CT colonography for screening of patients at increased risk for colorectal cancer: accuracy, patient acceptance and radiation issues
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Chapter 6

CT Colonography: Feasibility of Substantial Dose Reduction—Comparison of Medium to Very Low Doses in Identical Patients

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Abstract

In a feasibility study, the authors compared polyp detection and interobserver variability at computed tomographic (CT) colonography in 15 patients with doses ranging from medium to very low (12.00–0.05 mSv). At levels down to 2% of the medium dose, the mean detection of polyps 5 mm or larger remained at least 74%, while the number of false-positive results decreased and the interobserver agreement remained constant. Initial observations indicate that it is feasible to reduce the radiation dose required for CT colonography. Further studies are needed, however, to investigate the clinical value of very low–dose CT colonography.
Introduction

Computed tomographic (CT) colonography shows promise for colorectal cancer screening because of its accurate polyp detection and minimally invasive character (1–6). Findings in some studies (7–9) indicate that CT colonography is better accepted by patients than is colonoscopy and may encounter less reluctance than the screening tests that are currently recommended by the U.S. Multisociety Task Force: fecal occult blood test, double-contrast barium enema, sigmoidoscopy, and colonoscopy (10).

Unfortunately, exposure of asymptomatic subjects to radiation doses ranging from 4 to 12 mSv, as are used routinely today (11), with an estimated risk of one fatal cancer in 3,300–10,000 individuals aged 50 years (12), remains a major drawback. If the screening test requires regular repetition, the risk increases proportionally with the number of repetitions.

In clinical practice, the benefits of CT scanning for the patients generally outweigh the drawback of use of ionizing radiation. This balance, however, is very delicate in patients with a low potential benefit, as in the screening of asymptomatic people. Consequently, use of the lowest achievable dose for CT colonography will improve this balance and may serve implementation of this technique in colorectal cancer screening. This goal is facilitated by the recent introduction of CT scanners that enable use of lower doses than have been possible previously, a development driven by the present awareness of the potential danger of ionizing radiation (13–15).

To date, several investigators have studied the feasibility of low-dose protocols for CT colonography; their findings demonstrate that sensitivity and specificity are still satisfactory (11,16–19), even with an effective dose down to 1 mSv (18). However, the dose at which polyp detectability starts to decrease is still unknown, as is the lowest dose that is compatible with acceptable polyp detection.

The aim of this feasibility study was to compare polyp detection and interobserver variability at CT colonography with four low to very low doses (down to 0.05 mSv) with those at medium-dose (8–12 mSv) CT colonography.

Materials & Methods

Study Design To answer our research question, we compared a range of doses in identical patients and with identical readers. With such a design, any differences in polyp detectability can be attributed to variation in dose. Because we primarily focused on polyp detection in this feasibility study, we confined our study population to patients with polyps.
Patient Population For this study, we included prone and supine CT scans obtained in 15 patients with at least one polyp 5 mm or larger in largest dimension who had participated in an accuracy study of CT colonography. The Medical Ethics Committee of the Academic Medical Center, Amsterdam, the Netherlands, approved this accuracy study, and all patients gave written informed consent. Because the current study consisted of modification of data that had already been collected and no additional CT scans were obtained, the Medical Ethics Committee indicated that no additional approval from them and no additional informed consent from the patients were required.

All 15 patients were referred from the Academic Medical Center to undergo colonoscopy because of surveillance (personal or family history of colorectal polyps or cancer) or polypectomy. Ten men and five women (mean age, 59 years ± 13 [standard deviation]) were enrolled in the study. Mean age for the men was 55 years ± 12 and for the women was 67 years ± 12. All subjects used 4 L of macrogol bowel preparation (KleanPrep; Helsinn Birex Pharmaceuticals, Dublin, Ireland) prior to the examinations.

CT Colonography Each patient underwent imaging with a multissection CT scanner (Mx8000; Philips Medical Systems, Best, the Netherlands) in prone and supine positions. To distend the colon, approximately 2 L of air (13.4% volume of carbon dioxide) was insufflated manually. Before a patient underwent scanning, a preview image was obtained to estimate the distension; if necessary, additional air was insufflated with approval of the patient. CT was performed with the following parameters: 120 kV; collimation, 4.0 x 2.5 mm; rotation time, 0.75 second; pitch, 1.25; section thickness, 3.2 mm; and reconstruction interval, 1.6 mm. For all but one patient, 100 mAs was used. That patient was the last, who underwent CT after the overall milliamperesecond level was reduced for CT colonography, and 65 mAs was used. The effective dose for a complete examination was 8 mSv (at 65 mAs) or 12 mSv (at 100 mAs). The effective dose was estimated as an average for men and women by using a CT dosimetry calculator (ImPACT; Medicines and Healthcare Products Regulatory Agency, London, England). The calculated effective dose applied only to average-sized patients. For the same CT scanning parameters, the effective dose in heavier patients would be somewhat lower and that in thinner persons would be somewhat higher. At present, we do not have the facilities to perform patient-specific effective dose calculations.

