancers by improving visualization behind folds and curves. Other improvements include image-enhancing technologies to improve detection of flat lesions such as high-definition resolution, narrow-band imaging, and water infusion.¹⁶



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Figure 1. Three behind-folds visualizing colonoscopy technologies. **A**, the Third Eye Retroscope is advanced through the biopsy channel and provides a 180° retroflexed view on a second screen during withdrawal. **B**, The Full Spectrum Endoscope has 3 imagers and light emitting diode groups positioned at the front and at both sides of the distal tip of the colonoscope, providing a 330° view on 3 contiguous monitors. **C**, The EndoRings device is mounted on the distal tip of the colonoscope and consists of silicon circular wings that flatten the colonic folds during withdrawal.

TABLE 1. Demographic variables, indication for colonoscopy, and bowel preparation

	TERRACE study		FUSE study		CLEVER study		Pooled analysis	
	Standard colonoscopy first (N = 173)	Third Eye Retroscope first (N = 176)	Standard colonoscopy first (N = 88)	Full Spectrum Endoscope first (N = 97)	Standard colonoscopy first (N = 59)	EndoRings colonoscopy first (N = 57)	Standard colonoscopy first (N = 320)	Behind-folds visualizing colonoscopy first (N = 330)
Age, median (range), y	57 (26-83)	58 (23-79)	56 (22-70)	57 (21-70)	62 (40-74)	56 (40-75)	58 (22-83)	57.5 (21-79)
Female sex, no. (%)	63 (36%)	54 (31%)	46 (52%)	55 (57%)	29 (49%)	16 (28%)	138 (43%)	125 (38%)
Indication, no. (%)	N = 171*		N = 175*				N = 318*	N = 329*
Screening	91 (53%)	86 (49%)	53 (60%)	50 (52%)	17 (29%)	17 (30%)	161 (51%)	153 (47%)
Surveillance	36 (21%)	51 (29%)	16 (18%)	20 (21%)	19 (32%)	21 (37%)	71 (22%)	92 (28%)
Diagnostic workup	44 (26%)	38 (22%)	19 (22%)	27 (28%)	23 (39%)	19 (33%)	86 (27%)	84 (26%)
Bowel preparation score† median (interquartile range)	Ottawa scale		Ottawa scale		Boston scale		NA	NA
	4 (3-5)	4 (3-5)	3 (1.25-5.75)	3 (0-5.5)	8 (7-9)	8 (7-9)		

CLEVER, Multicenter, randomized, tandem evaluation of EndoRings colonoscopy; FUSE, Full Spectrum Endoscope; TERRACE, Third Eye Retroscope randomized clinical evaluation; N, number of patients; NA, not applicable.

*For 2 patients in the standard colonoscopy first group and 1 patient in the Third Eye Retroscope first group of the TERRACE study, the indication is missing.

†TERRACE¹⁷ and FUSE study¹⁸ reported bowel preparation scores according to the Ottawa bowel preparation scale (possible scores from 0-14 with lower scores indicating better preparation). The CLEVER study¹⁹ reported bowel preparation scores according to the Boston bowel preparation scale (possible scores ranging from 0-9, with higher scores indicating better preparation).

Three novel technologies aiming to optimize visualization behind colonic folds are the Third Eye Retroscope (Avantis Medical Systems Inc, Sunnyvale, Calif), Full Spectrum Endoscope (FUSE) colonoscope (EndoChoice Inc, Alpharetta, Ga), and the EndoRings device (EndoAid Ltd, Caesarea, Israel) (Fig. 1). These behind-folds visualizing technologies were recently evaluated in 3 independent, international, multicenter, randomized, back-to-back, tandem colonoscopy trials, and all 3 have been shown individually to significantly reduce polyp and adenoma miss rates compared with standard colonoscopy.¹⁷⁻¹⁹

The first version of the Third Eye Retroscope is inserted through the biopsy channel of the colonoscope and pro-

vides a retrograde view on a second screen during withdrawal of the colonoscope (Fig. 1A). In a multicenter randomized back-to-back tandem trial, the net additional percentage of adenomas detected with the Third Eye Retroscope was 23%.¹⁷

The FUSE colonoscope has 3 imagers and light-emitting diode groups, which are positioned at the front and at both sides of the distal tip of the colonoscope (Fig. 1B). The video images are shown on 3 contiguous monitors, creating a 330° field of view. The adenoma miss rate of FUSE has been found to be significantly lower than that of standard colonoscopy (7% vs 41%).¹⁸ However, a recent parallel randomized trial did not find differences

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