

## Gastrointestinal Imaging

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## Abbreviation:

CI = confidence interval

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## Colorectal Polyps: Detection with Low-Dose Multi-Detector Row Helical CT Colonography versus Two Sequential Colonoscopies<sup>1</sup>

**PURPOSE:** To prospectively evaluate the diagnostic accuracy of low-radiation-dose computed tomographic (CT) colonography for detection of colorectal polyps by using two sequential colonoscopies, with the second colonoscopy as the reference standard.

**MATERIALS AND METHODS:** The study was local ethics committee approved, and all patients gave written informed consent. Colonographic images were acquired by using a low-dose multi-detector row CT protocol (effective milliamperesecond setting, 10 mAs). Three observers interpreted the CT colonographic data separately and independently by using a two-dimensional technique. Initial conventional colonoscopy was performed by an endoscopist unaware of the CT colonographic findings. Second colonoscopy performed within 2 weeks by a colonoscopist aware of both the CT colonographic and the initial colonoscopic findings served as the reference standard. The sensitivities of CT colonography and initial colonoscopy were calculated on a per-polyp and a per-patient basis. Specificities and positive and negative predictive values also were calculated on a per-patient basis.

**RESULTS:** Eighty-eight patients underwent CT colonography and initial conventional colonoscopy on the same day. Per-polyp sensitivities were 62% and 83% for CT colonography and initial colonoscopy, respectively. Sensitivities for detection of polyps 6 mm in diameter or larger were 86% and 84% for CT colonography and initial colonoscopy, respectively. Initial colonoscopy failed to depict 16 polyps, six of which were correctly detected with CT colonography. For identification of patients with polyps 6 mm in diameter or larger, CT colonography and initial colonoscopy, respectively, had sensitivities of 84% and 90%, specificities of 82% and 100%, positive predictive values of 70% and 100%, and negative predictive values of 91% and 95%.

**CONCLUSION:** Low-dose CT colonography compares favorably with colonoscopy for detection of colorectal polyps 6 mm in diameter or larger, with markedly decreased performance for detection of polyps 5 mm in diameter or smaller.

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Computed tomographic (CT) colonography is a rapidly evolving imaging procedure in which CT data sets are used to produce two- and three-dimensional images of the colon. In recent years, this examination has emerged as a valid diagnostic colorectal cancer test (1-8). A limitation of the current published data on CT colonography is that conventional colonoscopy was used as the reference standard. There is compelling evidence that conventional colonoscopy, even when meticulously performed by experienced endoscopists, has a substantial miss rate in the detection of polyps (9-13). The limitations of currently available colonoscopes may hamper the visualization of mucosa in the proximal aspects of folds, flexures, and valves (12).

In addition, some small polyps may be difficult to identify because of their size, flat morphologic features, and/or lack of color contrast with the surrounding mucosa (14). Although several techniques to reduce the miss rate of colonoscopy (ie, high-magnification chromoscopy with dye spraying [15,16], cap-fitted colonoscopy [17], and wide-angle colonoscopy [12]) have been proposed, to our knowledge none has reached widespread use thus far.

Owing to the use of an imperfect reference standard in studies reported in the CT colonographic literature, the diagnostic performance of CT colonography possibly is underestimated. Specifically, it has been recently demonstrated that, in several instances, CT colonography depicts polyps that have been missed at conventional colonoscopy (13). Thus, some of the false-positive findings at CT colonography could be false-negative findings at conventional colonoscopy (8,18).

The ideal validation of a test for the identification of colorectal polyps, either CT colonography or conventional colonoscopy, would involve direct comparison with the findings at pathologic examination of the entire large bowel—a study that is impossible to perform (11). A method to create an enhanced reference-standard examination—a so-called segmental unblinding—was proposed by Pineau et al (18) and subsequently adopted in two recent studies (5,6). This method involves the incremental revealing of the CT colonographic findings to the endoscopist during colonoscopy as the colonoscope is withdrawn segment by segment, after the endoscopist has recorded his or her own independent observations (19). Therefore, if a polyp is identified in a given segment at CT colonography and is not seen at the “first-look” colonoscopy, the endoscopist has to reexamine the segment to resolve the discrepancy. However, if the CT colonographic result is negative, no further colonoscopic evaluation is performed (18).

To our knowledge, no study to investigate the performance of CT colonography with use of two sequential colonoscopies had been performed before the current investigation. With this approach, after complete initial colonoscopic and CT colonographic examinations, a complete second colonoscopy is performed and serves as the reference standard. Thus, the purpose of our study was to prospectively evaluate the diagnostic accuracy of low-radiation-dose

multi-detector row helical CT colonography for the detection of colorectal polyps by using two sequential colonoscopies, with the second colonoscopy as the reference standard.

## MATERIALS AND METHODS

The study was approved by the local ethics committee of the University of Rome-La Sapienza and conducted between November 2002 and December 2003. Written informed consent was obtained from all patients after the purpose and protocol of the study had been fully explained to them. This study was performed in accordance with the Declaration of Helsinki principles (20).

Patient inclusion criteria included the following: average-risk colorectal cancer screening performed, family history of colorectal carcinoma, personal or family history of colorectal polyps, follow-up of an abnormal screening test result (ie, positive guaiac-based stool test, barium enema examination, or sigmoidoscopy result) performed, evaluation of hematochezia performed, change in bowel movement habits, weight loss, abdominal pain, and/or iron deficiency-related anemia. Exclusion criteria included the following: history of familial adenomatous polyposis or hereditary nonpolyposis cancer syndromes, prior colorectal surgery, suspected inflammatory bowel disease, acute diverticulitis or bowel obstruction, rejection for conventional colonoscopy or CT colonography for any reason, medical condition that precluded the use of bowel preparation, inability to give informed consent, and/or pregnancy. Each patient included in the study underwent CT colonography followed by initial colonoscopy on the same day and second colonoscopy 7–14 days (average, 9.2 days) later.

### CT Colonographic Technique

The study participants underwent colonic cleansing by drinking 2 L of polyethylene glycol electrolyte solution (Isocolan; Bracco, Milan, Italy) and 10 mg of bisacodyl (Dulcolax; Boehringer Ingelheim, Florence, Italy) the day before the scheduled examinations. Bisacodyl was used to reduce the amount of fluid ingested by the patient and thus improve patient compliance (21).

The CT colonographic examinations were performed with a multi-detector row helical CT scanner (Somatom Plus 4 Volume Zoom; Siemens Medical Systems, Forchheim, Germany) 3–6 hours before

initial colonoscopy. CT colonography was performed with the patient in the prone and supine positions after intravenous administration of 20 mg of hyoscine-*N*-butylbromide (Buscopan; Boehringer Ingelheim). With the patient in the left lateral decubitus position, the colon was gently insufflated with room air, with a rubber catheter placed in the rectum according to patient tolerance. To prevent air leakage from the anus, the rectal tube was subsequently clamped and left in situ during imaging.

First, with the patient in the prone position, a scout CT image was obtained to estimate the adequacy of colonic distention. Further air insufflation was performed when collapsed bowel segments were observed. Before supine imaging, the colon was insufflated with additional air, again according to maximal patient tolerance, and colonic distention was verified on a second scout CT image. Air insufflation was performed in all patients by the same nurse.

The CT examinations were performed by using the following low-dose protocol, which was previously optimized for the CT scanner used in the present study by Iannaccone et al (22): 4 × 2.5-mm section collimation (effective section thickness, 3.0 mm), 1.0-mm reconstruction interval, 17.5 mm/sec table speed, gantry rotation time of 0.5 seconds, 140 kV, and effective milliamperesecond setting of 10 mAs. The ensuing total weighted CT dose index for the combined prone and supine image acquisitions was 2.74 mGy (22). The acquisition time ranged from 14 to 20 seconds. A resident who was not involved in CT colonographic data evaluation documented any complication associated with CT colonography.