Colonoscopy Within 2 hours after CT colonography, all patients underwent colonoscopy with a standard endoscope (CF-140L; Olympus, Tokyo, Japan). Four of
the colonoscopic examinations were performed by three gastroenterologists (including J.F.W.B.), who each had experience of 5 years or longer. The other 11 colonoscopic examinations were performed by eight gastroenterology fellows (four in their 1st year, two in their 2nd year, and two in their 3rd year) with the direct supervision of the attending gastroenterologist (J.F.W.B.). The endoscopists were blinded to results at CT colonography. During this examination, 13 patients received midazolam hydrochloride (Dormicum; Roche, Basel, Switzerland) and 11 received fentanyl citrate (Fentanyl-Janssen; Janssen Pharmaceuticals, Beerse, Belgium). A research fellow (R.E.v.G., a medical doctor but not a radiologist) recorded the examination on videotape. Polyps, if present, were scored with respect to the size, morphology, and segment (cecum, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum) in which they were located. Polyp size (largest dimension) was estimated by the endoscopist who performed colonoscopy on the basis of comparison with an open biopsy forceps of known size.

**Dose Reduction at CT** Radiation-dose reduction at CT scanning can be accomplished by reducing the number of photons to which the patient is exposed. As a consequence, image noise is increased. The number of photons can be reduced by reducing the tube current, increasing the pitch, or both. With the multissection CT scanner used in the current study, the tube current is automatically adjusted to the selected pitch, as the quantity effective milliampere-second level (tube current multiplied by the quotient of rotation time divided by pitch) is used; as a consequence, both patient dose and image noise depend on only the chosen (effective) milliampere-second value (20). In this study, CT colonographic examinations were simulated with a lower milliampere-second value and thus with a lower dose.

**Simulation of Low-Dose CT Colonography** To compare polyp detection and interobserver variability at CT colonography with medium and lower doses in the same 15 patients, we used an established simulation technique (11,21,22) to obtain four additional lower-dose CT colonographic images in each patient. Findings in a previous study (22) demonstrate that simulated lower-dose CT scans obtained with a similar method cannot be distinguished from genuine lower-dose scans.

The simulation method consists of controlled increase of noise in the colonoscopic raw CT transmission data prior to reconstruction of the images. The essence of the simulation method used in the current study is the following (21). First, the number of
photons corresponding to each transmission measurement was determined by using calibration measurements with rectangular water-filled phantoms and calculations of the attenuation of the CT x-ray spectrum in water. Next, the number of detected photons corresponding to a lower milliampere-second value was simulated by generating a Poisson deviate with the appropriate lower mean value. Finally, this Poisson deviate was converted back into a transmission measurement that corresponded to the desired lower tube current time. In this simulation, the electronics noise floor and other noise sources apart from quantum noise were not taken into account. The procedure was validated with CT scans obtained at various milliampere-second levels in water-filled phantoms by comparing the standard deviations of the simulated and real CT images. For very low milliampere-second levels (less than 15 mAs, with which no scans can be obtained with the multissection CT scanner used in this study), the procedure was validated with CT scans obtained in water-filled phantoms by using Monte Carlo simulations in which the complete measurement and reconstruction process was taken into account.

In practice, a research fellow (R.E.V.C.) extracted the raw transmission data from the multissection CT scanner, increased the noise of the raw data off-line by using software written by the physicist (H.W.V.), reentered the modified raw data into the multissection CT scanner, and made reconstructions by using the standard reconstruction software. The resulting CT images simulate scans acquired with reduced milliampere-second level and thus with proportionally reduced dose. Scans were simulated at 25.0, 6.3, 1.6, and 0.4 mAs, which correspond to effective doses for prone and supine scans together of 3.0, 0.8, 0.2, and 0.05 mSv, respectively. The two lowest doses are not yet achievable in clinical practice, but they are technically possible. Reduction by a factor of four for consecutive milliampere-second levels has the consequence that, to a first approximation, the noise level is doubled in the corresponding CT scans.

