CT colonography as surveillance technique for patients at increased risk for colorectal cancer

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Citation for published version (APA):
Jensch, S. (2009). CT colonography as surveillance technique for patients at increased risk for colorectal cancer.

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Chapter 2

Image Quality and Patient Acceptance of Four Regimen with Different Amounts of Mild Laxatives for CT Colonography

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Dennis Pot
Jan Peringa
Shandra Bipat
Jasper Florie
Rogier E. van Gelder
Jaap Stoker

Abstract

**Purpose:** The purpose of our study was to prospectively evaluate image quality and patient acceptance of CT colonography (CTC) with fecal tagging using different levels of catharsis.

**Methods:** Forty consecutive increased-risk patients were randomized. Group 1 received orally 20 mg of bisacodyl, group 2 received 30 mg of bisacodyl, group 3 received 20 mg of bisacodyl and 8.2 g of magnesium citrate, and group 4 received 30 mg of bisacodyl and 16.4 g of magnesium citrate. All patients used a 2-day low-fiber diet and received diatrizoate meglumine and barium for fecal tagging. One reviewer blindly scored subjective image quality (fecal tagging, amount of residual feces [liquid or solid], luminal distention, and image readability) on a 5- to 6-point scale using a 2D review technique. The mean and SD of attenuation of tagging were measured as well as the relative SD as a measure of homogeneity. Furthermore, patient acceptance (burden related to diarrhea, abdominal pain, flatulence, and overall burden) was evaluated. Ordinal regression, generalized estimating equations, and parametric and nonparametric tests were used for analysis.

**Results:** Image readability was evaluated as good or excellent in all examinations except one in group 2 (non-diagnostic) and two in group 3 (moderate). Group 2 contained more feces than group 4 ($p = 0.04$). With regard to mean attenuation and homogeneity of tagging, no significant differences were observed between groups. Group 4 experienced more severe diarrhea than groups 1 and 2 and higher overall burden than groups 1 and 3 ($p < 0.042$).

**Conclusion:** The mildest preparation with 20 mg of bisacodyl provided good image quality of CTC images. Increasing the amount of laxatives did not improve image quality or tagging characteristics but was associated with a lower patient acceptance.
Introduction

CT colonography (CTC) is being investigated as a possible screening technique for the detection of colorectal polyps and cancer [1–5]. However, the requisite cathartic bowel preparation, which is often described by patients as the most burdensome aspect of colonic examinations [6–8], might diminish patients’ willingness to participate in a screening program [9–11]. Labeling of fecal material with a contrast agent (fecal tagging) has enabled the use of limited bowel preparation regimens containing no or only limited amounts of laxatives [12]. So far, feasibility studies investigating CTC with reduced catharsis have shown promising results with regard to image quality and patient acceptance [13–17]. In addition, one large accuracy study that used no cathartics has been published that reported excellent results with regard to polyp detection [18].

For labeling fecal material, three types of tagging agents are available: barium and nonionic and ionic iodinated contrast agents. Barium is traditionally used for solid fecal matter tagging and iodinated contrast agents are used to tag residual fluid. Furthermore, a variety of mild laxatives, for example, bisacodyl sodium or magnesium citrate [13, 14], can be added to reduce the amount of fecal matter in the colon. At present, no consensus exists about which contrast agent should be used and whether mild cathartics should be added to the tagging regimen, and if so, in what dose [19].

We hypothesized that a higher level of catharsis would improve image quality but reduce patient acceptance. Our objective was to determine the optimal dosage of laxatives for CTC with limited bowel preparation with regard to both image quality and patient acceptance. Therefore, we compared image quality and patient acceptance between four regimens with increasing levels of mild catharsis, using bisacodyl and magnesium citrate as laxative agents. Although some studies have compared image quality of CTC with and without laxatives [20, 21], to our knowledge, our study is the first that has investigated the effect of different amounts of mild laxatives in CTC.

Materials and Methods

Study population

Forty consecutive adult patients with an increased risk for colorectal cancer (i.e., a personal or family history of colorectal polyps or cancer) were included in this study.
between October 2004 and January 2005. All patients were scheduled to undergo a conventional colonoscopy for polyp detection at the endoscopic departments of the Academic Medical Center or the Onze Lieve Vrouwe Gasthuis. Exclusion criteria were a personal history of inflammatory bowel disease or familial adenomatous polyposis, prior allergic reaction to an iodine-containing contrast agent, colorectal polyps or cancer at prior endoscopy that were not removed, or participation in a research project that involved ionizing radiation within 12 months preceding the CTC examination. On the day of the CTC examination, patients were asked to indicate whether they had symptoms of colorectal disease (i.e., abdominal pain, hematochezia, or altered bowel habits) and if so, which symptoms were present. No formal power calculation was performed in this feasibility study and, for practical reasons, 40 patients were studied. The institutional review board of both hospitals gave approval for this feasibility study of 40 patients. All patients gave written informed consent.

