CT colonography in faecal occult blood test positives
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Reducing the oral contrast dose in CT colonography: Evaluation of faecal tagging quality and patient acceptance

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Submitted


**ABSTRACT**

**Purpose:** To evaluate what amount of iodine tagging oral contrast medium is necessary for an optimal computed tomography colonography limited bowel preparation without using laxatives.

**Materials and Methods:** Faecal occult blood test positive patients were randomly selected for one of three iodine bowel preparations: 1) 3*50 mL meglumine ioxithalamate (45 g I), 2) 4*25 mL meglumine ioxithalamate (30 g I) or 3) 3*25 mL (22.5 g I) meglumine ioxithalamate. Two experienced readers assessed the tagging quality per colonic segment on a 5-point scale and the presence of adherent stool. Also semi-automatic density and homogeneity measurements were performed. Patient acceptance was assessed with questionnaires.

**Results:** Per preparation group 15 patients were included. The quality of tagging was insufficient (score 1-2) in 0% of segments in group 1, 4% in group 2 and 5% in group 3 (p<0.001 compared to group 1). In group 1 in 11% of the segments adherent stool was present compared to 49% in group 2 and 41% in group 3 (p<0.001). Tagging density was 610, 514 and 533 HU in group 1, 2 and 3 respectively (p=0.065). Homogeneity was 85, 102 and 90 SD HU in group 1, 2 and 3 respectively (p=0.011). In group 1 two patients experienced no burden after contrast agent ingestion compared to one patient in group 2 and nine patients in group 3 (p=0.017).

**Conclusion:** A dose of 3*50 mL meglumine ioxithalamate is advisable for an optimal tagging quality despite beneficial effects on the patient acceptance in patients receiving a lower dose.
INTRODUCTION

High quality bowel preparation is essential in order to accurately detect colorectal polyps and carcinomas using computed tomography colonography (CT colonography). Several different CT colonography bowel preparation techniques have been evaluated in previous studies, including cathartic bowel preparation such as polyethylene glycol or sodium phosphate. However, oral contrast medium alone can also be used to ‘tag’ the residual faeces. Cathartic preparations often lead to excessive diarrhoea with concomitant patient discomfort, but preparation with an oral tagging agent has been proven to produce sufficient faecal tagging whilst minimising the unwanted side effect of diarrhoea. It is important to improve patient experience with the bowel preparation because this can increase compliance with CT colonography examinations, especially in the context of screening.

Tagging-only bowel preparations can consist of barium or iodine contrast tagging or a combination of both. The advantage of barium tagging is that it does not induce the diarrhoea which can result from the oral intake of high-osmolarity iodinated contrast media. However, barium tags mainly the solid stool and not the liquid components, which can lead to inhomogeneous tagging. On the contrary, a high-osmolarity iodine contrast medium softens the stool, causing a more homogeneous mixing with the iodine and thereby improving ease of CT colonography reading.

In a study of Iannacone et al. a two-day preparation with iodine tagging only (in total 74g iodine) was required for optimal polyp detection. Other studies have shown that a one-day preparation with iodine tagging is sufficient for optimal tagging and polyp detection. In the study by Campanella et al. iodine was administered only on the morning before the CT colonography (total iodine load 18.5 g) following a two-day preparation with a mild laxative. In order to minimize diarrhoea and keep the instructions to the patient as simple as possible, however, a minimal iodine dose without laxatives would be preferable. No previous study has used a minimal iodine dose lower than 30 mg without any laxatives.

The aim of this study was to assess the feasibility of a laxative free and low iodine load tagging bowel regimen for CT colonography. Patients received different bowel preparations and the tagging quality of the residual stool, patient acceptance and ease of interpretation of the CT colonography examination were then evaluated.