### CT Colonographic Image Analysis

Three gastrointestinal radiologists (R.I., C.C., F.M.), who were unaware of both the specific indications for CT colonography and the results of the initial colonoscopic examination, separately and independently reviewed each case directly on a dedicated workstation by using a software package with volume-rendering capabilities (Vitre; Vital Images, Plymouth, Minn). These observers had previously interpreted approximately 400 (R.I.), 200 (C.C.), and 100 (F.M.) CT colonographic cases with endoscopic correlation. The findings in each patient were prospectively recorded by the three observers before second colonoscopy was performed.

For image analysis, the observers were

asked to use a previously validated time-efficient technique (23,24). In brief, the initial analysis entailed reviewing magnified two-dimensional transverse CT images. When a suspected polyp was detected on the two-dimensional transverse CT images, coronal and sagittal CT images and three-dimensional endoluminal views were evaluated to confirm the finding. If no suspected polyp was identified at review of the transverse images, no further image analysis was performed. The presence, location, size, and morphologic features of all suspected polyps were documented. Polyps were measured on the transverse CT images by using an electronic ruler.

To specify the location of each polyp, the colon was divided into six segments: cecum, ascending colon and hepatic flexure, transverse colon and splenic flexure, descending colon, sigmoid colon, and rectum. With regard to morphologic features, all polyps were classified as pedunculated, sessile, or flat. Flat polyps were defined as those with a base at least twice as long as the height. Sessile polyps were those that did not meet the criteria to be classified as flat and did not have a stalk. Pedunculated polyps had an identifiable stalk. All polyps seen at CT colonography were photographed, and the colonographic images were stored in digital format. The image interpretation time for each CT colonographic examination was recorded with a stopwatch.

### Initial Conventional Colonoscopy

All colonoscopies were performed by one of two staff endoscopists (A.L., E.F.) with extensive and comparable colonoscopic experience (each having interpreted more than 5000 cases prior to this study). Both endoscopists were unaware of the CT colonographic findings. Two endoscopists participated in the study because the sensitivity of colonoscopy has been shown to vary between examiners (25) and because variation in examination technique is potentially responsible for the nondetection of polyps (26). To avoid bias, the two endoscopists alternated between performing the first and second examinations. All examinations were performed while the patients were sedated. Sedation was induced with intravenous administration of midazolam hydrochloride (Versed; Hoffmann-La Roche, Nutley, NJ).

The endoscopist performed conventional colonoscopy with a standard videocolonoscope (model C240 or CV-1; Olympus Optical, Tokyo, Japan). The en-

doscopist was asked to pass the instrument tip to the cecum and withdraw the endoscope segment by segment for the detection of polyps. Cecal intubation was verified on the basis of the identification of the appendiceal orifice, triradiate cecal fold, and ileocecal valve and the findings at biopsy of the small bowel after intubation of the terminal ileum. The presence, location, size, and morphologic features of all colorectal polyps were documented. All polyps were photographed. The width of each lesion was estimated to the nearest millimeter by means of visual comparison with the known diameter (4 mm) of an opened biopsy forceps that was pushed against the polyp; the height was estimated by placing the closed forceps tip (2.1 mm) adjacent to the lesion. This allowed subsequent calculation of the height-to-width ratio for each polyp, which is important in assessing the flat morphologic features of polyps.

The location of each polyp was mapped within the same six colonic segments used in CT colonographic analysis. The morphologic criteria for polyps at colonoscopy were the same as those at CT colonography. During the initial conventional colonoscopic examination performed on the same day as but after CT colonography, no polyp was sampled at biopsy or resected. In addition, a resident who was not involved in CT colonographic data evaluation was present to document any complication associated with initial colonoscopy.

### Second Conventional Colonoscopy

Each second colonoscopic procedure was performed by the endoscopist who did not perform the first examination. The bowel preparation before colonoscopy and the technique used were the same as those described for the first colonoscopic examination. The location, size, and morphologic criteria used for polyp assessment also were the same as those used for the first colonoscopy. The endoscopist who performed the second colonoscopic examination was aware of the findings of both initial colonoscopy and CT colonography. Specifically, to facilitate polyp-to-polyp matching with the lesions depicted at second colonoscopy, the initial colonoscopic images and the CT colonographic images—together with the reference images of the identified polyps—were reviewed before the second colonoscopy. To solve any potential discrepancy in the polyp-to-polyp matching, the endoscopist who per-

formed the first colonoscopic examination and one radiology resident who was aware of the results derived by the three CT observers also were present. The complications associated with the second colonoscopic procedure also were recorded.

### Histologic Features of Polyps

All polyps were sampled at biopsy or resected during the second colonoscopy. The histologic appearances of all polyp specimens were evaluated by the same pathologist, who had 11 years of experience. Histologically, polyps were classified as nonneoplastic (including hyperplastic, inflammatory, and juvenile polyps) or neoplastic (including tubular, villous, tubulovillous, serrated, and microtubular adenomas; carcinomas in situ; and invasive carcinomas) (27).

### Data Analyses

Results were calculated in two ways: by using individual polyp detection—that is, per-polyp analysis—and by using patient detection—that is, per-patient analysis. For per-polyp analysis, the results of the second colonoscopy—in terms of the location, size, and morphologic features of the depicted polyps—were considered the reference standard against which the findings at initial colonoscopy and CT colonography were compared. For a given polyp to be considered a true-positive match between second colonoscopy and either CT colonography or initial colonoscopy, the location, size, and morphologic features of the polyp had to be considered.

With regard to location and morphologic features, a polyp detected at CT colonography or first colonoscopy was considered to be concordant with one seen at second colonoscopy if it was located in the same or an adjacent colonic segment (with the exception of polyps in the cecum, for which no margin of error was allowed) and had the same morphologic features, compared with the polyp seen at second colonoscopy. Precise matching of polyps according to size criteria was rarely possible because of the known measurement error with conventional colonoscopy and the unknown measurement error with CT colonography (5,18). Thus, for a given polyp to meet the size criteria, the size measured at CT colonography or initial colonoscopy had to be within a 50% margin of error of the size determined at second colonoscopy (5,6,18).

Each polyp that was seen at second colonoscopy but not documented at CT colonography or initial colonoscopy was classified as a false-negative finding of CT colonography or initial colonoscopy, respectively. In cases in which additional polyps that were not seen at first colonoscopy were identified at second colonoscopy, the two endoscopists jointly discussed the possible reason(s) for the initial nonvisualization (ie, a polyp situated behind a colonic fold, an area of interest that was difficult to assess for anatomic reasons, or perceptual error). If a polyp was depicted at CT colonography or initial colonoscopy but not confirmed at second colonoscopy, it was deemed to be a false-positive finding of CT colonography or initial colonoscopy, respectively.

After the comparisons, a retrospective review of all false-negative and false-positive CT colonographic findings was jointly performed by the three observers and a study supervisor (R.P.) to determine the reasons for the diagnostic errors. In addition, because of the potential range of size measurements for a given polyp among the three observers, a consensus reading was performed to determine the CT colonographic size of each polyp. Therefore, the average results given throughout this report refer to the polyp sizes estimated during this consensus reading.

For per-patient analysis, the overall results of CT colonography or initial colonoscopy were compared with the overall results of second colonoscopy for each patient. A patient was considered to have true-positive findings at CT colonography or initial colonoscopy if the given examination depicted at least one polyp that was seen at second colonoscopy on the basis of the location, size, and morphologic criteria described earlier.