Bowel Preparation
A low-fiber diet was prescribed for all patients for 2 days before the CTC examination. No specific meal kit was used. Through a customized computer program, patients were randomized into one of four groups using a randomization lock design (Table 1).

<table>
<thead>
<tr>
<th>Group</th>
<th>Barium Sulphate\textsuperscript{a} (mL) (40% w/v)</th>
<th>Diatrizoate Meglumine\textsuperscript{b} (mL) (200 mgI/mL)</th>
<th>Bisacodyl\textsuperscript{c} (mg)</th>
<th>Magnesium Citrate\textsuperscript{d} (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>80</td>
<td>110</td>
<td>20</td>
<td>-</td>
</tr>
<tr>
<td>II</td>
<td>80</td>
<td>110</td>
<td>30</td>
<td>-</td>
</tr>
<tr>
<td>III</td>
<td>80</td>
<td>110</td>
<td>20</td>
<td>8.2</td>
</tr>
<tr>
<td>IV</td>
<td>80</td>
<td>110</td>
<td>30</td>
<td>16.4</td>
</tr>
</tbody>
</table>

Note—Dash (—) indicates not applicable.
\textsuperscript{a}Dosage: 2 days before CTC, 20 mL at dinner and 1 day before CTC, 20 mL at breakfast, lunch, and dinner.
\textsuperscript{b}Dosage: 1 day before CTC, 10 mL at breakfast and 20 mL at lunch and dinner; on the day of CTC, 60 mL at breakfast.
\textsuperscript{c}Dosage: 16 hours before CTC, 10 mg of orally administered bisacodyl for groups 1 and 3 and 20 mg for groups 2 and 4; on the day of CTC, all groups received 10 mg of bisacodyl orally at breakfast.
\textsuperscript{d}Dosage: 18 hours before CTC, groups 3 and 4 received magnesium citrate in the displayed dose.

Preparations contained solely orally administered bisacodyl or bisacodyl in combination with magnesium citrate (LoSo Prep, E-Z-EM) as laxative agents, and the
extent of catharsis gradually increased from group 1 to group 4. We did not include a laxative-free regimen because such regimens have been shown to result in insufficient image quality [20, 21]. The most extensive preparation (group 4) contained a combination of bisacodyl and magnesium citrate in a dosage that is commercially available as a preparation kit for CT colonography (LoSo Prep) and is considered a mild preparation [13, 14]. Tagging consisted of barium sulfate, 40% weight per volume (Tagitol V, E-Z-EM) and diatrizoate meglumine with an iodine concentration of 200 mg/mL. Patients were not informed of the content of the other regimens.

**CT Colonography**

The CTC examination was performed in the supine and prone positions on an Mx8000 4-MDCT scanner (Philips Medical Systems) with the following parameters: 120 kV; collimation, 4 × 2.5 mm; rotation time, 0.75 second; pitch, 1.25; slice thickness, 3.2 mm; and reconstruction interval, 1.6 mm. Patients with a circumference < 103 cm were scanned with 50 mAs (n = 15); patients with a circumference > 103 cm, with 70 mAs (n = 25). A total of 20 mg of butyl scopolamine bromide (Buscopan, Boehringer Ingelheim) (n = 22) or, if contraindicated, 1 mg of glucagon hydrochloride (GlucaGen, Novo Nordisk) (n = 17) was administered IV immediately before scanning. In one patient neither was administered because of contraindications. On average, 4 L of carbon dioxide (CO2) was insufflated via an automatic insufflator (PROTOCO2L, E-Z-EM) to achieve adequate distention. The time that patients spent in the CT room was recorded with a stopwatch.