MATERIALS AND METHODS

Patients were offered colonoscopy at the gastroenterology department as the result of a positive faecal occult blood test (FOBT) in the second round of a large bowel cancer pilot screening study that invited 10,000 average risk persons between 50 and 75 years to participate. At the outpatient clinic all patients with a positive FOBT were informed about the CT colonography study and asked to participate. Exclusion criteria were: patients who were unable to give informed consent, patients with terminal illness, patients with
colorectal carcinoma symptoms within the last three months, colonoscopy in the previous two years, examinations with radiation exposure in the last 12 months, iodine contrast allergy, hyperthyroidism and pregnancy. After written informed consent for CT colonography had been obtained, patients were allocated to one of three preparation groups (see Table 1 for further details).

### Table 1 Three different preparation regimes for CT colonography

<table>
<thead>
<tr>
<th>Prepartion 1</th>
<th>Day -1</th>
<th>Day CTC</th>
<th>Total Iodine dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2* 50 mL Telebrix: at lunch and dinner</td>
<td>-1*50 mL Telebrix 1.5h before CTC</td>
<td>150 ml</td>
<td>45 g I</td>
</tr>
<tr>
<td>-low-fiber diet</td>
<td>-Only liquid foods before CTC</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Preparation 2</th>
<th>Day -1</th>
<th>Day CTC</th>
<th>Total Iodine dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>-3*25 mL Telebrix: at breakfast, lunch and dinner</td>
<td>-1*25 mL Telebrix 1.5h before CTC</td>
<td>100 ml</td>
<td>30 g I</td>
</tr>
<tr>
<td>-low-fiber diet</td>
<td>-Only liquid foods before CTC</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Preparation 3</th>
<th>Day -1</th>
<th>Day CTC</th>
<th>Total Iodine dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>-2* 25mL Telebrix at lunch and dinner</td>
<td>-1*25 ml Telebrix 1.5h before CTC</td>
<td>75 ml</td>
<td>22.5 g I</td>
</tr>
<tr>
<td>-low-fiber diet</td>
<td>-Only liquid foods before CTC</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CTC: CT colonography

Allocation to a preparation group occurred sequentially: the first included patient enrolled in the study received preparation 1, second patient preparation 2, third preparation 3, fourth preparation 1 etc. The preparation schemes all consisted of the ingestion of meglumine-ioxithalamate (Telebrix Gastro 300 mg I/ml; Guerbet, Cedex, France) and a low-fibre diet on the day before CT colonography. On the day of CT colonography examination patients were only allowed to take drinks and liquid foods before the examination and they had to take their last bottle of Telebrix. Approval of the Medical Ethics Committee of our institution was obtained.

**CT colonography examination**

Before the examination a smooth muscle relaxant was injected intravenously (20 mg butylscopolamine bromide (Buscopan; Boehringer-Ingelheim, Ingelheim, Germany); or when contraindicated 1 mg Glucagon (Glucagen; Novo-Nordisk, Bagsvaerd, Denmark)). Approximately 3 litres of CO2 gas were insufflated via a rectal catheter into the colon, using an automated insufflator (Bracco, PROTOCO2L insufflator, New York, USA). All the examinations were performed using a 64-slice CT scanner (Brilliance, Philips Medical Systems, Best, the Netherlands). A low dose protocol with 25 ref mAs was used with z-axis tube modulation and automatic current selection. Slice collimation was 64*0.625 mm, pitch 1.2, slice thickness 0.9 mm, rotation time 0.4s and tube voltage 120 kV. Patients were scanned in supine and prone position.

**Evaluation of tagging quality**

Tagging quality was assessed on the supine scans alone by two experienced CT colonography readers (ML, experience of 500 CT colonography examinations with
colonoscopy verification; FZ, experience of 125 CT colonography examinations with colonoscopy verification) using several subjective scores. The subjective scores were used to determine the amount and consistency of the faecal residue, the tagging quality (5-point scale), the largest piece of untagged faecal material, the presence of adherent stool and the influence of the tagging quality on polyp detection (see Table 2). The evaluations were done per colonic segment: coecum, ascending, transverse, descending colon, sigmoid and rectum. Furthermore, the more experienced reader rated the distension per segment of the supine scans on a four point scale: 1) poor distension, 0-25% of maximal diameter distended; 2) moderate distension, 25-50% of maximal diameter; 3) sufficient distension, 50-75% of maximal diameter; 4) good distension, 75-100% of maximal diameter.