**Noise Reduction Filters for Very Low Milliampere-Second Level**

Lowering of the milliampere-second level increases the image noise, if all other parameters are kept constant. For the lowest simulated milliampere-second values used in this study, this increase in noise was such that the two-dimensional images (Fig 1) and especially the three-dimensional images (Fig 2) had very poor quality. Therefore, smoothing of images at a simulated lower milliampere-second level was required to counteract this increase in noise. For reconstruction of the original CT data obtained with 100 and 65 mAs, a standard reconstruction filter was used (filter C of the multissection
Figure 1 A-H. Effect of dose reduction and smoothing on transverse CT images. Images obtained in 60-year-old male patient with 8-mm polyp (arrow) in ascending colon, with 100-mAs colonoscopy and with simulated lower milliampere-second values, without and with Gaussian in-plane filters for the three lowest doses. A, 100 mAs. B, 25 mAs. C, 6.3 mAs. D, 6.3 mAs with filter. E, 1.6 mAs. F, 1.6 mAs with filter. G, 0.4 mAs. H, 0.4 mAs with filter. Image noise increases with decreasing tube current time. Filtered images (D, F, H) have smoother appearance than do corresponding unfiltered images (C, E, G).
CT scanner). The simulated images obtained at lower milliampere-second levels were reconstructed with the smoothest reconstruction filter available (filter A of the multisection CT scanner). For the lowest three doses, additional in-plane smoothing of the CT images was used by convolving the images with a Gaussian kernel with $\sigma = 0.6$ mm (6.3 mAs) and $\sigma = 1.2$ mm (1.6 and 0.4 mAs). This amount of smoothing was chosen empirically to keep the noise in the images approximately constant with decreasing tube current times, down to the simulated 1.6-mAs images. To not reduce the spatial resolution

*Figure 2 A-F.* Effect of smoothing filters on three-dimensional volume-rendered CT images in 50-year-old male patient with 5-mm sigmoid polyp (arrow in A) obtained without (A, C, E) and with (B, D, F) Gaussian in-plane filter. A, 6.3 mAs (0.8 mSv), B, 6.3 mAs (filter $\sigma = 0.6$ mm), C, 1.6 mAs (0.2 mSv), D, 1.6 mAs (filter $\sigma = 1.2$ mm), E, 0.4 mAs (0.05 mSv), F, 0.4 mAs (filter $\sigma = 1.2$ mm). Note that application of a filter is essential for detection of polyps in very low-dose data.
any further, we used the same filters for the 0.4- and 1.6-mAs simulated images. Figures 3 and 4 demonstrate the effect of lowering milliamper-second levels in combination with image smoothing on the visibility of a 15- and 5-mm polyp, respectively.

**Evaluation of CT Colonographic Data** An abdominal radiologist (observer 1, C.Y.N.) and a research fellow (observer 2, J.F., a medical doctor but not a radiologist), each with experience with more than 80 CT colonographic examinations, recorded the number of polyps detected and measured their size in CT colonographic images obtained with the five doses, in five separate readings. These observers were unaware of colonoscopic findings and disease prevalence. The readings started with the very low-dose data and, subsequently, data with increasing doses were evaluated. At least 4 weeks passed between the two readings (range, 4–6 weeks).

To further reduce memory bias, data were reviewed on the basis of segments. For this purpose, the colon was divided into six segments: cecum, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum. To perform this division, partitions were inserted in the three-dimensional images at the boundaries between the segments, and therefore the observers could not look beyond the segment

**Figure 3.** Images of 15-mm polyp in 60-year-old male patient at colonoscopy and at CT colonography with five doses. Top row: Left: Colonoscopic image shows 15-mm polyp in ascending colon (arrow). Middle: CT colonographic image obtained at 100 mAs. Right: CT colonographic image obtained at 25 mAs. Bottom row: Left: CT colonographic image obtained at 6.3 mAs. Middle: CT colonographic image obtained at 1.6 mAs. Right: CT colonographic image obtained at 0.4 mAs. Although image quality decreases, polyp visibility is unimpaired.
Figure 4. Images of 5-mm polyp in 57-year-old male patient at colonoscopy and at CT colonography with five doses. Top row: Left: Colonoscopic image shows 5-mm polyp (arrow) in transverse colon. Middle: CT colonographic image obtained at 100 mAs. Right: CT colonographic image obtained at 25 mAs. Bottom row: Left: CT colonographic image obtained at 6.3 mAs. Middle: CT colonographic image obtained at 1.6 mAs. Right: CT colonographic image obtained at 0.4 mAs. Image quality decreases and polyp visibility is affected at lowest doses as a result of increased image noise and smoothing.

being evaluated. Prone and supine images obtained in each segment were evaluated successively. At each of the five readings, the paired images of the segment were evaluated in a new random order.

Ninety segments were examined; 33 (37%) of them contained at least one polyp. Of these 33 segments, 13 contained only polyps smaller than 5 mm and 20 contained polyps 5 mm or larger. Among the latter segments, five contained a polyp that was 10 mm or larger.