**Conventional Colonoscopy**

Colonoscopy was performed 4–30 days (mean, 17 days) after CTC. Bowel preparation for colonoscopy consisted of 3 (n = 2), 4 (n = 36), or 6 L (n = 2) of polyethylene glycol–electrolyte solution (Klean-Prep, Helsinn Birex Pharmaceuticals) administered the day before the examination. Patients received midazolam (n = 28), fentanyl (n = 20), or alfentanil (Rapifen, AstraZeneca) (n = 6) on request. Buscopan was administered IV to all patients. The colonoscopy was performed either by an experienced gastroenterologist or surgeon or by a resident under the direct supervision of a staff member. During the examination, a research nurse involved in our study was present.
Chapter 2

Outcome Parameters

*Subjective image quality*

The CTC data were evaluated by a research fellow in CTC who was blinded to all clinical data, including the bowel preparation used. The reviewer had a prior experience of 150 non-tagged cathartic-prepared CTC examinations with colonoscopic verification.

A primary 2D evaluation technique (axial views) was applied using multiplanar reformatted (MPR) images and 3D endoluminal views for problem solving (ViewForum 5.1, Philips Medical Systems). No electronic cleansing software was

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**Figure 1.** Axial multiplanar reformatted coronal and endoluminal 3D images show subjective evaluation in four different patients with various grades of fecal tagging

A. In 50-year-old man with abdominal pain and family history of colorectal cancer, reviewer evaluated fecal tagging as excellent.
B. In 51-year-old woman with history of colorectal polyps, reviewer evaluated fecal tagging as good.
C. In 61-year-old man with history of colorectal cancer, reviewer evaluated fecal tagging as moderate.
D. In 72-year-old man with history of colorectal cancer, reviewer evaluated fecal tagging as poor.
applied. The reviewer filled out a standardized questionnaire for every examination with regard to image quality. Table 2 displays the scoring system used by the reviewer. The image quality parameters of fecal tagging (Fig. 1), luminal distention, amount of fecal residue (combined estimation for liquid and solid feces), and image readability were scored by the reviewer for the complete (supine and prone together) examination. This evaluation was considered the subjective image quality assessment on a per-patient basis. The same image quality parameters were again evaluated on a per-segment basis. To this end, the colon was divided in six segments: cecum; ascending, transverse, descending, and sigmoid colon; and rectum. Fecal tagging and the amount of fecal material were evaluated only with the patient in the supine position because we presumed these parameters would not be influenced by a position change. However, because alteration of the position of the patient might substantially influence distention of different colonic segments [22, 23], luminal distention and segmental image readability were again evaluated with the patient in the prone position. Furthermore, to examine the effect of increasing catharsis on the consistency of fecal material, the reviewer scored the ratio between feces with a solid consistency and feces with a liquid consistency. This was performed on a per-segment basis with the patient in the supine position. A 5-point scale was applied: 1, 0–20% solid; 2, 21–40% solid; 3, 41–60% solid; 4, 61–80% solid; and 5, 81–100% solid. If no stool was present in a segment, no evaluation of consistency was performed for that particular segment.

**Numeric evaluation of degree and homogeneity of tagging**

To evaluate the quality of fecal tagging, the mean and SD of attenuation of tagged material (in Hounsfield units) were measured on seven separate slices that were randomly selected by a computer program (Windows Excel 2002, Microsoft) for every patient. To this end, a resident in the fourth year of training, who was blinded as to the preparation used, placed a region of interest (ROI) of at least 60 mm² in the area that contained the most fecal material on the randomly picked axial slices. The resident recorded whether the ROI was placed in liquid stool, stool adherent to the colon wall, or solid stool. The mean and SD of attenuation values within the ROIs were then calculated by our CTC software (ViewForum 5.1) (Fig. 2). If not enough fecal material was present to draw an ROI, the randomization program provided another slice for evaluation. The SD of attenuation values of tagged material is a measure of homogeneity. However, because the mean attenuation of tagging can vary considerably among patients, we considered the relative SD (SD / mean) to be
a better measure of homogeneity. After all, by adapting the window width when viewing images, tagging with a larger mean attenuation value and a large SD may have a similar visual appearance to tagging with a smaller attenuation value and a proportionally smaller SD. Furthermore, separate assessments were performed for solid, adherent, and liquid feces.

**Interpretation time**

The time needed to interpret a complete examination for polyp detection, excluding report time and image quality evaluation, was recorded with a stopwatch by the reviewer. Because of the limited number of patients and the expected low prevalence of polyps in our cohort, performance characteristics were not part of our study design and are not discussed in this article.