Table 2 Subjective scores of tagging quality

| Total amount of faecal residue per segment | 1. 0-25% of the lumen filled with faecal residue | 2. >25-50% of the lumen filled with faecal residue | 3. >50-75% of the lumen filled with faecal residue | 4. >75-100% of the lumen filled with faecal residue |
| Consistency of faecal residue | 1. liquid | 2. partly solid/partially liquid | 3. solid |
| Quality of tagging | 1. insufficient preparation; all residual faeces inhomogeneously tagged | 2. poor preparation; 1-<25% homogeneously tagged | 3. moderate preparation; 25-<50% homogeneously tagged | 4. sufficient preparation; 50 to <75% homogeneously tagged | 5. good preparation; 75-100% homogeneously tagged |
| Largest piece of untagged stool | 1. no untagged stool | 2. <6 mm untagged stool piece | 3. 6-<10 mm untagged stool piece | 4. ≥10 mm untagged stool piece |
| Presence of adherent stool | 1. Yes, adherent ("sticky") stool present | 2. No |
| Influence of quality of tagging on polyp detection | 1. diagnostic images for polyps of all sizes | 2. diagnostic images only for polyps ≥6 mm | 3. diagnostic images only for polyps ≥10 mm | 4. non-diagnostic images, polyps ≥10 mm can be missed |

In addition, automatic density measurements were performed with specialized software (View Forum, Philips, Best, Netherlands). All voxels having a density >200 HU were considered to be faeces. Measurements were performed automatically in every 10mm perpendicular to the colon path and the mean values for density (HU) and homogeneity (SD of HU) were calculated per colonic segment. The colonic segments had been defined by a radiology research fellow (ML), by defining the borders of each segment in one sample colon. Ratios of the length per segment related to the total colonic length were calculated and applied to all CT colonographies in this study. All automatic measurements were checked by the research fellow. When measurements in a segment were inadequate
due to faecal remnants with a density below 200 HU, the radiology research fellow performed manual measurements of the faecal residue with three ROI’s placed in the segment. The slices in which the ROIs were placed were randomly selected by using a computer program (Windows Excel 2003, Microsoft). Only ROI’s with a surface larger than 30 mm² were measured. As the density and homogeneity can vary between patients and the combination of both measurements is important, we also calculated the relative homogeneity (=SD HU/mean HU).

**Polyp detection**

Two experienced CT colonography readers (ML, FZ; see previous paragraph) performed polyp detection at CT colonography before the colonoscopy. Images were read in primary 2D read (window setting 1500, -250 HU) with 3D problem solving on specialized software (View Forum, Philips, Best, Netherlands). A secondary 3D fly-through was also performed after the 2D read for additional evaluation. The lesions detected were classified as pedunculated, sessile or flat and were measured using electronic callipers in the largest diameter in multiplanar reformatted (MPR) images. No consensus read was performed and all lesions of ≥6 mm found by the CT colonography readers were unblinded during the colonoscopy. Reading times for the primary 2D and additional 3D read were registered.

**Colonoscopy**

Colonoscopies were performed by experienced gastroenterologists or gastroenterology-fellows under supervision. All patients received 2 L of polyethylene glycol electrolyte solution (Moviprep; Norgine Limited, Mid Glamorgan, United Kingdom) with a low-fibre diet for bowel preparation. Analgesics (fentanyl, Fentanyl-Janssen; Janssen Pharmaceuticals, Beerse, Belgium) and sedation (midazolam, Dormicum; Roche, Basel, Switzerland) were used as standard in all patients. The polyps detected at CT colonography were revealed per colonic segment to the colonoscopists according to the technique of segmental unblinding. Polyp size was estimated using opened biopsy forceps and the colonoscopy was videotaped from the caecum to enable matching of the colonoscopy and CT colonography polyps by a radiology research fellow (ML). Lesion histology was classified according to the Vienna classification.18