In the present study, CT colonographic data were evaluated with a primary three-dimensional display mode. Data from a previous study (23), as well as from our own preliminary experience, indicate that with primary three-dimensional display modes a better polyp visualization is achieved than that with primary two-dimensional displays. To achieve optimal colon surface visibility, we used three-dimensional unfolded cubic projections (24). This method comprises the evaluation of a sequence of preprocessed three-dimensional unfolded cubic projections of the prone and supine CT data with the ability to further investigate suspected lesions with two-dimensional images. All CT colonographic data were volume rendered (threshold, −750 HU; ramp, 80 HU). The
observers measured the lesions they detected in the two-dimensional images because, with the software we used, this was more time efficient than measurement in three-dimensional images. The evaluation was performed with a workstation (EasyVision; Philips Medical Systems).

**Definitions of True- and False-Positive Findings** Another research fellow (R.E.v.G.) compared all findings at CT colonography with those at colonoscopy, which was the reference standard, by means of direct visual comparison of the recorded CT colonographic images and the videotaped colonoscopic images. This research fellow had previously matched CT colonographic and colonoscopic findings in more than 100 patients but was not involved in the review of CT colonographic images (performed by C.Y.N. and J.F.). A polyp detected at CT colonography was labeled as a true-positive finding if it corresponded exactly to a polyp detected at colonoscopy in terms of location (segment: cecum; ascending, transverse, descending, and sigmoid colon; and rectum), morphology, and size. Because estimates of the size of polyps at colonoscopy tend to have errors, we accepted a margin of error of 3 mm for polyps smaller than 5 mm and a margin of 5 mm for polyps 5 mm or larger. All other findings at CT colonography were classified as false-positive.

**Statistical Analysis** *Detection parameters.*—Polyp sensitivity at each dose was defined as the number of true-positive findings relative to the total number of polyps. Because polyp specificity cannot be defined, we report the number of false-positive findings and the segment specificity, defined as the number of segments without polyps at CT colonography relative to the number of segments without polyps at colonoscopy.

Although some investigators advocate the removal only of polyps 10 mm or larger (25), clinicians and patients are unlikely to accept the fact that lesions between 5 and 10 mm remain undetected (26,27). Therefore, we used 5 mm as the main cutoff in the present study. Because this matter is a subject of continuous discussion, however, we also used 10 mm as a cutoff in the analysis of true- and false-positive findings.

The true-positive findings were subdivided on the basis of the size estimated by the endoscopists, and the false-positive findings were subdivided on the basis of the measurements made by each observer on the CT images.
Stratification of polyp sensitivity according to pelvic and abdominal location.—In the pelvic region, the noise level is generally higher than that in other parts of the abdomen because of the larger lateral dimensions of the pelvis and the presence of bone structures. The effect of dose reduction on image quality will therefore be most severe in this region. For this reason, we performed an additional analysis to study the effect of dose reduction on sensitivity for polyps 5 mm or larger in segments in the pelvis (cecum, sigmoid colon, and rectum) and those in the abdomen (ascending, transverse, and descending colon).

Differences in polyp detection between the colonoscopic and lower-dose CT colonographic data were assessed with the McNemar test for paired proportions. Because few polyps were 10 mm or larger, differences in detection of these polyps between colonoscopic and lower-dose scans could not be assessed. Differences in polyp sensitivity between the pelvic and abdominal regions were assessed at each dose with the Mann-Whitney test. All analyses were performed separately for each observer.

Interobserver agreement.—Interobserver agreement analysis was performed on the basis of segment for each dose. Observers were considered to agree if they recorded one or more polyps in the same segment, regardless of whether these findings were true- or false-positive. If both observers recorded no findings in the same segment, they were also considered to agree. The statistic with 95% confidence interval was calculated. The values were interpreted on the following basis: $\kappa < 0.20$, poor agreement; $\kappa = 0.21$–0.40, fair agreement; $\kappa = 0.41$–0.60, moderate agreement; $\kappa = 0.61$–0.80, good agreement; $\kappa = 0.81$–1.00, very good agreement.

Interpretation time.—The time required to interpret findings in each segment was registered automatically with the workstation. Interpretation times for segments in the same patient were added to obtain patient interpretation times. Differences in interpretation times between the colonoscopic and lower-dose CT colonographic images were assessed with the paired-samples $t$ test for each observer separately.