### Statistical Analyses

All statistical analyses were conducted by using commercially available software (SPSS for Windows, version 11.0.0; SPSS, Chicago, Ill). For per-polyp analysis, the sensitivity and corresponding 95% confidence interval (CI) of both CT colonography and initial colonoscopy were calculated on the basis of the total number of polyps (ie, neoplastic and nonneoplastic polyps combined) and on the basis of the number of neoplastic polyps only. The specificity of the examinations for the detection of individual polyps could

**TABLE 1**  
Demographic Characteristics and Indications for Colonoscopy in 88 Patients

Characteristic or Indication	Value
Men	55 (62)
Women	33 (38)
Mean age (y)*	62.4 (50–74)
Indication for colonoscopy	
Asymptomatic patients	38 (43)
Screening	12 (14)
Personal history of polyps	11 (12)
Family history of colorectal cancer	9 (10)
Abnormal screening test result <sup>†</sup>	6 (7)
Symptomatic patients	50 (57)
Hematochezia	13 (15)
Change in bowel movement habits	12 (14)
Weight loss	10 (11)
Abdominal pain	8 (9)
Iron deficiency–related anemia	7 (8)

Note.—Unless otherwise noted, data are numbers of patients and numbers in parentheses are percentages.

\* Numbers in parentheses are the age range.

<sup>†</sup> Includes positive result of guaiac-based stool test ( $n = 4$ ), barium enema examination ( $n = 1$ ), or sigmoidoscopy ( $n = 1$ ).

**TABLE 2**  
Distribution of Polyps according to Size, Location, and Histologic Type

Polyp Location and Histologic Type	Polyp Size*			Total
	≤5 mm	6–9 mm	≥10 mm	
Rectum				
Neoplastic	3	1	1	5
Nonneoplastic	5	3	1	9
Total	8	4	2	14
Sigmoid colon				
Neoplastic	4	5	3	12
Nonneoplastic	10	3	2	15
Total	14	8	5	27
Descending colon				
Neoplastic	4	2	1	7
Nonneoplastic	7	1	0	8
Total	11	3	1	15
Transverse colon and splenic flexure				
Neoplastic	1	2	1	4
Nonneoplastic	6	1	0	7
Total	7	3	1	11
Ascending colonic and hepatic flexure				
Neoplastic	5	1	0	6
Nonneoplastic	5	1	1	7
Total	10	2	1	13
Cecum				
Neoplastic	1	3	1	5
Nonneoplastic	6	3	0	9
Total	7	6	1	14
All colonic segments				
Neoplastic	18	14	7	39
Nonneoplastic	39	12	4	55
Total	57	26	11	94

\* Data are numbers of polyps.

not be calculated because the total number of true-negative polyps could not be assessed (5).

For per-patient analysis, the sensitivity, specificity, positive predictive value, and negative predictive value of both CT colonography and initial colonoscopy,

with corresponding 95% CIs, were calculated.

In this study, per-polyp and per-patient analysis data were calculated according to size thresholds (6,19), with separate evaluations for polyps 5 mm in diameter or smaller, 6 mm in diameter or

**TABLE 3**  
**Sensitivity of CT Colonography (for Three Observers) and Initial Colonoscopy for Individual Polyp Detection**

Parameter	Polyp Size						All
	≤5 mm	≥6 mm	≥7 mm	≥8 mm	≥9 mm	≥10 mm	
<b>Observer 1</b>							
Sensitivity, all polyps	51 (29/57)	84 (31/37)	88 (23/26)	94 (17/18)	100 (14/14)	100 (11/11)	64 (60/94)
95% CI	38%, 63%	69%, 92%	71%, 96%	74%, 99%	79%, 100%	74%, 100%	54%, 73%
Sensitivity, neoplastic polyps	50 (9/18)	81 (17/21)	93 (14/15)	100 (11/11)	100 (9/9)	100 (7/7)	67 (26/39)
95% CI	29%, 71%	60%, 92%	70%, 99%	74%, 100%	70%, 100%	65%, 100%	51%, 79%
<b>Observer 2</b>							
Sensitivity, all polyps	47 (27/57)	86 (32/37)	88 (23/26)	94 (17/18)	100 (14/14)	100 (11/11)	63 (59/94)
95% CI	23%, 43%	72%, 94%	71%, 96%	74%, 99%	79%, 100%	74%, 100%	53%, 72%
Sensitivity, neoplastic polyps	44 (8/18)	81 (17/21)	87 (13/15)	100 (11/11)	100 (9/9)	100 (7/7)	64 (25/39)
95% CI	25%, 66%	60%, 92%	62%, 96%	74%, 100%	70%, 100%	65%, 100%	48%, 77%
<b>Observer 3</b>							
Sensitivity, all polyps	42 (24/57)	86 (32/37)	88 (23/26)	89 (16/18)	93 (13/14)	100 (11/11)	60 (56/94)
95% CI	30%, 55%	72%, 94%	71%, 96%	67%, 97%	69%, 99%	74%, 100%	50%, 69%
Sensitivity, neoplastic polyps	39 (7/18)	71 (15/21)	80 (12/15)	100 (11/11)	100 (9/9)	100 (7/7)	56 (22/39)
95% CI	20%, 61%	50%, 86%	55%, 93%	74%, 100%	70%, 100%	65%, 100%	41%, 71%
<b>Initial colonoscopy</b>							
Sensitivity, all polyps	82 (47/57)	84 (31/37)	85 (22/26)	83 (15/18)	86 (12/14)	91 (10/11)	83 (78/94)
95% CI	71%, 90%	69%, 92%	67%, 94%	61%, 94%	60%, 96%	62%, 98%	74%, 89%
Sensitivity, neoplastic polyps	83 (15/18)	91 (19/21)	87 (13/15)	82 (9/11)	89 (8/9)	86 (6/7)	87 (34/39)
95% CI	61%, 94%	71%, 97%	62%, 96%	52%, 95%	57%, 98%	49%, 97%	73%, 94%

Note.—Data are percentages. For sensitivity data, the numbers used to calculate the percentages are in parentheses. Each 95% CI corresponds to the directly preceding sensitivity value. Data are presented separately for all polyps (ie, neoplastic and nonneoplastic polyps combined) and for neoplastic polyps alone.

larger, 7 mm in diameter or larger, 8 mm in diameter or larger, 9 mm in diameter or larger, and 10 mm in diameter or larger.

Interobserver reliability for both the detection of individual polyps and the detection of patients with polyps at CT colonography was evaluated by calculating  $\kappa$  statistics for multiple observers with use of nonweighted binary  $\kappa$  statistic values. A  $\kappa$  value of 0.01–0.20 was considered to indicate minor agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, high agreement; and 0.81–1.00, excellent agreement.

## RESULTS

From November 2002 to December 2003, a total of 503 patients were referred to our institution for conventional colonoscopy and met the criteria for enrollment in the study. Of these 503 patients, 398 declined to participate. Of the 105 remaining patients, 11 were subsequently excluded because of failure of the CT scanner on the day of the scheduled CT colonographic examination and six were excluded because the cecum was not reached at initial colonoscopy; thus, the completion rate (ie, cecal intubation rate) was 94% (88/[88 + 6]). The remaining 88 patients underwent a complete CT colonographic examination and two sequential colonoscopic examinations and

therefore constituted the final study population. The demographic characteristics of these patients and their indications for colonoscopy are given in Table 1. Overall, 38 (43%) patients were asymptomatic and the remaining 50 (57%) patients were scheduled to undergo conventional colonoscopy for the evaluation of symptoms.

### Second Conventional Colonoscopy

Second colonoscopy (Table 2) was performed 7–14 days (average, 9.2 days) after the first colonoscopic examination. Cecal intubation was achieved in all patients. No complication occurred during second colonoscopy. Of the 88 patients enrolled in the study, 42 (48%) showed no evidence of having polyps. A total of 94 polyps were identified in the remaining 46 (52%) patients: 23 patients had a single polyp; 11, two polyps; and 12, three or more polyps. Of the 94 polyps, 57 (61%) were 1–5 mm in diameter; 26 (28%), 6–9 mm in diameter; and 11 (12%), 10 mm or greater in diameter. With regard to morphologic features, 36 (38%) polyps were categorized as pedunculated; 53 (56%) polyps, as sessile; and five polyps (5%), as flat.