**Patient experience**

Patients were asked to fill out a questionnaire on the day of the CTC examination with regard to the burden and side effects of the CTC preparation—that is, flatulence, abdominal pain, and diarrhea—as well as the discomfort caused by the intake of contrast material and laxative agents on a 5-point scale (Table 2). To understand if the everyday bowel habits of patients were of influence on image quality parameters, patients were asked to fill out their normal frequency of defecation: 1, more than one defecation per day; 2, once per day; 3, once per 2 days; 4, once in 3 days; 5, less than one defecation per 3 days; and 6, less than one defecation per 5 days. On the
### Table 2. Scales Used by Observer to Rate Image Quality and by Patients to Rate Burden and Preference

<table>
<thead>
<tr>
<th>Observer</th>
<th>Scale</th>
</tr>
</thead>
</table>
| Fecal tagging<sup>a</sup> | a = Poor, not interpretable  
| | b = Moderate, diagnostic with untagged feces < 10 mm  
| | c = Good, diagnostic with untagged feces < 6 mm  
| | d = Very good, diagnostic without limitations  
| Presence of feces<sup>a</sup> | a = Large amount of feces, segment fully filled  
| | b = Moderate amount of feces, ≈ 50% of lumen filled  
| | c = Small amount of feces  
| | d = Only layer on wall  
| | e = No feces at all  
| Luminal distention<sup>a,b</sup> | a = Collapsed  
| | b = Poorly distended  
| | c = Only moderately distended, but segment is distended over its full length  
| | d = Good  
| | e = Very good  
| Image readability<sup>a,b</sup> | a = Poor, not diagnostic  
| | b = Moderate, diagnostic for lesions ≥ 10 mm  
| | c = Good, diagnostic for lesions ≥ 6 mm  
| | d = Excellent, no limitations  

<table>
<thead>
<tr>
<th>Patients</th>
<th>Scale</th>
</tr>
</thead>
</table>
| Burden caused by intake of bisacodyl, magnesium citrate, barium sulfate, diatrizoate meglumine | a = None  
| | b = Mild  
| | c = Moderate  
| | d = Severe  
| | e = Extreme  
| Side effects: diarrhea, flatulence, abdominal pain, overall burden | a = None  
| | b = Mild  
| | c = Moderate  
| | d = Severe  
| | e = Extreme  
| Most burdensome preparation | CT colonography (CTC) or conventional colonoscopy  
| Most burdensome examination | CT colonography (CTC) or conventional colonoscopy  
| Most burdensome event | Bowel preparation prior to conventional colonoscopy  
| | Limited bowel preparation prior to CTC  
| | CTC examination  
| | Conventional colonoscopy examination  
| Preference for CTC or conventional colonoscopy examination in the future | Definitely CTC  
| | Probably CTC  
| | Possibly CTC  
| | Indifferent  
| | Possibly conventional colonoscopy  
| | Probably conventional colonoscopy  
| | Definitely conventional colonoscopy  

<sup>a</sup>Subjective image quality parameters were scored per patient and per segment in the supine position.  
<sup>b</sup>Luminal distention and image readability were again evaluated on a per-segment basis in the prone position.
day of the colonoscopy, patients filled out a questionnaire with regard to the burden associated with the bowel preparation for colonoscopy (Table 2).

Patient preference
Five weeks after colonoscopy, patients were sent a questionnaire in which they were asked which preparation had been most burdensome (CTC or conventional colonoscopy) and which examination (CTC or conventional colonoscopy) they would prefer in the future, and they were asked to indicate the most burdensome event of both examinations (Table 2). The patient preference and experience questionnaires were designed by the department of social medicine and had previously been used in two studies that were performed in our institution [7, 24].

Statistical Analysis
Subjective image quality
With regard to the per-patient analysis, possible differences in image quality parameters between the four preparations were assessed using ordinal regression analysis. In this analysis, first the preparation with the highest regression coefficient was determined; this was subsequently used as the reference group. With regard to the per-segment analysis, ordinal regression analysis was applied using generalized estimating equations (GEE) to revise the data clustering and dependency [25]. This was done because more than one segment was obtained from each patient. The link function was set at log link, and an independent working correction matrix was used. Furthermore, associations between normal defecation frequency and subjective image quality parameters were tested with the chi-square test. If significant associations were present, additional ordinal regression analyses using GEE for revising the patient’s normal defecation frequency were performed. Associations between the subjective image quality parameters (e.g., association between fecal tagging and the amount of residual feces) within each group were assessed using the chi-square test.

Numeric evaluation of degree and homogeneity of tagging
Because more than one measurement of Hounsfield units and SD was obtained from each patient, linear regression analysis was applied using GEE to revise the data clustering and dependency. Furthermore, ROIs were placed at random and were not evenly distributed among segments. This might have resulted in differences in measured homogeneity because of the physiologic variation of mean tagging
attenuation within a given patient due to the normal dehydrating action of the colon. Therefore, the GEE analysis was adjusted to correct for this segmental distribution. Furthermore, because liquid material tends to be more homogeneously tagged than solid material, the GEE analysis was adjusted to correct for stool consistency (solid, adherent, or liquid feces). For each group, estimates of means with corresponding standard errors could be calculated from the results (intercept and slopes) obtained by the analysis.