**Questionnaires**

All patients received four questionnaires with questions relating to patient experience of the preparation and the examination itself. In the first questionnaire, which was completed at home before the examinations, patients were asked about their normal daily stool consistency and frequency of defecation. The second questionnaire was completed directly after the CT colonography, and included questions about the experience of iodine contrast agent ingestion and the effect of the bowel preparation, as measured on a 5-point scale (1=not unpleasant, 2=minimally unpleasant, 3=moderately unpleasant, 4=severely unpleasant to 5=extremely unpleasant). Patients were also asked to indicate their preference for the CT colonography or the colonoscopy bowel preparation (as indicated on a 7 point scale: 1=definitely CTC – 7=definitely colonoscopy). The final questionnaire was sent to the patient’s home two weeks after the last examination. Patients were asked
which aspects of the examination were most difficult to tolerate and also whether activities of daily living were limited prior to the examination.

**Statistical analysis**

Participant characteristics, including age, sex, normal stool consistency and prior experience with colonoscopy were compared by means of proper statistics (e.g. Student-T-test, Chi-square test) depending on the type of data (e.g. continuous data, binomial data respectively).

Tagging quality outcomes were analysed in different ways. The subjective scores for the amount of residual faeces, consistency of residual faeces, colonic distension, presence of adherent stool, quality of tagging and influence on polyp detection by both reviewers were added and were compared performing the Chi-square trend test. The interobserver variability for the tagging quality was determined by giving percentages of total agreement in both observers. The calculation of kappa statistics was hampered by the low prevalence of certain scores resulting in unequal distributions in the crosstabs.\(^{19}\)

The density and homogeneity of the residual stool and the SD/HU ratios were compared by using an ANOVA-test (normal distribution) and for the pairwise comparisons the Student T test was used.

The number of true positive lesions at CT colonography for lesions larger than or equal to 6 mm was determined. Lesions included adenomatous, hyperplastic and inflammatory polyps and colorectal carcinomas. Comparison of the CT colonography and colonoscopy findings was performed using segmental unblinding during colonoscopy by a research fellow (ML; previous experience of matching 325 cases). A true positive CT colonography polyp had a size within 50% margin of the corresponding colonoscopy polyp, was located in the same segment as at colonoscopy, or in an adjacent segment as at colonoscopy and resembled in morphology compared to the lesion seen on the videotaped colonoscopy in morphology. Furthermore the number of technical false negatives (lesions that were retrospectively not visible at CT colonography), perceptive false negatives (lesions that were retrospectively visible at CT colonography) and the number of false positives were retrospectively determined by this research fellow. Due to the relatively low patient numbers per group and the relatively low number of findings, no statistical analysis was performed. Reading times were compared using the Student-T-test.

From the questionnaires, patient experience of the preparation, especially regarding diarrhoea, and patient preference for a preparation regime were compared by using a Chi-square trend test.

Statistical analyses were performed using SPSS version 15.0.1 for Windows (SPSS) and Excel Windows version 2003. For analysis, a p-value of <0.05 was considered as statistical significant.
RESULTS

In total there were 80 eligible FOBT positive patients; one patient was excluded because of Graves disease and another 24 patients did not want to take part in this study, mainly because of the anticipated burden of the additional CT colonography examination. Finally 45 patients were included, 15 patients in each of the three preparation groups (see flowchart in fig. 1). In group 1, the number of males/females was 7/8, in group 2 7/8 and in group 3 11/4 (p>0.05 for all comparisons among the three groups). Mean ages in group 1, 2 and 3 were 62 years (SD 6.8), 62 years (SD 5.9) and 62 years (SD 7.4) respectively (p>0.05). Stool consistency prior to this study was hard in two patients in each group and soft in seven patients in each group. The other patients had a variable stool consistency (p>0.05). In group 1 four patients had had a previous colonoscopy. In group 2 this were two and in group 3 one patient. During the CT colonography examination Buscopan was used in 39 patients, Glucagon in four patients and in two patients no smooth muscle relaxant was used. The distension was rated insufficient (score 1 or 2) in one segment in group 1, four segments in group 2 and three segments in group 3. No complications occurred during the bowel preparation or the CT colonography examination.