The histologic types of all 94 polyps were successfully classified. Nonneoplastic histologic features were found in 55 (58%) polyps, all of which proved to be hyperplastic. The 39 (42%) remaining

polyps were neoplastic and included 26 (28%) tubular adenomas, six (6%) tubulovillous adenomas, two (2%) serrated adenomas, three (3%) carcinomas in situ, and two (2%) invasive carcinomas.

### Initial Conventional Colonoscopy

No complications were associated with the initial colonoscopic examination. Overall, initial colonoscopy (Table 3) yielded a per-polyp sensitivity of 83%, with a sensitivity of 87% for the detection of neoplastic polyps. Initial colonoscopy “missed” 16 polyps (diameter range, 4–14 mm) that were depicted at second colonoscopy, for a total miss rate of 17%. Five (four tubular adenomas and one tubulovillous adenoma; diameter range, 5–14 mm) of these 16 missed polyps were neoplastic. Thus, the neoplastic polyp miss rate of initial colonoscopy was 13% (five of 39 polyps). The reasons for missed polyps at initial colonoscopy were a blind spot (ie, the polyp was located behind a colonic fold) in 12 cases and perceptual error in the remaining four cases. All polyps found at initial colonoscopy were confirmed and resected at second colonoscopy—that is, there were no false-positive findings at initial colonoscopy.

Table 4 shows the results of initial colonoscopy for the identification of patients with colorectal polyps according to polyp size. At per-patient analysis, initial

**TABLE 4**  
Performance Values for CT Colonography (for Three Observers) and Initial Colonoscopy in Identifying Patients with Colorectal Polyps

Parameter	Polyp Size						All
	≤5 mm	≥6 mm	≥7 mm	≥8 mm	≥9 mm	≥10 mm	
<b>Sensitivity</b>							
Observer 1	76 (13/13+4) 53%, 90%	86 (25/25+4) 69%, 94%	91 (20/20+2) 72%, 98%	94 (16/16+1) 73%, 99%	100 (14/14) 78%, 100%	100 (10/10) 72%, 100%	83 (38/38+8) 69%, 91%
Observer 2	76 (13/13+4) 53%, 90%	83 (24/24+5) 66%, 92%	91 (20/20+2) 72%, 98%	94 (16/16+1) 73%, 99%	100 (14/14) 79%, 100%	100 (10/10) 72%, 100%	80 (37/37+9) 67%, 89%
Observer 3	71 (12/12+5) 47%, 87%	83 (24/24+5) 66%, 92%	91 (20/20+2) 72%, 98%	94 (16/16+1) 73%, 99%	100 (14/14) 79%, 100%	100 (10/10) 72%, 100%	78 (36/36+10) 64%, 88%
Initial colonoscopy	100 (17/17) 82%, 100%	90 (26/26+3) 74%, 96%	86 (19/19+3) 67%, 95%	82 (14/14+3) 59%, 94%	86 (12/12+2) 60%, 96%	90 (9/9+1) 60%, 98%	94 (43/43+3) 83%, 98%
<b>Specificity</b>							
Observer 1	100 (71/71) 95%, 100%	83 (49/49+10) 72%, 91%	91 (60/60+6) 82%, 96%	96 (68/68+3) 88%, 99%	99 (73/73+1) 93%, 100%	100 (78/78) 95%, 100%	76 (32/32+10) 62%, 87%
Observer 2	100 (71/71) 95%, 100%	83 (49/49+10) 72%, 91%	92 (61/61+5) 84%, 97%	97 (69/69+2) 90%, 99%	99 (73/73+1) 93%, 100%	100 (78/78) 95%, 100%	76 (32/32+10) 62%, 87%
Observer 3	100 (71/71) 95%, 100%	80 (47/47+12) 67%, 88%	89 (59/59+7) 80%, 95%	94 (67/67+4) 86%, 98%	97 (72/72+2) 91%, 99%	99 (77/77+1) 93%, 100%	71 (30/30+12) 56%, 83%
Initial colonoscopy	100 (71/71) 95%, 100%	100 (59/59) 94%, 100%	100 (66/66) 94%, 100%	100 (71/71) 95%, 100%	100 (74/74) 95%, 100%	100 (78/78) 95%, 100%	100 (42/42) 92%, 100%
<b>Positive predictive value</b>							
Observer 1	100 (13/13) 77%, 100%	71 (25/25+10) 55%, 84%	77 (20/20+6) 58%, 89%	84 (16/16+3) 62%, 94%	93 (14/14+1) 70%, 99%	100 (10/10) 72%, 100%	79 (38/38+10) 66%, 88%
Observer 2	100 (13/13) 77%, 100%	71 (24/24+10) 54%, 83%	80 (20/20+5) 61%, 91%	89 (16/16+2) 67%, 97%	93 (14/14+1) 70%, 99%	100 (10/10) 72%, 100%	79 (37/37+10) 65%, 88%
Observer 3	100 (12/12) 75%, 100%	67 (24/24+12) 50%, 80%	74 (20/20+7) 55%, 87%	80 (16/16+4) 58%, 92%	88 (14/14+2) 64%, 97%	91 (10/10+1) 62%, 98%	75 (36/36+12) 61%, 85%
Initial colonoscopy	100 (17/17) 82%, 100%	100 (26/26) 87%, 100%	100 (19/19) 83%, 100%	100 (14/14) 79%, 100%	100 (12/12) 75%, 100%	100 (9/9) 70%, 100%	100 (43/43) 92%, 100%
<b>Negative predictive value</b>							
Observer 1	95 (71/71+4) 87%, 98%	92 (49/49+4) 82%, 97%	97 (60/60+2) 89%, 99%	99 (68/68+1) 92%, 100%	100 (73/73) 95%, 100%	100 (78/78) 95%, 100%	80 (32/32+8) 65%, 90%
Observer 2	95 (71/71+4) 87%, 98%	91 (49/49+5) 80%, 96%	97 (61/61+2) 89%, 99%	99 (69/69+1) 92%, 100%	100 (73/73) 95%, 100%	100 (78/78) 95%, 100%	78 (32/32+9) 63%, 88%
Observer 3	93 (71/71+5) 86%, 97%	90 (47/47+5) 79%, 96%	97 (59/59+2) 89%, 99%	98 (67/67+1) 92%, 100%	100 (72/72) 95%, 100%	100 (77/77) 95%, 100%	75 (30/30+10) 60%, 86%
Initial colonoscopy	100 (71/71) 95%, 100%	95 (59/59+3) 87%, 98%	96 (66/66+3) 88%, 99%	96 (71/71+3) 89%, 99%	97 (74/74+2) 91%, 99%	99 (78/78+1) 93%, 100%	93 (42/42+3) 82%, 98%

Note.—Data are percentages. The numbers used to calculate the percentages are in parentheses. The corresponding 95% CI is on the second line.

colonoscopy had a sensitivity of 94%, a specificity of 100%, a positive predictive value of 100%, and a negative predictive value of 93%.

### CT Colonography

No complication occurred during the CT colonographic examinations. The mean time required for data interpretation was 10 minutes (range, 8–15 minutes).

The κ values for agreement among the three observers indicated moderate to high agreement on a per-polyp basis and high to excellent agreement on a per-patient basis (Table 5).