Differences with a $P$ value less than .05 were considered significant. Software (SPSS for Windows, version 11.0; SPSS, Chicago, Ill) was used for all statistical tests.
Results

Colonoscopy At colonoscopy, 116 polyps were detected, and 27 were 5 mm or larger (medium and large) and five were 10 mm or larger (large). Twelve polyps 5 mm or larger were located in the abdominal segments (median size, 6 mm; range, 5–15 mm), and 15 polyps 5 mm or larger were located in the pelvic segments (median size, 5 mm; range, 5–20 mm).

CT Colonography True- and false-positive lesions. — True- and false-positive findings at CT colonography for all milliampere-second levels are listed in Table 1. Detection of polyps of all sizes decreased significantly (P < .05) with decreasing milliampere-second level, except at 25 mAs for observer 1. Down to 1.6 mAs, the mean sensitivity for polyps 5 mm or larger decreased slightly but remained equal to or higher than 74%, as shown in Figure 5. For observer 1, sensitivity for polyps 5 mm or larger varied from 85% to 78%, whereas for observer 2 this parameter varied from 81% to 70%. At the lowest

Table 1. True and false positive results of CT colonography with five dose levels

<table>
<thead>
<tr>
<th>Lesions according to size</th>
<th>CS</th>
<th>CT colonography</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>100 mAs*</td>
<td>25 mAs</td>
</tr>
<tr>
<td>True positive.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All sizes</td>
<td>116</td>
<td></td>
</tr>
<tr>
<td>Observer 1</td>
<td>63 (56)</td>
<td>61 (53)</td>
</tr>
<tr>
<td>Observer 2</td>
<td>56 (48)</td>
<td>44 (38)</td>
</tr>
<tr>
<td>≥ 5 mm</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Observer 1</td>
<td>23 (85)</td>
<td>21 (78)</td>
</tr>
<tr>
<td>Observer 2</td>
<td>22 (81)</td>
<td>20 (74)</td>
</tr>
<tr>
<td>≥ 10 mm</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Observer 1</td>
<td>5 (100)</td>
<td>4 (80)</td>
</tr>
<tr>
<td>Observer 2</td>
<td>4 (80)</td>
<td>4 (80)</td>
</tr>
<tr>
<td>False positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All sizes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observer 1</td>
<td>99</td>
<td>80</td>
</tr>
<tr>
<td>Observer 2</td>
<td>58</td>
<td>30</td>
</tr>
<tr>
<td>≥ 5 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observer 1</td>
<td>31</td>
<td>28</td>
</tr>
<tr>
<td>Observer 2</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>≥ 10 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observer 1</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Observer 2</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

Note. — Findings were in 15 patients with 116 polyps. Numbers in parentheses are percentages (polyp sensitivities). Statistical differences were assessed with McNemar test for both observers separately. CS, colonoscopy. CS numbers indicate polyp numbers. * One patient underwent CT colonography at 65 mAs. †P < .05 compared with original 100-mAs CT colonographic data.
milliampere-second level, sensitivity for polyps 5 mm or larger decreased to 44% for observer 1 and to 52% for observer 2. None of the differences in detection of polyps 5 mm or larger between the 100 mAs and simulated lower milliampere-second data were significant, except between 100 and 0.4 mAs ($P < .05$), for both observers. Detection of large polyps was between 80% and 100% at all milliampere-second levels.

The total number of false-positive findings decreased with decreasing milliampere-second level for both observers but increased again at the lowest milliampere-second level for observer 2. The decrease was mainly caused by a reduction in small false-positive findings, while also for observer 1 the number of medium-sized false-positive findings decreased. The number of large false-positive findings remained roughly constant for both observers. There is a large difference in the number of false-positive findings between the observers, especially at 100 and 25 mAs.

**Segment specificity.**—Table 2 shows the segment specificity. Specificity regarding the correct identification of segments without polyps increased or remained constant, except at 0.4 mAs. Concerning segments without polyps 5 mm or larger, specificity improved for observer 1 from 79% at 100 mAs to 93% at 0.4 mAs and for observer 2 was between 90% and 96% at all milliampere-second levels. Specificity for segments without polyps 10 mm or larger was between 96% and 99% at all milliampere-second levels for both observers.