**Patient experience and preference**

Differences in patient experience (burden) were analyzed using ordinal regression analysis and the preparation with the lowest regression coefficient (most burdensome) as the reference group. The chi-square test was used to test for significant differences in patients’ indications of the most burdensome preparation and examination (CTC or conventional colonoscopy) between groups. Patient preference for either CTC or colonoscopy was tested using the chi-square test after the data were first dichotomized as preference for CTC versus preference for colonoscopy.

**Interpretation time**

Differences in interpretation times for the different preparations were tested for significance using the independent samples Student’s t test. Statistical analyses were performed with SPSS version 12.0.2 for Windows (SPSS) and SAS version 8.02 for Windows (SAS Institute). The Proc Genmod command was used to apply the generalized estimating equations. A p-value of < 0.05 was considered to indicate a statistically significant difference.

**Results**

All patients included in this study accepted randomization. Eleven patients were randomized into group 1, 10 patients into group 2, 10 patients into group 3, and nine patients into group 4. Twenty-seven patients were men (67.5%) and 13 patients were women (32.5%), with an average age of 62 years (age range, 40–83 years). Fourteen (35%) patients had symptoms (abdominal pain, 6; hematochezia, 4; and altered bowel habits, 4), and 26 (65%) patients were asymptomatic. Thirty-three (83%) patients had a personal history of colorectal polyps (n = 21), cancer (n = 6), or both (n = 6). A total of 11 patients had undergone surgery for a colorectal cancer:
right-sided hemicolectomy \((n = 1)\), transverse colectomy \((n = 2)\), low anterior resection \((n = 7)\), total mesorectal excision \((n = 1)\). Thirty of 38 patients who filled out the questionnaire with regard to bowel frequency had a defecation frequency of one defecation or more per day, five patients had a defecation frequency of once in 2 days, two patients (groups 2 and 3) had a frequency of once in 3 days, and one patient had a bowel frequency of once in 3–5 days (group 2). Because one patient had undergone a hemicolectomy, a total of 476 bowel segments were available for analysis (per position: group 1, 66 segments; group 2, 58; group 3, 60; and group 4, 54 segments). The average room examination time for CTC was 15 minutes.

**Subjective image quality**

On a per-patient basis \((n = 40)\), no significant differences were found between groups with regard to image quality. All examinations were evaluated as good (diagnostic for lesions \(\geq 6 \text{ mm}\)) or excellent (diagnostic with no limitations) image readability. Only one examination (group 2) was of nondiagnostic value (because of poor distention) and two examinations (group 3) were of moderate image readability (because of moderate fecal tagging) (Table 3). Within each group, a higher degree of homogeneity was significantly associated with better image readability \((p < 0.006)\).

**Table 3.** Overall Image Readability of 40 Complete (Supine and Prone) CT Colonography Examinations

<table>
<thead>
<tr>
<th>Group</th>
<th>Excellent; No Limitations</th>
<th>Good; Diagnostic for Lesions (\geq 6 \text{ mm})</th>
<th>Moderate; Diagnostic for Lesions (\geq 10 \text{ mm})</th>
<th>Poor; Not Diagnostic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 ((n=11))</td>
<td>5</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2 ((n=10))</td>
<td>3</td>
<td>6</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>3 ((n=10))</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>4 ((n=9))</td>
<td>5</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Note—Data are number of examinations that were subjectively evaluated by the reviewer.*

For group 2, poorer distention was associated with decreased image readability \((p = 0.002)\). On a per-segment basis, significantly more residual feces was present in group 2 in comparison with group 4 \((p = 0.04)\). No other significant differences in image quality were found between groups (Fig. 3). Fecal material was significantly more liquid in group 4 in comparison with groups 1, 2, and 3 \((p = 0.004, p = 0.002, \ldots)\).
and \( p < 0.001 \) (Fig. 4). A significant association was observed between daily bowel habits and the amount of residual feces in the colon for groups 2 and 3 \( (p < 0.0001) \). In other words, a lower defecation frequency in normal life was associated with a higher amount of residual feces in our study. Subsequently, when the normal defecation frequency of patients was included in the GEE analysis, the finding that group 2 contained more residual feces than group 4 was no longer significant \( (p = 0.160) \).