Fig. 1 Flow-chart of the study

Quality of tagging
The total amount of faecal residue was highest in group 1; 23% of all segments were filled with >25% of faecal residue in group 1 versus 17% in group 2 and 11% in group 3 (for group 1 vs. 3: p=0.001). All subjective evaluation scores of the tagging quality with corresponding p-values are presented in Table 3. The consistency of the faeces was mainly...
fluid in all segments, but in group 2 and 3 the faeces had a solid consistency in a significantly larger number of segments than in group 1. The quality of tagging was insufficient to moderate (score 1-3) in 1% of segments in group 1, in 14% of segments in group 2 and in 8% in group 3 (comparisons between groups yielded p-values <0.05; see Table 3 for exact values). When comparisons were made per colonic segment, all segments in group 1, except the sigmoid colon, had significantly higher scores than in group 2. No significant differences per colonic segment were found for group 1 compared to group 3. In fig. 2 examples of different quality scores are presented.

Table 3 Tagging quality scored by readers for all segments

<table>
<thead>
<tr>
<th></th>
<th>Preperation 1</th>
<th>Preperation 2</th>
<th>Preperation 3</th>
<th>p-values</th>
<th>Agreement observers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total amount of faecal residue segment</td>
<td>0-&lt;25%</td>
<td>77%</td>
<td>83%</td>
<td>89%</td>
<td>1 vs 2: 0.099</td>
</tr>
<tr>
<td>Consistency of faecal residues</td>
<td>Liquid</td>
<td>87%</td>
<td>53%</td>
<td>55%</td>
<td>1 vs 2: &lt;0.001</td>
</tr>
<tr>
<td>Quality of tagging</td>
<td>1 (insufficient)</td>
<td>0%</td>
<td>2%</td>
<td>1%</td>
<td>1 vs 2: &lt;0.001</td>
</tr>
<tr>
<td>Largest piece of untagged stool</td>
<td>No untagged</td>
<td>83%</td>
<td>62%</td>
<td>74%</td>
<td>1 vs 2: &lt;0.001</td>
</tr>
<tr>
<td>Presence of adherent stool</td>
<td>Yes</td>
<td>11%</td>
<td>49%</td>
<td>41%</td>
<td>1 vs 2: &lt;0.001</td>
</tr>
<tr>
<td>Influence of quality of tagging on polyp detection</td>
<td>1 (diagnostic)</td>
<td>89%</td>
<td>61%</td>
<td>67%</td>
<td>1 vs 2: &lt;0.001</td>
</tr>
</tbody>
</table>

The percentages of segments per tagging quality score are presented (results of both readers are added). Agreement between both observers is presented in the last column. P-values are given for all groups compared.

When considering the largest piece of untagged stool we found an untagged stool piece ≥6mm in 4% of the segments in group 1. For group 2 this was in 16% of all segments and for group 3 in 6% (comparisons between groups yielded p-values <0.05). In group 1 in only 11% of the segments adherent stool was present. This was significantly higher in group 2 (49% adherent stool) and group 3 (41%). Also the influence of the tagging quality on polyp detection was rated better in group 1 compared to group 2 and 3. The
interobserver variation for all qualitative imaging scores varied between 71% and 85% (see Table 3).

Fig. 2 Examples of subjective tagging quality scores

**Fig. 2a** Example of a CT colonography with good tagging quality and the ascending colon filled with 50-75% of tagged faeces (preparation group 1). **Fig. 2b** Moderate tagging quality in the cecum and ascending colon (preparation group 2). **Fig. 2c** Poor tagging quality in the ascending colon, sagittal image (preparation group 2). Furthermore both observers found untagged stool particles of ≥10mm.