| Table 2. Segment specificity of CT colonography at five dose levels (100 to 0.4 mAs; 12 to 0.05 mSv) |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Lesions according to size       | CS                              | CT colonography                 |
|                                 | 100 mAs*                        | 25 mAs                          | 6.3 mAs                         | 1.6 mAs                         | 0.4 mAs                         |
| Segment specificity             |                                 |                                 |                                 |                                 |                                 |
| -without polyps                 | 57                              |                                 |                                 |                                 |                                 |
| Observer 1                      | 38 (67)                         | 38 (67)                         | 45 (79)                         | 47 (82)                         | 44 (77)                         |
| Observer 2                      | 41 (72)                         | 49 (86)                         | 48 (84)                         | 48 (84)                         | 34 (60)                         |
| -without polyps ≥ 5 mm          | 70                              |                                 |                                 |                                 |                                 |
| Observer 1                      | 55 (79)                         | 59 (84)                         | 59 (84)                         | 61 (87)                         | 65 (93)                         |
| Observer 2                      | 64 (91)                         | 66 (94)                         | 64 (91)                         | 63 (90)                         | 67 (96)                         |
| -without polyps ≥ 10 mm         | 85                              |                                 |                                 |                                 |                                 |
| Observer 1                      | 82 (96)                         | 82 (96)                         | 82 (96)                         | 82 (96)                         | 83 (98)                         |
| Observer 2                      | 83 (98)                         | 84 (99)                         | 84 (99)                         | 83 (98)                         | 84 (99)                         |

Note. CS, colonoscopy. CS cata are numbers of segments without polyps. CT colonography data are numbers of true-negative segments. Numbers in parentheses are percentages (segment specificity). * One patient underwent CT colonography at 65 mAs.
Polyp sensitivity according to pelvic and abdominal location.—Table 3 and Figure 5 demonstrate the sensitivity for polyps 5 mm or larger stratified according to polyp location (pelvic or abdominal). Detection of polyps was slightly lower in the pelvic region than in the abdominal region. This difference was most evident at the lowest milliampere-second level. At 6.3 mAs, the difference between the abdominal and pelvic sensitivity was significant for observer 2. At 0.4 mAs, the difference was significant for both observers ($P < .05$).

![Figure 5](image-url)

**Figure 5.** Mean sensitivity for polyps 5 mm or larger (27 polyps in 15 patients) at five doses for all locations (x) and for abdominal (▲, 12 polyps) and pelvic (□, 15 polyps) regions separately. Overall sensitivity decreases slightly but remains 74% or more to 1.6 mAs and then decreases more sharply. Detection of abdominal and pelvic polyps slightly decreases. Only significant difference in pelvic polyp detection was between 100 and 0.4 mAs ($P < .05$).

**Table 3.** Polyp sensitivity for lesions ≥ 5 mm according to pelvic and abdominal localization at five dose levels (100 to 0.4 mAs; 12 to 0.05 mSv)

<table>
<thead>
<tr>
<th>Polyp sensitivity</th>
<th>CS</th>
<th>CT colonography</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>100 mAs*</td>
<td>25 mAs</td>
</tr>
<tr>
<td>Pelvic region §</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Observer 1</td>
<td>11 (92)</td>
<td>11 (92)</td>
</tr>
<tr>
<td>Observer 2</td>
<td>11 (92)</td>
<td>10 (83)</td>
</tr>
<tr>
<td>Abdominal region ‡</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Observer 1</td>
<td>12 (80)</td>
<td>10 (67)</td>
</tr>
<tr>
<td>Observer 2</td>
<td>11 (73)</td>
<td>10 (67)</td>
</tr>
</tbody>
</table>

Note. — CT colonography data are numbers of true-positive polyps. Numbers in parentheses are percentages (polyp sensitivity). CS, colonoscopy. CS data indicate polyp numbers. * One patient underwent CT colonography at 65 mAs. †Significant difference in polyp detection between abdominal and pelvic regions for observer 2 at 6.3 mAs and for both observers at 0.4 mAs ($P < .05$). ‡Ascending, transverse, and descending colon. §Cecum, sigmoid colon, and rectum. || Significant difference in polyp detection compared with 100-mAs data ($P < .05$).
In both regions, the sensitivity decreased slightly with decreasing milliampere-second level. Only the difference in pelvic polyp detection between 100 and 0.4 mAs was significant for both observers ($P < .05$).

**Interobserver analysis.**—Results of interobserver analysis are given in Table 4. The statistics for CT colonography were good at all milliampere-second levels, except for the lowest value for which the statistic was moderate.

**Table 4. Inter-observer analysis for CT colonography with five dose levels**

<table>
<thead>
<tr>
<th>Data</th>
<th>100 mAs*</th>
<th>25 mAs</th>
<th>6.3 mAs</th>
<th>1.6 mAs</th>
<th>0.4 mAs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kappa statistic (95% CI)</td>
<td>0.73 (0.59-0.87)</td>
<td>0.65 (0.51-0.80)</td>
<td>0.68 (0.52-0.83)</td>
<td>0.69 (0.54-0.85)</td>
<td>0.49 (0.32-0.66)</td>
</tr>
<tr>
<td>Number of concordant segments (%) †</td>
<td>78 (87)</td>
<td>74 (82)</td>
<td>76 (84)</td>
<td>77 (86)</td>
<td>67 (74)</td>
</tr>
</tbody>
</table>

* One patient underwent CT colonography at 65 mAs. †Total number, 90.