CT colonography (Table 3) yielded a mean per-polyp sensitivity for the three observers of 62% ((60 + 59 + 56)/[94 + 94 + 94]), with a mean sensitivity for neoplastic polyp (Fig 1) detection of 62% ((26 + 25 + 22)/[39 + 39 + 39]). With the analysis focused on polyps 6 mm in di-

**TABLE 5**  
Agreement between Observers Regarding Presence or Absence of Individual Colorectal Polyps and Identification of Patients with Colorectal Polyps

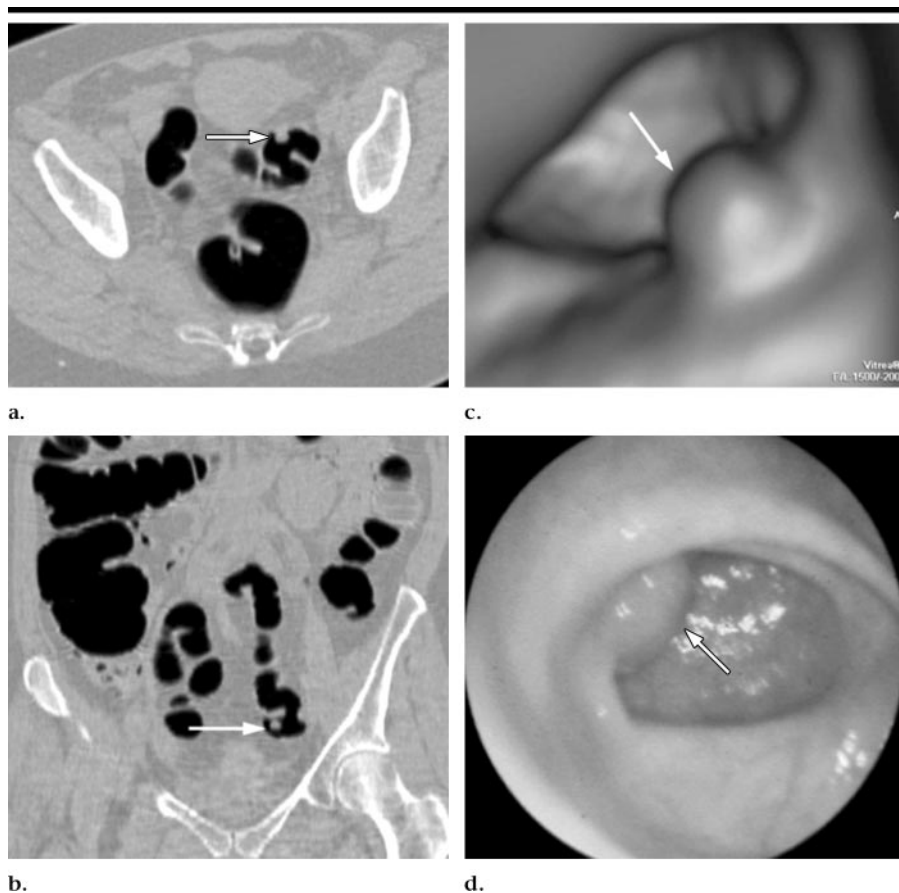
Agreement Analysis	Observer 1 vs Observer 2	Observer 2 vs Observer 3	Observer 1 vs Observer 3
Per polyp	0.63	0.59	0.51
Per patient	0.79	0.79	0.81

Note.—Data are κ values.

iameter or larger, CT colonography yielded a substantially increased detection rate: The mean sensitivity for the three observers was 86% ((31 + 32 + 32)/[37 + 37 + 37]), with a mean sensitivity for neoplastic polyp detection of 78% ((17 + 17 + 15)/[21 + 21 + 21]). Notably, all 11 neoplastic polyps 8 mm in diameter or larger were correctly identified by the three observers, yielding a sensitivity of 100%.

In addition, CT colonography correctly depicted six of the 16 polyps (three ≤5 mm polyps, two 8-mm polyps, and one 14-mm polyp) that were not seen at initial colonoscopy but were confirmed and resected at second colonoscopy. Four of these six polyps were neoplastic (three adenomas, one tubulovillous adenoma) (Fig 2).

CT colonography yielded 34, 35, and 38 false-negative findings for observers 1,



**Figure 1.** Seven-millimeter-diameter polyp (arrow) in 68-year-old woman. (a) Transverse CT colonographic image shows the polyp with round borders in the sigmoid colon. (b) Coronal CT colonographic image clearly shows the polyp. (c) Three-dimensional volume-rendered endoluminal CT image clearly demonstrates the polyp's sessile structure. (d) Initial conventional colonoscopic image shows the polyp, which was removed at second colonoscopy and found to be a tubular adenoma at histologic analysis.

2, and 3, respectively. At retrospective analysis, no clear cause of error (Table 6) could be determined for 26, 26, and 28 of these false-negative findings, respectively, because the polyps could not be seen in a well-distended and adequately cleansed colonic segment (Fig 3). CT colonography also yielded 19, 20, and 24 false-positive findings for observers 1, 2, and 3, respectively. At retrospective analysis, the most frequent cause of error was residual fecal material (Fig 4).

The results of the three observers and CT colonography in the identification of patients with colorectal polyps according to polyp size are summarized in Table 4. At per-patient analysis, CT colonography yielded a mean sensitivity for the three observers of 80% ( $[38 + 37 + 36]/[46 + 46 + 46]$ ), a mean specificity of 75% ( $[32 + 32 + 30]/[42 + 42 + 42]$ ), a mean positive predictive value of 78% ( $[38 + 37 + 36]/[48 + 47 + 48]$ ), and a mean

negative predictive value of 78% ( $[32 + 32 + 30]/[40 + 41 + 40]$ ).

## DISCUSSION

Our study results show that low-dose CT colonography has an excellent diagnostic performance in the detection of colorectal polyps 10 mm in diameter or larger, with a sensitivity of 100%: 11 of 11 polyps were correctly detected on CT colonographic images by the three CT observers. Even when the cutoff polyp size was reduced to 6 mm, CT colonography had a mean sensitivity of 86% ( $[31 + 32 + 32]/[37 + 37 + 37]$ ) for the three observers, which was slightly superior to the sensitivity of initial colonoscopy (84%) in our study and in the upper range of values for CT colonography reported in the literature (1–8). This finding is of pivotal clinical importance because polyps 6 mm in diameter or larger

have the highest probability of being malignant (28).

In contrast, although the sensitivity of initial colonoscopy remained stable (sensitivity for detection of polyps  $\leq 5$  mm, 82%), the diagnostic performance of CT colonography decreased substantially when polyps 5 mm in diameter or smaller were considered (mean sensitivity, 47%  $[29 + 27 + 24]/[57 + 57 + 57]$  for the three observers). This finding is in agreement with several previous reports (1,7,29). In our study, 26, 26, and 28 polyps 5 mm in diameter or smaller could not be detected with CT colonography, even at retrospective analysis. Because a substantial proportion of these small polyps missed at CT colonography were hyperplastic, one possible explanation for the nonvisualization of such lesions could be their soft consistency, which favors the effacement against the colonic mucosa once the colon is distended with air (1,30).

In our study, however, the sensitivities of CT colonography for the detection of all polyps (ie, neoplastic and nonneoplastic polyps combined) and for the detection of neoplastic polyps only were relatively stable. This indicates that diminutive lesions, regardless of their histologic type, are difficult to detect at CT colonography. However, the minority of such small polyps are malignant (31–33), and the adenoma-to-carcinoma transformation is believed to take at least 10 years on average (34,35). Thus, the clinical importance of identifying such small polyps is controversial.

It is perhaps more important that all of the flat polyps in our series were missed at CT colonography. Although only five such lesions were identified, there is increasing evidence that flat adenomas are extremely difficult to detect at CT colonography (7,8,36–38) because they cause only minimal alterations of the colonic mucosa. In this regard, it should be emphasized that even conventional colonoscopy has limited capability to depict flat lesions without the supplementary use of special techniques, such as high-magnification chromoscopy and dye spraying (16). In addition, the clinical importance of flat adenomas is still controversial because their prevalence and malignant potential are unclear (39).