The average density of the tagged faeces in all colonic segments was 610 HU in preparation group 1, 514 HU in group 2 and 533 HU in group 3 (p=0.065, using the ANOVA test). In the descending colon the density was significantly higher in group 1 compared to the two other groups. The average homogeneity was 85 SD HU, 102 SD HU and 90 SD HU (p=0.011) in the three groups respectively. Ratios of the relative homogeneity (HU SD/mean HU) were 0.14, 0.21 and 0.18 (p=0.015) respectively. For the descending colon in both groups 2 and 3, the relative homogeneity ratio was higher compared to group 1. In Table 4 the values are presented per segment and significant differences between groups per segment are also indicated.
Table 4 Tagging density and homogeneity measurements

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Density (mean HU)</th>
<th>p-value</th>
<th>Homogeneity (SD HU)</th>
<th>p-value</th>
<th>Relative Homogeneity (SD HU/mean HU)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Cecum</td>
<td>575</td>
<td>439</td>
<td>551</td>
<td>0.064</td>
<td>86</td>
<td>103</td>
</tr>
<tr>
<td>Ascending</td>
<td>602</td>
<td>478†</td>
<td>499</td>
<td>0.048</td>
<td>82</td>
<td>105†</td>
</tr>
<tr>
<td>Transverse</td>
<td>633</td>
<td>588</td>
<td>571</td>
<td>0.552</td>
<td>77</td>
<td>95†</td>
</tr>
<tr>
<td>Descending</td>
<td>666</td>
<td>555†</td>
<td>534†</td>
<td>0.035</td>
<td>81</td>
<td>89</td>
</tr>
<tr>
<td>Sigmoid</td>
<td>609</td>
<td>541</td>
<td>519</td>
<td>0.262</td>
<td>93</td>
<td>97</td>
</tr>
<tr>
<td>Rectum</td>
<td>569</td>
<td>481</td>
<td>411</td>
<td>0.122</td>
<td>94</td>
<td>120</td>
</tr>
<tr>
<td>Total</td>
<td>610</td>
<td>514</td>
<td>533</td>
<td>0.065</td>
<td>85</td>
<td>102†</td>
</tr>
</tbody>
</table>

†indicates a significant difference when compared to values of group 1.

Polyp detection

In group 1, 17 lesions ≥6 mm were found at segmental unblinded colonoscopy in six patients. In group 2 there were 17 lesions in seven patients and, in group 3, 17 lesions in seven patients. Both observers detected 10 lesions in group 1, nine lesions in group 2 and 16 lesions in group 3 (see table 5 for all true positive and false negative lesions). In group 1, five lesions were missed due to a technical error by both observers (i.e. retrospectively not visible at the CT colonography); three sessile lesions and two flat lesions. Group 2 also contained five lesions missed due to a technical error; two sessile lesions and three flat lesions. In group 3, the one lesion missed was a pedunculated lesion. All perceptive errors made by both observers were lesions that were retrospectively hardly visible. See fig. 3 for two examples of lesions.

Observer 1 had a reading time of 10’58” (SD 2’52”) in group 1, 12’10” (SD 3’00”) in group 2 and 13’37” (SD 4’48”) in group 3 (comparisons between groups yielded p-values >0.05). For observer 2 this was 18’17” (SD 6’35”), 19’03” (SD 7’46”) and 18’37” (SD 5’22”) for group 1, 2 and 3 respectively (p>0.05).

Fig. 3 False negative and true positive polyps Fig. 3a: Pedunculated polyp 8 mm in the ascending colon retrospectively detected at CT colonography (perceptive false negative). Left is the supine axial image, right the prone axial image.
Fig. 3b: Carcinoma (neuro-endocrine tumour) of 12 mm in the rectum detected at CT colonography but only seen after segmental unblinding at colonoscopy. Left is the prone axial image, right is 3D image.