**Table 5. Mean patient interpretation times in CT colonography with five dose levels**

<table>
<thead>
<tr>
<th>Observer</th>
<th>100 mAs*</th>
<th>25 mAs</th>
<th>6.3 mAs</th>
<th>1.6 mAs</th>
<th>0.4 mAs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24'18&quot;</td>
<td>22'49&quot;</td>
<td>22'53&quot;</td>
<td>22'13&quot; †</td>
<td>23'50&quot;</td>
</tr>
<tr>
<td>2</td>
<td>21'05&quot;</td>
<td>19'29&quot;</td>
<td>19'15&quot; †</td>
<td>19'03&quot; †</td>
<td>23'16&quot; †</td>
</tr>
</tbody>
</table>

Note.—Observer 1; Observer 2. Data are minutes:seconds. Statistical differences in interpretation times between original dose (100 mAs) and simulated lower doses were assessed for each observer individually with paired-samples $t$ test. * One patient underwent CT colonography at 65 mAs. †$P < .05$ compared with original 100-mAs CT colonographic data.

**Interpretation time.**—Mean patient interpretation times for each observer are given in Table 5. Mean interpretation times at 6.3 mAs for observer 2 and at 1.6 mAs for both observers were significantly lower than those at 100 mAs ($P < .05$).

**Discussion**

Results in this feasibility study indicate that extremely low doses may suffice at CT colonography. This finding might serve other investigators who study the diagnostic value of very low–dose CT colonography in colorectal cancer screening. With doses down to 0.2 mSv, the mean sensitivity for polyps 5 mm or larger showed a slight but not significant decrease and remained at least 74%, and the interobserver agreement remained constant. Sensitivity values for polyps 5 mm or larger with radiation doses down to 0.2 mSv were within the ranges reported in previous studies (3–6) about the diagnostic accuracy of CT colonography.
The influence of dose on the detectability of polyps depends on their size, which therefore will play an important role in the determination of radiation dose. A significant decrease in sensitivity for polyps 5 mm or larger was found only at 0.05 mSv, whereas sensitivity for polyps 10 mm or larger did not decrease. Owing to the small number of polyps 10 mm or larger, however, we were not able to statistically assess the latter observation.

In the present feasibility study, we aimed to find the order of magnitude of the lowest dose that is compatible with acceptable polyp detection. To guarantee internal validity, we applied five doses in 15 patients to make sure that the differences in polyp visibility were purely a result of the differences in dose. A potential disadvantage of this setup is that memory bias may have been present. We applied three strategies to reduce this potential bias. First, we employed an interval of at least 4 weeks between two subsequent readings. Second, data for each segment were evaluated separately and in a random order to further reduce memory bias. Finally, the readings started with the lowest dose followed by successively higher doses. Because of the large difference between doses, it is extremely improbable that, even if the observer still had any memory of the previous reading, this information would assist interpretation of the new version with a lower noise level.

This study design has some disadvantages, particularly regarding the possibility of generalizing these findings to a clinical setting. Because the potential future role of CT colonography is in the selection of patients with at least one polyp of a certain size but not in the identification of each polyp, our outcome parameters do not directly apply to clinical practice. Also, because we primarily aimed to find the lowest dose compatible with acceptable polyp detection, a prerequisite for potential implementation of CT colonography, we confined our population to patients with polyps, and consequently patient specificity could not be calculated. It is conceivable, however, that the relative effect of dose reduction on segment specificity in the present study is comparable to that on patient specificity. Future studies, performed in a consecutive surveillance or screening population, that also include patients without polyps are required to establish the clinical value of very low-dose CT colonography in terms of patient sensitivity, specificity, and predictive values.

The number of false-positive findings decreased with decreasing dose in this study. The increased noise and the smoothing that was applied in the images obtained with the three lowest doses may have restrained observers from considering small irregularities as polyps.
In this study, both observers had a high number of false-positive findings, especially at 100-mAs and simulated 25-mAs CT colonography. This result appears to be at least partially caused by the unexpectedly high number of segments that were contaminated with fecal residue. Most false-positive lesions were smaller than 5 mm, but one observer detected a considerable number of false-positive lesions that were 5 mm or larger. Because these false-positive findings were confined to 15 of 70 segments without polyps 5 mm or larger, the segment specificity was still considerable (79%).

Although segment specificity for both readers was similar, the experienced abdominal radiologist had a much higher number of false-positive findings than did the research fellow. Because both observers had comparable experience in CT colonography, the cause of this discrepancy is not clear.