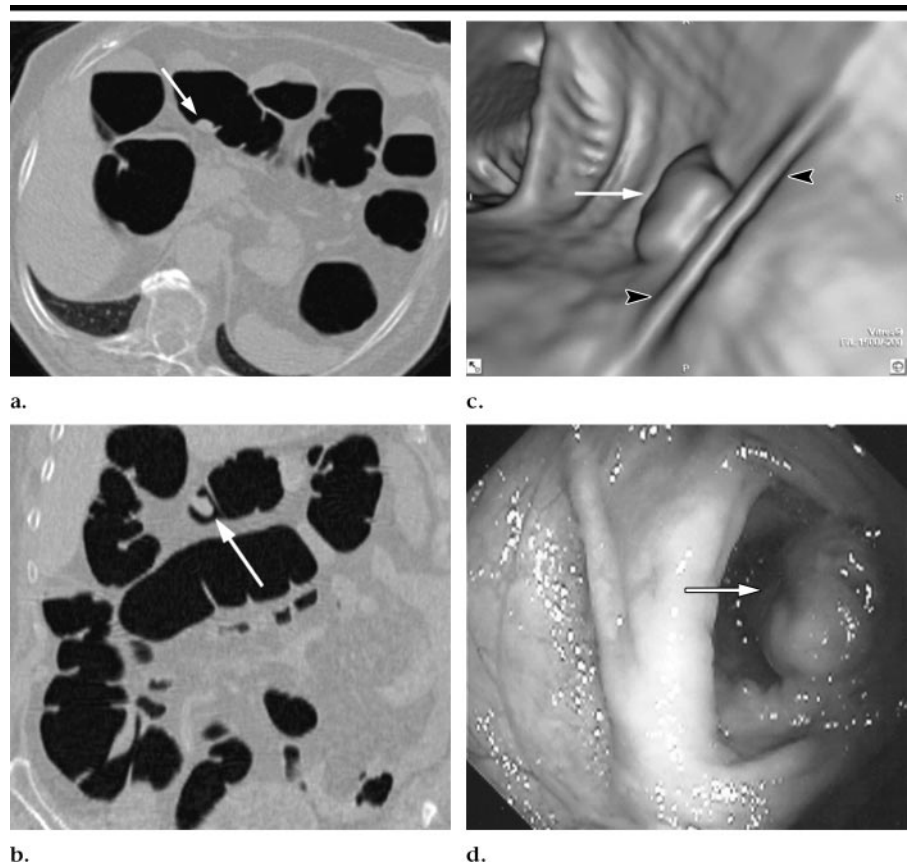
Another important issue that emerged from our research is that false-positive CT colonographic findings are relatively frequent: The three observers had 19, 20, and 24 false-positive findings in our study. In agreement with the findings of two recent studies (40,41), the most fre-

quent cause of the false-positive cases in our study was the presence of residual fecal material. Small fecal residue often adheres to the colonic mucosa and is too small to contain gas bubbles (a finding consistent with fecal material). Thus, such residue is often indistinguishable from polyps and thus has the potential to prompt many unnecessary colonoscopic examinations (42).

Although per-polyp analysis is important for determining which polyps will most likely be identified or missed with CT colonography, from a clinical point of view per-patient analysis is far more important because it enables the use of CT colonography to preselect those patients with polyps who might benefit from colonoscopy (5,8). In this regard, the diagnostic performance of CT colonography was comparable to that of initial colonoscopy in terms of sensitivity, specificity, and positive and negative predictive values for the identification of patients with polyps 10 mm in diameter or larger. Moreover, the negative predictive value of low-dose CT colonography—that is, its effectiveness in the identification of patients who did not need to undergo colonoscopy—was approximately equal to the negative predictive value of initial colonoscopy in the identification of patients with polyps 6 mm in diameter or larger (91% for CT colonography vs 95% for initial colonoscopy). This finding has important clinical implications for CT colonography as a potential screening tool because 46%–85% of screening colonoscopies do not reveal clinically important abnormalities (43,44).

Moreover, our study results demonstrate that low-dose CT colonographic images are interpreted with moderate to high interobserver agreement on a per-polyp basis and with high to excellent agreement on a per-patient basis among observers with different levels of experience. The three observers had previously interpreted approximately 400, 200, and 100 CT colonographic cases with endoscopic correlation in our series. The reproducibility of our results was thus demonstrated. These results correlate with the findings of other authors (6,45) but differ from those reported by Johnson et al (38). It is possible that the interobserver variability in our study was reduced, compared with that in the Johnson et al (38) study, owing to the use of thin-section multi-detector row helical CT image acquisitions.

One of the major strengths of our study was the use of two sequential colonoscopies to evaluate the performance of CT colonography. The performance of a sec-



**Figure 2.** Fourteen-millimeter-diameter polyp (arrow) in 62-year-old man. (a) Transverse CT colonographic image shows the polyp with round borders in the transverse colon. (b) Coronal CT colonographic image findings confirm the presence of the polyp. (c) Three-dimensional volume-rendered endoluminal CT image clearly demonstrates that the polyp is located behind a colonic fold (arrowheads). (d) Second conventional colonoscopic image shows the polyp. Despite its relatively large size, this polyp was missed at initial colonoscopy and difficult to detect even at second colonoscopy owing to its location behind the colonic fold. Histologic evaluation revealed this polyp to be a tubulovillous adenoma.

ond complete colonoscopic examination by an experienced endoscopist who was aware of the CT colonographic and initial colonoscopic findings yielded a greatly improved reference standard compared with the reference standards used in the majority of studies reported in the CT colonographic literature. It is conceivable that, although second colonoscopy may depict some polyps missed at the first examination, it may fail to depict other missed polyps (10,13). However, it can be assumed that after two colonoscopic procedures performed by two experienced endoscopists and CT colonography, the probability of having missed polyps in our cohort was minimal.

In addition, the use of two sequential colonoscopies yielded important information about the performance of conventional colonoscopy. In agreement with previous study (9,10,12,13) findings, our study results show that conven-

tional colonoscopy has a substantial miss rate in the identification of colorectal polyps. The overall miss rate was 17% in our study: 16 of 94 polyps were not seen prospectively. In our series, 16 polyps (five neoplastic, 11 nonneoplastic) that were missed at initial colonoscopy were identified at second colonoscopy. Six of these polyps, four of which were neoplastic, were seen at CT colonography. Thus, if initial colonoscopy had been the reference standard, these six polyps would have been wrongly classified as false-positive findings at CT colonography. In agreement with the recent findings of Pickhardt et al (13), the most frequent reason for missed polyps at initial colonoscopy in our study was the location of polyps behind colonic folds (in 12 [75%] of 16 cases).