Table 5 Polyp detection

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Detection ≥6mm</th>
<th>Technical FN</th>
<th>Perceptive FN</th>
<th>FP ≥6mm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reader 1</td>
<td>Reader 2</td>
<td>Reader 1</td>
<td>Reader 2</td>
</tr>
<tr>
<td>1</td>
<td>9/17</td>
<td>10/17</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>53%</td>
<td>59%</td>
<td>(29-77)</td>
<td>(35-82)</td>
</tr>
<tr>
<td>2</td>
<td>9/17</td>
<td>8/17</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>53%</td>
<td>47%</td>
<td>(29-77)</td>
<td>(23-71)</td>
</tr>
<tr>
<td>3</td>
<td>16/17</td>
<td>16/17</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>94%</td>
<td>94%</td>
<td>(83-100)</td>
<td>(83-100)</td>
</tr>
</tbody>
</table>

Perceptive false negatives were visible in retrospect at CT colonography, whereas technique related errors were not. Between brackets 95% Confidence Intervals are given. FN: false negative; FP: false positive.

Patient acceptance

Questionnaires 1 and 2 were filled in by all patients, questionnaire 3 was not filled in by two patients and questionnaire 4 was not returned by four patients. In groups 1 and 2, 14 patients experienced diarrhoea after ingestion of the contrast agent versus 10 patients in group 3 (p=0.067). In group 1 two patients experienced no arduous side-effects in regard to the effect of the oral contrast agent, with one patient in group 2 and nine patients in group 3 also reporting no arduous side-effects (see fig. 4; p=0.017). Patients in group 1 and 2 tolerated the preparation and examination significantly less well than group 3.
Fig. 4 Symptoms experienced due to the effect of the contrast agent

In each group the patients were asked about their experience after contrast ingestion. No differences between groups existed (p-value: 0.017). On the y-axis the percentages of patients are presented.

Furthermore most patients in all groups preferred the CT colonography bowel preparation compared to the colonoscopy bowel preparation with no difference in preference for the three groups (fig. 5; p=0.222). When patients were asked which aspect of the whole examination was most difficult to tolerate, patients found the insufflation of CO2 for the CT colonography most arduous (67% in group 1, 62% in group 2 and 55% in group 3 (see fig. 6a). For colonoscopy the bowel preparation was the most poorly tolerated aspect, 57% in group 1, 46% in group 2 and 58% in group 3 (see fig. 6b).

Fig. 5 Preference of patients for CT colonography or colonoscopy bowel preparation

Patients were asked about their preference for bowel preparation; whether they would prefer to undergo the CT colonography or the colonoscopy bowel preparation. No differences between preparation groups existed (p-value: 0.222). On the y-axis the percentages of patients per group are presented. CTC: CT colonography; OC: optical colonoscopy
DISCUSSION

Our findings suggest that preparation 1, starting one day before the CT colonography and using three 50 ml doses of an iodine contrast agent (meeglumine ioxithalamate; 45 g I), results in a good tagging quality. When only half of this dose is used, the patient tolerance increases significantly but the tagging quality declines with an increase in the amount of adherent and solid faeces. In addition, when the semi-automated measurements were considered, we found a significantly better homogeneity and relative homogeneity (SD HU/mean HU) in the first group that had taken the three 50 ml doses of the iodine contrast agent.

When a tagging only preparation is used for CT colonography, it is important that homogeneous mixing with the faeces is obtained without untagged faecal remnants. This increases ease of image interpretation, resulting in optimal polyp detection, increased specificity and improved reading efficiency.² We found that the first preparation group that received in total 45 g I, had the best tagging quality rated by the observers. In the other groups with 30 g I or 22.5 g I, the tagging quality was rated significantly poorer, although, a large number of colonic segments still had an optimal score. In addition, more pieces of untagged stool were found in these groups. When considering the semi-automatic measurements, we found better homogeneity in the first preparation group compared to group 2. No large differences were observed in the density values but we combined these values with the homogeneity values (SD HU) to calculate the relative homogeneity (SD HU/mean HU). This value corrects for differences in mean density and represents the quality of tagging. For example, a low mean density of 200 HU with homogeneity of 80 SD HU, will result in a higher ratio of relative homogeneity (ratio=0.4) compared to a mean density of 600 HU with 80 SD HU (ratio=0.13). This relative homogeneity is an important tool for comparing the effects of differences in homogeneity and density.⁴ In group 2 and 3 we found significantly higher ratios compared to group 1.