**Numeric evaluation of degree and homogeneity of tagging**

The degree of tagging, expressed as the mean attenuation of tagged material, decreased when more laxatives were used (Table 4); however, this decrease was not statistically significant (all \( p \geq 0.253 \)). A gradual decrease in mean SD of pixel values was also found from group 1 to group 4. This decline, however, was not significant between groups (all \( p \geq 0.067 \)). Furthermore, the relative SD (SD / mean) did not differ significantly among groups (all \( p \geq 0.157 \)), indicating no difference in homogeneity of tagging among groups.

![Figure 3. Graphs show subjective image quality scores on per-segment basis](image)

Fecal tagging and amount of feces were scored on supine images (for group 1, 66 segments; group 2, 58 segments; group 3, 60 segments; and group 4, 54 segments). Distention and diagnostic readability were scored on supine and prone images (132, 120, 210, and 108 segments, resp.). Group 2 performed significantly poorer with regard to amount of residual feces in comparison with group 4 \( (p = 0.04) \).
Regardless of the preparation, the relative SD was significantly higher for solid feces (0.22) versus adherent (0.16) or liquid (0.14) feces, showing that tagging was less homogeneous for solid feces than for adherent stool ($p = 0.008$) or liquid feces ($p = 0.001$) (Table 5).

**Interpretation time**

The mean interpretation time for group 1 was 16 minutes, for group 2 was 24 minutes, for group 3 was 26 minutes, and for group 4 was 21 minutes (all $p \geq 0.107$).

**Patient Experience**

All patients experienced diarrhea except for three patients in group 2. The burden of diarrhea was evaluated as none or mild by six patients (55%) in group 1, six patients (60%) in group 2, four patients (40%) in group 3, and one patient (11%) in group 4. Diarrhea was considered significantly more burdensome in group 4 than in groups 1 ($p = 0.042$) and 2 ($p = 0.031$) but not compared with group 3 ($p = 0.179$).

With regard to abdominal pain and flatulence, no significant differences were found among groups. With regard to abdominal pain ($n = 37$), one patient in group 4 had severe abdominal pain, and two patients (groups 2 and 4) had moderate abdominal pain. The remaining patients had little ($n = 6$) or no ($n = 28$) pain. With regard to flatulence ($n = 37$), one patient in group 4 experienced a severe burden, one patient in group 2 had a moderate burden, and the other patients experienced little ($n = 5$) or no ($n = 30$) burden.
The total burden of the bowel preparation was rated as none or mild by all patients (100%) in group 1, nine (90%) in group 2, eight (80%) in group 3, and five (55%) in group 4—a significantly higher total burden in group 4 than in groups 1 (p = 0.002) and 3 (p = 0.02). No significant difference (p = 0.082) was found between groups 2 and 4, most likely because one patient in group 2 rated the CTC bowel preparation as extremely burdensome. This patient stated, before the CTC preparation, an explicit preference for the colonoscopy preparation because in his opinion that preparation was simpler and shorter. Excluding this patient, a significantly lower overall burden (p = 0.04) was found for group 2 in comparison with group 4. Most patients experienced no or only a mild burden with regard to the intake of barium (32/34),
diatrizoate meglumine (36/40), bisacodyl (34/37), or magnesium citrate (9/15), with no significant differences between the groups.

### Patient Preferences

Except four patients (one in group 2 and three in group 3), all patients found colonoscopy a more burdensome examination than CTC. If patients were asked what examination they would prefer in the future, most patients (30/40) indicated a preference for CTC, two patients were indifferent, and eight patients preferred conventional colonoscopy (Fig. 5). The reasons patients preferred colonoscopy were: direct polypectomy ($n = 4$), shorter preparation time ($n = 2$), false-positive CTC ($n = 1$), and no particular reason ($n = 1$). No significant differences in preference were observed among the groups. All (100%) patients in group 1, nine (90%) patients in group 2, eight (80%) in group 3, and seven (78%) patients in group 4 preferred CTC bowel preparation over the polyethylene glycol preparation, with no significant differences among groups ($p = 0.054$). In all groups, most patients evaluated the

### Table 5. Tagging characteristics for stool consistency regardless of the preparation

<table>
<thead>
<tr>
<th></th>
<th>Mean (HU)</th>
<th>SD</th>
<th>Relative SD (SD/mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solid consistency</td>
<td>737</td>
<td>143$^a$</td>
<td>0.22$^b$</td>
</tr>
<tr>
<td>Adherent consistency</td>
<td>688</td>
<td>97</td>
<td>0.16</td>
</tr>
<tr>
<td>Liquid consistency</td>
<td>631</td>
<td>79</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Note—Data in parentheses are number of measurements.