Pelvic polyp sensitivity was slightly lower than abdominal polyp sensitivity. This difference may be a result of the higher noise level in the pelvic region and the more difficult interpretation of lesions in the tortuous sigmoid colon. This difference was significant at the lowest dose. Hence, dose reduction may be more complicated in the pelvis. The consequences of this finding must be further elucidated, especially in view of the possibilities of state-of-the-art CT scanners to adjust the tube current to the scan region. For constant overall image quality, tube current must be adjusted to the girth of the patient (11,28).

We adjusted the image smoothing to the dose, as would be done in clinical practice. After smoothing, the 6.3- and 1.6-mAs images had a noise level similar to that in the 25-mAs images, at the expense of spatial resolution. The in-plane resolution of CT images is usually adjusted by the choice of the reconstruction filter. The amount of smoothing required could not be obtained with the reconstruction filters available on the multisectiion CT scanner. Therefore, additional filtering was obtained with spatial-domain filtering of the CT scans. Equivalent results have been obtained with either of these methods (29,30).

The lowest tube current times that were tested in this study (1.6 and 0.4 mAs) cannot yet be realized in clinical practice. Until recently, the possibility of CT scanning with very low doses was hampered by the presence of an electronics noise floor in the preamplifiers of the CT detectors, which increased the noise in the CT scans disproportionally at the lowest doses (31). CT scanners that were introduced during the past year profit from the development of improved detector technology, and scans can be acquired at a minimum of 3–5 mAs. Further reduction of milliampere-second level is technically possible and, as findings in the present study indicate, may be
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clinically useful.

The results of our study concur with those in other studies and extend them to substantially lower doses. Cohnen and colleagues (18) compared sensitivity and specificity with medium and very low-dose scan protocols (12 and 1 mSv, respectively) in two groups of patients suspected of having colorectal polyps or cancer. They found that the performance for polyps 5 mm or larger was similar: 89% (eight of nine polyps) and 94% (17 of 18 polyps) with the medium and very low doses, respectively. Iannaccone and colleagues (19) determined the accuracy for CT colonography performed with a 2-mSv scan protocol. They found excellent sensitivity and specificity, with detection of six of six polyps larger than 10 mm, nine of nine colorectal cancers, and no false-positive findings. These data are similar to previously reported results about the accuracy of CT colonography. A drawback of both studies is that the investigators did not compare different doses in identical patients, which means that other factors could account for the similar sensitivity and specificity that were observed. Our approach enables such a comparison without the drawbacks of acquisition of CT scans in the same patients at several doses and thus exposure to additional ionizing radiation.

Rigorous reduction of radiation dose may hamper the potential benefit of CT colonography to depict extracolonic findings because the image quality of solid organs is substantially deteriorated. However, the primary aim of CT colonography is the selection of patients with polyps, and therefore we did not take extracolonic findings into account.

The burdensome bowel preparation that was used in the present study may be redundant in the near future. Results of recent studies (32,33) show that the addition of contrast agents to several low-fiber diets enables distinction of bowel wall from bowel contents. In another study (34), intravenous contrast media were used to improve the conspicuity of the bowel wall and medium-sized polyps. The use of contrast agents may be incompatible with very low-dose CT because of the relatively low contrast between contrast material–enhanced and unenhanced structures.

Although CT colonography holds promise for colorectal cancer screening, the prospect of exposure of large numbers of asymptomatic individuals to intermediate doses of ionizing radiation, probably more than once in their lives, may hamper implementation in screening programs.

Exposure to ionizing radiation may induce cancer in the exposed individual after a latent period of up to a few decades. The risks of effective doses in the magnitude presently employed for CT colonography (4–12 mSv) remain uncertain (35) but cannot
be disregarded, and therefore it is generally agreed that radiologists should aim for the lowest dose required for the diagnostic task.

In the case of CT scans obtained with an effective dose of approximately 0.2 mSv, which may be feasible on the basis of findings in the present study, the problems with exposure to ionizing radiation may be substantially reduced. Compared with the radiation doses of 4–12 mSv that are used routinely today (11), future doses would be reduced 20- to 60-fold.

Generalizability of findings in the present study may be limited because we employed a primary three-dimensional display mode as opposed to the primary two-dimensional display mode used by the majority of researchers. Although the two-dimensional images were less affected by the dose reduction than were the three-dimensional images, the effects of dose reduction on primary two-dimensional performance remain to be determined.

We conclude that findings in this feasibility study indicate that the effective dose in CT colonography can probably be considerably decreased without substantial impairment of detection of polyps 5 mm or larger and interobserver agreement. Future studies are needed to investigate the clinical value of CT colonography at a very low dose in a cohort of consecutive surveillance or screening patients.
References