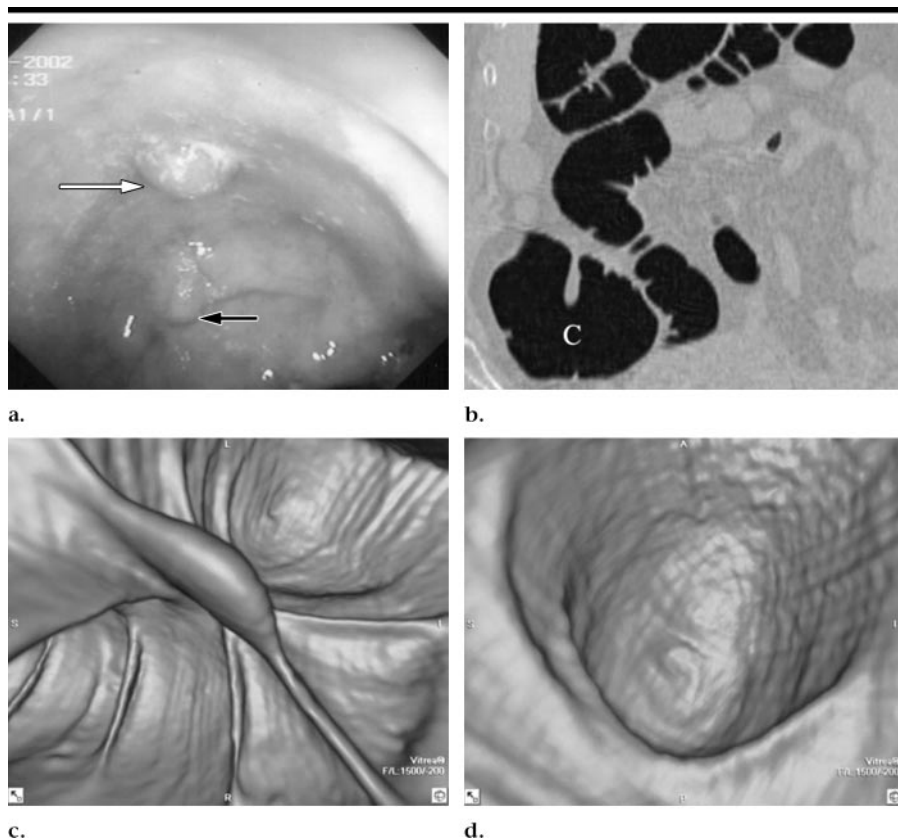
Because both endoscopists in our study had extensive colonoscopic experience (as indicated by cecal intubation rates of

**TABLE 6**  
**Causes of False-Positive and False-Negative Findings in Individual Polyp Detection at CT Colonography**

Finding Type	Total No. of Findings	Perceptual Error	Fecal Material	Residual Fluid	Collapsed Bowel	Thick Fold	Motion Artifact	No Clear Cause*
False-negative								
Observer 1	34	3	1	3	1	0	0	26
Observer 2	35	3	2	2	2	0	0	26
Observer 3	38	4	2	2	2	0	0	28
False-positive								
Observer 1	19	0	12	0	0	7	0	0
Observer 2	20	0	12	0	0	8	0	0
Observer 3	24	0	14	0	0	9	1	0

Note.—Data are numbers of false-negative or false-positive findings due to the given causes.

\* Polyp could not be seen in a well-distended and adequately cleansed colonic segment retrospectively.



**Figure 3.** Two polyps, 8 and 4 mm in diameter, in 63-year-old man. (a) Initial conventional colonoscopic image shows the 8-mm polyp (white arrow) within the cecum. The 4-mm polyp (black arrow) can also be seen. These polyps were not detected at CT colonography by the three observers, and both were confirmed and removed at second colonoscopy. At histologic analysis, these lesions were shown to be hyperplastic polyps. (b) Coronal CT colonographic image obtained at retrospective analysis shows no abnormality in the well-distended cecum (C). (c) Three-dimensional volume-rendered endoluminal CT image obtained at retrospective analysis clearly shows the anatomy of the cecum, but no polyp is depicted. (d) Another three-dimensional volume-rendered endoluminal CT image obtained at retrospective analysis reveals no abnormality of the cecal mucosa.

94% and 100% at initial and second colonoscopy, respectively), the miss rate of conventional colonoscopy confirms that colonoscopy is an imperfect reference standard. Therefore, an improved reference standard is needed for accurate

assessment of the performance of CT colonography (18,19).

As a possible way to create an improved reference standard, so-called segmental unblinding has been described (18) and adopted (5,6). This method has

the important advantage of enabling both initial evaluation and reevaluation of a colonic segment during the same endoscopic session, so only one colonoscopic procedure is needed. However, this approach also has certain limitations: First, if a polyp is not seen at CT colonography and at first-look colonoscopy, a second colonoscopic look is not performed (18). Second, owing to a learning effect, this technique may hamper the comparison of diagnostic performance between colonoscopy and CT colonography, because if the endoscopist misses a polyp in a specific segment, he or she may unintentionally adjust the examination approach during assessment of the remaining segments (8). Third, segmental unblinding with same-day colonoscopy may be difficult to perform at many centers owing to logistic reasons, because the CT colonographic report must be available within a few hours. This can be difficult to achieve in routine clinical practice, especially if three CT observers are needed to prospectively assess interobserver variability.

The limitations of our study require comment. First, similar to what has been reported regarding colonoscopy and the expertise of endoscopists (44), there is increasing evidence that greater observer experience is associated with increased CT colonographic performance (4). In our study, the three observers had greater-than-average experience in CT colonographic data interpretation, having interpreted approximately 400, 200, and 100 cases with endoscopic correlation. Therefore, further studies are needed to confirm the diagnostic performance of low-dose CT colonography when its findings are interpreted by less experienced readers.

In addition, instead of monobasic sodium phosphate monohydrate com-



**Figure 4.** Four-millimeter-diameter false-positive lesion (arrow) in 64-year-old woman. (a) Transverse CT colonographic image shows the lesion in the sigmoid colon. (b) Sagittal CT colonographic image findings confirm the presence of the lesion. (c) Three-dimensional volume-rendered endoluminal CT image clearly shows the lesion. Although all three observers reported this lesion to be a polyp, it was not seen at first or second colonoscopy. This lesion is believed to represent fecal residue.

bined with dibasic sodium phosphate heptahydrate, polyethylene glycol electrolyte solution and bisacodyl were used for cathartic preparation. The monobasic sodium phosphate monohydrate–dibasic sodium phosphate heptahydrate preparation has been demonstrated to leave a drier colonic surface compared with the polyethylene glycol preparation (46). However, in our study, residual fluids were rarely responsible for diagnostic errors at CT colonography.

In conclusion, our study results show that the performance of low-dose multi-detector row helical CT colonography compares favorably with that of conventional colonoscopy in the detection of colorectal polyps 6 mm in diameter or larger and has markedly decreased performance in the detection of polyps 5 mm in diameter or smaller. The high negative predictive value of CT colonography can be used to exclude the presence of clinically important colorectal polyps in the majority of patients and thus potentially to reduce the number of negative-result colonoscopies performed. Further studies are needed to determine which lesion cutoff size is clinically acceptable and the appropriate time interval for repeat CT colonography when lesions smaller than this cutoff size are detected.