No studies have previously been performed using these small amounts of iodine contrast agent and a short preparation time, without the addition of laxatives. Some earlier studies have shown, however, that excellent results can be obtained for polyp detection and tagging quality with a two-or one-day preparation.¹⁴,¹⁵,²⁰ Furthermore the study of Campanella et al. showed that a dose of 18.5 g I just before CT colonography and two days of preparation with a laxative agent was also sufficient for adequate tagging.¹⁶ Due to the smaller amounts of contrast agent in the second and third group of patients in this study, the colon in those patients contained a lower concentration of the contrast agent which probably resulted in a lower amount of faecal residue but also led to less stool softening and thus more solid faecal remnants and more adherent (or ‘sticky’) faeces. Although overall quality in the second and third preparation groups was rated less, only a few segments were not considered to be diagnostic for finding polyps of ≥6mm and only one segment was not diagnostic for finding polyps ≥10mm. Thus for a relatively large number of patients preparation with only 22.5 g of iodine contrast agent might be sufficient for an adequate polyp detection.
Chapter 4 | Reduction of the CT colonography oral contrast dose

Most unpleasant aspect CT colonography

Not many studies have calculated the effect of minimal bowel preparation on polyp detection although Iannacone et al. used a preparation of in total 200 ml iodine contrast (74 g I) and found a very high sensitivity of 86% for polyps $\geq$6mm.\textsuperscript{14} As patient numbers were too small in our study, we did not calculate sensitivity differences between preparation groups but the most important aspect of this study was to evaluate the tagging quality rather than evaluate polyp detection.

High amounts of iodine in tagging agents will induce diarrhoea and consequently will reduce patient tolerance of the examination.\textsuperscript{15} This can negatively influence patient compliance, especially in the context of population screening.\textsuperscript{11} In this study it was shown that a low amount of contrast agent started at lunch on the day before the CT colonography is tolerated better by patients than preparation with twice the amount of contrast agent or a preparation which starts at breakfast the day before. When patients were asked to indicate their preference for the CT colonography or the colonoscopy preparation, nearly all patients preferred the CT colonography preparation. This is consistent with results of earlier studies that showed that patients tolerate reduced...
preparation better than cathartic preparation.\textsuperscript{6,7,21,22} Furthermore we used a low-fibre diet in our study because earlier research in our hospital has confirmed that a low-fibre diet can increase the tagging quality.\textsuperscript{23}

Reading times increased somewhat for both readers over the three preparation groups, but differences were not significant. An increase in reading times could indicate that the images are more difficult to read because of the decreased tagging quality.

This study has some weaknesses; primarily the low number of patients included in each preparation group. However, the numbers are sufficient to address the primary outcome measures, and therefore evaluation of the tagging quality in the CT colonography examinations could be performed as previous studies on bowel preparation have done.\textsuperscript{4,7,16}

Due to the low number of polyps a meaningful comparison of performance in polyp detection between the groups was not possible. Another weakness of this study is that only an iodine preparation was tested and no barium contrast agent was assessed. As it has already been shown that iodine in small amounts results in homogeneous mixing in contrast to barium contrast agents\textsuperscript{7,20} we focussed only on reducing the amount of iodine tagging to produce a shorter preparation time. Small amounts of iodine are absorbed in the colon so the use of oral iodine contrast agents can result in mild allergic or rarely in severe anaphylactic reactions.\textsuperscript{24-26} As our patients took their iodine contrast agent at home, we wanted to avoid the risk on anaphylactic reactions so all patients with a previous iodine contrast allergy were excluded from the study. No complications due to the bowel preparation occurred in this study.

To conclude, we found that the iodine preparation with the largest amount of iodine contrast agent (45 g I) had the best results on tagging quality with the lowest number of untagged stool particles. The results for measured density and homogeneity were also most favourable in the group with the largest amount of tagging agent. Further decrease of the iodine dose does not seem advisable, despite the beneficial effects on the patient acceptance.

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References