$^a$ SD was significantly higher for solid than for adherent ($p = 0.041$) or liquid ($p = 0.005$) feces.

$^b$ Relative SD was significantly higher for solid than for adherent ($p = 0.008$) or liquid ($p = 0.001$) feces.

### Table 6. Most Burdensome Event for 40 Patients

<table>
<thead>
<tr>
<th>Group</th>
<th>CTC Bowel Preparation</th>
<th>CTC Examination</th>
<th>Conventional Colonoscopy Bowel Preparation</th>
<th>Conventional Colonoscopy Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>1</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>1</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>0</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>

Note—Appraisal by patients 5 weeks after CT colonography (CTC) and conventional colonoscopy. Most patients ($n = 30$) indicated the bowel preparation for colonoscopy as the most burdensome event regardless of the bowel preparation used for CTC.
bowel preparation for colonoscopy \((n = 30)\) or colonoscopy itself \((n = 5)\) as the most burdensome event, with no significant differences among the groups (Table 6).

### Discussion

In this feasibility study regarding image quality and patient acceptance, we investigated four different dosages of mild laxatives, consisting of bisacodyl (a bowel stimulant) and magnesium citrate (a hyperosmotic saline laxative), to prepare patients for CTC. Our results showed good to excellent image readability of CTC examinations \((37/40)\) regardless of the preparation used. Increasing the amounts of laxatives did not lead to a higher attenuation of tagging or to more homogeneous tagging, and subjective image quality did not show significant improvement. A higher dosage of laxatives was significantly associated with a higher burden of diarrhea and a higher overall burden of the bowel preparation. Nevertheless, irrespective of the amount of laxatives for CTC, the majority of patients \((35/40)\) preferred the bowel preparation for CTC over the cleansing laxative bowel preparation (polyethylene glycol) for colonoscopy.

In two previous studies, the same or a higher dose of magnesium citrate (without bisacodyl) as used in our group 4, was used; both reported significantly better image quality of CTC images compared with images made without the use of laxatives [20, 21]. Magnesium citrate liquefies residual feces and decreases the amount of remaining feces. This is associated with better readability [21] and can be expected to lead to increased homogeneity of tagged material. In concordance with these
studies, we expected that image quality would gradually improve in our study and be best with group 4.

In our study, however, a higher level of catharsis resulted in neither better image quality nor improvement of tagging characteristics (subjective or numeric). Our data showed that residual feces in group 4 was more liquefied compared with the other groups (all $p \leq 0.004$), but the relative SD (SD / mean) did not decrease, indicating that homogeneity did not improve. A decline, although not significant ($p \geq 0.253$), of the mean attenuation of the tagged material from group 1 to group 4 was observed that we did not anticipate. The lower attenuation values in groups with more catharsis might be explained because lower concentrations of contrast agent were present as a result of dilution caused by the hyperosmotic effect of magnesium citrate.

Regardless of the preparation, solid feces was less homogeneously tagged than liquid stool. However, we believe that homogeneity of solid feces was still satisfactory in all groups. Attenuation of solid feces was high (group 1, 1,030 H; group 2, 634 H; and group 3, 485 H) with relatively small SDs (215, 140, and 74, respectively) and nearly constant relative SDs (0.18, 0.21, and 0.23, respectively). As a result, the lowest attenuation value of tagged solid material was still well above soft-tissue density in all groups.

Most segments (88%) contained no or only small amounts of feces. Furthermore, no decrease in the amount of fecal material was observed using a higher dose of laxatives. This is in contrast with the results of Dachman et al. [21], who found no feces in only 65% of segments using magnesium citrate. That we used a combination of barium and diatrizoate meglumine for tagging purposes instead of only barium might explain this difference. Probably the laxative side effect of diatrizoate meglumine combined with (small amounts of) laxatives caused relatively clean colons with good homogeneity of tagged feces.