#### References

- Fenlon HM, Nunes DP, Schroy PC 3rd, Barish MA, Clarke PD, Ferrucci JT. A comparison of virtual and conventional colonoscopy for the detection of colorectal polyps. *N Engl J Med* 1999;341:1496–1503.
- Fletcher JG, Johnson CD, Welch TJ, et al. Optimization of CT colonography technique: prospective trial in 180 patients. *Radiology* 2000;216:704–711.
- Yee J, Akerkar GA, Hung RK, Steinauer-Gebauer AM, Wall SD, McQuaid KR. Colorectal neoplasia: performance characteristics of CT colonography for detection in 300 patients. *Radiology* 2001;219:685–692.
- Johnson CD, Toledano AY, Herman BA, et al. Computerized tomographic colonography: performance evaluation in a retrospective multicenter setting. *Gastroenterology* 2003;125:688–695.
- Pineau BC, Paskett ED, Chen GJ, et al. Virtual colonoscopy using oral contrast compared with colonoscopy for the detection of patients with colorectal polyps. *Gastroenterology* 2003;125:304–310.
- Pickhardt PJ, Choi JR, Hwang I, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. *N Engl J Med* 2003;349:2191–2200.
- Macari M, Bini EJ, Jacobs SL, et al. Colorectal polyps and cancers in asymptomatic average-risk patients: evaluation with CT colonography. *Radiology* 2004;230:629–636.
- Van Gelder RE, Nio CY, Florie J, et al. Computed tomographic colonography compared with colonoscopy in patients at increased risk for colorectal cancer. *Gastroenterology* 2004;127:41–48.
- Hixson LJ, Fennerty MB, Sampliner RE, McGee D, Garewal H. Prospective study of the frequency and size distribution of polyps missed by colonoscopy. *J Natl Cancer Inst* 1990;82:1769–1772.
- Rex DK, Cutler CS, Lemmel GT, et al. Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. *Gastroenterology* 1997;112:24–28.
- Bensen S, Mott LA, Dain B, Rothstein R, Baron J; for the Polyp Prevention Study Group. The colonoscopic miss rate and true 1-year recurrence of colorectal neoplastic polyps. *Am J Gastroenterol* 1999;94:194–199.
- Rex DK, Chadalawada V, Helper DJ. Wide angle colonoscopy with a prototype instrument: impact on miss rates and efficiency as determined by back-to-back colonoscopies. *Am J Gastroenterol* 2003;98:2000–2005.
- Pickhardt PJ, Nugent PA, Mysliwiec PA, Choi JR, Schindler WR. Location of adenomas missed by optical colonoscopy. *Ann Intern Med* 2004;141:352–359.
- Brooker JC, Saunders BP, Shah SG, et al. Total colonic dye-spray increases the detection of diminutive adenomas during routine colonoscopy: a randomized controlled trial. *Gastrointest Endosc* 2002;56:333–338.
- Rembacken BJ, Fujii T, Cairns A, et al. Flat and depressed colonic neoplasms: a prospective study of 1000 colonoscopies in the UK. *Lancet* 2000;355:1211–1214.
- Hurlstone DP, Cross SS, Adam I, et al. A prospective clinicopathological and endoscopic evaluation of flat and depressed colorectal lesions in the United Kingdom. *Am J Gastroenterol* 2003;98:2543–2549.
- Matsushita M, Hajiro K, Okazaki K, Takakuwa H, Tominaga M. Efficacy of total colonoscopy with a transparent cap in comparison with colonoscopy without the cap. *Endoscopy* 1998;30:444–447.
- Pineau BC, Paskett ED, Chen GJ, Durkalski VL, Espeland MA, Vining DJ. Validation of virtual colonoscopy in the detection of colorectal polyps and masses: rationale for proper study design. *Int J Gastrointest Cancer* 2001;30:133–140.
- Dachman AH, Zalis ME. Quality and consistency in CT colonography and research reporting. *Radiology* 2004;230:319–323.
- 41st World Medical Assembly Declaration of Helsinki. Recommendations guiding physicians in biomedical research involving human subjects. *Bull Pan Am Health Organ* 1990;24:606–609.
- Adams WJ, Meagher AP, Lubowski DZ, King DW. Bisacodyl reduces the volume of polyethylene glycol solution required for bowel preparation. *Dis Colon Rectum* 1994;37:229–233.
- Iannaccone R, Laghi A, Catalano C, et al. Detection of colorectal lesions: lower-dose multi-detector row helical CT colonography compared with conventional colonoscopy. *Radiology* 2003;229:775–781.
- Dachman AH, Kuniyoshi JK, Boyle CM, et al. CT colonography with three-dimensional problem solving for detection of colonic polyps. *AJR Am J Roentgenol* 1998;171:989–995.
- Macari M, Milano A, Lavelle M, Berman P, Megibow AJ. Comparison of time-efficient CT colonography with two- and three-dimensional colonic evaluation for detect-

- ing colorectal polyps. *AJR Am J Roentgenol* 2000;174:1543-1549.
25. Rex DK, Rahmani EY, Haseman JH, Lemmel GT, Kaster S, Buckley JS. Relative sensitivity of colonoscopy and barium enema for detection of colorectal cancer in clinical practice. *Gastroenterology* 1997;112:17-23.
  26. Rex DK. Colonoscopic withdrawal technique is associated with adenoma miss rates. *Gastrointest Endosc* 2000;51:33-36.
  27. Rubio CA, Jaramillo E, Lindblom A, Fogt F. Classification of colorectal polyps: guidelines for the endoscopist. *Endoscopy* 2002;34:226-236.
  28. Rex DK. Virtual colonoscopy: time for some tough questions for radiologists and gastroenterologists. *Endoscopy* 2000;32:260-263.
  29. Macari M, Bini EJ, Xue X, et al. Colorectal neoplasms: prospective comparison of thin-section low-dose multi-detector row CT colonography and conventional colonoscopy for detection. *Radiology* 2002;224:383-392.
  30. Bertoni G, Sassatelli R, Conigliaro R, et al. Visual "disappearing phenomenon" can reliably predict the nonadenomatous nature of rectal and rectosigmoid diminutive polyps at endoscopy. *Gastrointest Endosc* 1994;40:588-591.
  31. Nusko G, Mansmann U, Altendorf-Hofmann A, Groitl H, Wittekind C, Hahn EG. Risk of invasive carcinoma in colorectal adenomas assessed by size and site. *Int J Colorectal Dis* 1997;12:267-271.
  32. Bond JH. Clinical relevance of the small colorectal polyp. *Endoscopy* 2001;33:454-457.
  33. Aldridge AJ, Simson JN. Histological assessment of colorectal adenomas by size: are polyps less than 10 mm in size clinically important? *Eur J Surg* 2001;167:777-781.
  34. Winawer SJ, Zauber AG, Ho MN, et al; for the National Polyp Study Workgroup. Prevention of colorectal cancer by colonoscopic polypectomy. *N Engl J Med* 1993;329:1977-1981.
  35. Hofstad B, Vatn N. Growth rate of colon polyps and cancer. *Gastrointest Endosc Clin N Am* 1997;7:345-363.
  36. Rex DK, Vining D, Kopecky KK. An initial experience with screening for colon polyps using spiral CT with and without CT colography (virtual colonoscopy). *Gastrointest Endosc* 1999;50:309-313.
  37. Fidler JL, Johnson CD, MacCarty RL, Welch TJ, Hara AK, Harmsen WS. Detection of flat lesions in the colon with CT colonography. *Abdom Imaging* 2002;27:292-300.
  38. Johnson CD, Harmsen WS, Wilson LA, et al. Prospective blinded evaluation of computed tomographic colonography for screen detection of colorectal polyps. *Gastroenterology* 2003;125:311-319.
  39. Hurlstone DP, Brown S, Cross SS. The role of flat and depressed colorectal lesions in colorectal carcinogenesis: new insights from clinicopathological findings in high-magnification chromoscopic colonoscopy. *Histopathology* 2003;43:413-426.
  40. Yee J, Kumar NN, Hung RK, Akerkar GA, Kumar PR, Wall SD. Comparison of supine and prone scanning separately and in combination at CT colonography. *Radiology* 2003;226:653-661.
  41. Edwards JT, Mendelson RM, Fritschi L, et al. Colorectal neoplasia screening with CT colonography in average-risk asymptomatic subjects: community-based study. *Radiology* 2004;230:459-464.
  42. Ferrucci JT. Colon cancer screening with virtual colonoscopy: promise, polyps, politics. *AJR Am J Roentgenol* 2001;177:975-988.
  43. Lieberman DA, Weiss DG, Bond JH, Ahnen DJ, Garewal H, Chejfec G; for Veterans Affairs Cooperative Study Group 380. Use of colonoscopy to screen asymptomatic adults for colorectal cancer. *N Engl J Med* 2000;343:162-168.
  44. Imperiale TF, Wagner DR, Lin CY, Larkin GN, Rogge JD, Ransohoff DF. Risk of advanced proximal neoplasms in asymptomatic adults according to the distal colorectal findings. *N Engl J Med* 2000;343:169-174.
  45. McFarland EG, Pilgram TK, Brink JA, et al. CT colonography: multiobserver diagnostic performance. *Radiology* 2002;225:380-390.
  46. Macari M, Lavelle M, Pedrosa I, et al. Effect of different bowel preparations on residual fluid at CT colonography. *Radiology* 2001;218:274-277.