Increasing the amounts of laxatives did not improve subjective image quality but did increase the burden perceived by patients. In our study, most patients experienced diarrhea, regardless of the preparation used. These observations are not in line with the previously discussed study by Zalis et al. [20]. In that study, only one of 22 patients reported mild transient diarrhea after preparation with magnesium citrate. Two important differences between the studies may explain this discrepancy. First, we used ionic iodinated contrast material, which is known to have a strong osmotic effect, instead of a nonionic contrast agent. Second, in our study, all patients

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received bisacodyl, whereas in the Zalis et al. study, no bisacodyl was administered at all. It is likely that a combination of both factors led to some degree of diarrhea. Although diarrhea was present in all preparations, the burden of diarrhea and the overall burden of the preparation significantly increased with higher doses of laxatives. In fact, one could argue whether laxatives should be added at all to the preparation if ionic contrast agents are used in high concentrations. At the time of the writing of this article, we no longer add any form of laxatives to the preparation, and we believe this has not impaired the image quality of CTC.

An interval of 5 weeks was applied after colonoscopy to ask patients about their preference because the memory of adverse reactions may decrease over time [7, 8, 24]. The majority of patients (75%) preferred CTC as a colorectal examination and considered the polyethylene glycol–electrolyte solution for colonoscopy the most unpleasant factor (75%). In our institution, this bowel preparation is used by the gastroenterologists for all patients because it is safe to use and rigorously cleans the colon. Other bowel preparations for colonoscopy, such as an osmotic laxative ([sodium phosphates solution] Phospho-soda, Fleet), are considered more patient-friendly [26, 27]. Had these been used in our study, they might have caused a shift in patient preference toward colonoscopy. A disadvantage of Phospho-soda is that it can cause electrolyte imbalance and is contraindicated in patients with congestive heart failure or renal failure [28, 29].

Several limitations of our study must be considered. A limited cohort of 40 patients, randomized into four groups, participated in this study. Despite the relatively low numbers of patients per group, we did find a significantly higher patient burden with increasing laxative dosage. With regard to image quality, no trend of improvement in quality was observed with more catharsis. However, in group 2, segments contained significantly more feces compared with group 4. This was mainly attributed to the fact that two of the three patients in our study with a relatively low defecation frequency in normal life were placed in group 2. Despite more feces present in the colon, image readability of the examinations was not significantly affected. Although our data are limited, this might suggest that with adequate tagging, patients with bowel habits of one defeation in 3–5 days can be prepared with minimal amounts of laxatives without affecting image quality. Furthermore, all patients without diarrhea (n = 3) were in group 2. Patients were not asked about compliance with the preparation. Because non-compliance could have contributed to more residual feces in group 2 but could also provide a possible explanation for the moderate image quality in two patients in group 3, we considered that a limitation of our study.
Furthermore, only one observer subjectively evaluated all data on image quality. It is possible that another observer would rate the data differently. Another possible qualifier is that we did not include a full catharsis regimen as a reference standard to which the studied preparations were compared. However, we believe that for this study a clinically relevant scoring system was constructed with regard to image quality of the examinations: using classifications as not diagnostic, diagnostic for all lesions, diagnostic for lesions ≥ 6 mm, or only diagnostic for lesions ≥ 10 mm.

The experience of the reviewer before our study consisted of 150 cathartic CTC examinations, and consequently image quality of these examinations served as a reference standard for the reviewer. With regard to patient experience, the bowel preparation used for colonoscopy in our study was a full cathartic bowel preparation using a polyethylene glycol–electrolyte solution that can also be used for CTC. Most patients in all groups indicated the colonoscopy preparation as more burdensome when compared with the CTC bowel preparation.

We used an iodine-based contrast medium for fecal tagging in addition to barium. Some investigators prefer using only barium because of the side effects and possible adverse reactions to iodine-based contrast agents [10]. However, we believe that a combination of both contrast agents resulted in adequate tagging of both solid and liquid feces as stated in other studies [2, 29]. Although the laxative side effect of an iodine-based contrast agent will probably increase the patient burden in some way, an advantage is that CTC images are easier to interpret and a possible cleansing algorithm might be more effective [20, 30]. Finally, in our study we focused on image quality. Polyp conspicuity was not investigated. So far, one larger study without catharsis has reported an excellent sensitivity of 90% and specificity of 92% for patients with polyps of any size [18]. Although further research is warranted, these results underscore our findings that good image quality can be obtained with small amounts of laxatives.

We conclude that CTC with limited bowel preparation, using barium and ionic iodinated contrast agents for fecal tagging, requires only minimal doses of laxatives—in our study only 20 mg of bisacodyl—to obtain good image quality and minimize patient burden. This is important because a mild bowel preparation will undoubtedly increase patient willingness to participate in a screening program.
Acknowledgments

We thank Karin Horsthuis for her critical review of this manuscript and Henk W. Venema for his help with the data analysis and critical review of this manuscript.

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