The Performance of CTC

Didier Bielen

CONTENTS

2.1 Introduction 17
2.2 CT Colonography 18
2.3 Our Experience 19
2.3.1 Patient Acceptance 19
2.3.2 Polyp Detection 20
2.3.3 Referral to Optical Colonoscopy 22
2.3.4 Interpretation 23
2.3.5 CAD 23
2.3.6 Polyp Measurements 25
2.3.7 The Issue of Radiation 25
2.4 Conclusion 26
References 26

Introduction

In Western Europe and the United States, colorectal carcinoma (CRC) remains the second leading cause of cancer-related death (Jemal et al. 2005; Ferlay et al. 2007). In Belgium, each year 7,700 new colorectal cancers are diagnosed (De Laet et al. 2006). Fortunately, the majority of these cancers originate from pre-existing benign lesions from the mucosal lining of the bowel wall. These “adenomatous polyps” have the potential to progress into a malignant lesion, a carcinoma, over a period of 10 years, the dwelling time (Stryker et al. 1987). Identification and subsequent removal of these adenomas by way of endoscopy determines a significant decrease in the incidence of CRC (Winawer et al. 1993). Once a cancer has been diagnosed, the 5-year survival declines significantly. This justifies a population-based screening for the early detection of the disease. Such screening tests should be sufficiently accurate, i.e. be able to detect polyps ≥10 mm, be acceptable to “patients”, be feasible in clinical practice, and be neither harmful nor too expensive. The test should be cost-effective where the potential benefits must outweigh the costs.

Depending on genetic and environmental factors, the risk for cancer transformation is variable and associated with the histological characteristics of a polyp, in particular the villous component of a lesion or the flat aspect of a lesion. But since these histological characteristics can only be determined after the removal of a lesion, it would be more convenient to determine this risk prior to removal. Unfortunately, most of these characteristics can be evaluated only after polyp resection, either surgically or after an endoscopy. Further, endoscopic polyp resection has both an inherent procedural risk and an additional risk because of the need for pharmacological sedation (Bowles et al. 2004).
The clinically important polyp seems to be a lesion measuring at least 6 mm. The rationale behind this is the fact that the majority of polyps \( \leq 5 \) mm are hyperplastic and harbour a risk of malignancy of less than 1%, while larger polyps \( \geq 10 \) mm harbour a risk of 10%, which further increases with size (NUSKO et al. 1997). Additional risk factors are the histological characteristics, with a risk of nearly 30% for tubulo-villous and villous lesions vs. 3.9% for tubulous polyps, and lesion location, with a risk of 6.4% for right-sided lesions, 8.0% for left-sided lesions and 23.0% for lesions in the rectum (NUSKO et al. 1997). Considering small (\( < 5 \) mm) and intermediate (6–9 mm) lesions, follow-up studies showed that there is a tendency to grow for polyps \( < 5 \) mm, and a tendency to regress for those \( > 5 \) mm (HOFSTAD et al. 1994). In this series, only one lesion showed an increase in diameter \( > 10 \) mm.

For practical reasons, the main determinant of the risk for CRC is believed to be the polyp's size (WINAWER et al. 1997). While small adenomas (\( < 10 \) mm) have a negligible potential for short-term degeneration, the so-called advanced adenomas, i.e. those with a diameter \( \geq 10 \) mm, and/or \( \geq 20\% \) villous component and/or high-grade dysplasia, carry a significantly increased risk of cancer (SHINYA and WOLFF 1979).

The prevalence of such adenomas in 20–40% of the population aged \( \geq 60 \) years (IMPERIALE et al. 2000) offers opportunities for secondary prevention or screening for risk stratification and subsequent patient management based on the polyp size.

Such screening tests should be sufficiently accurate for detecting polyps \( \geq 10 \) mm, be acceptable to the otherwise healthy persons to be screened, be feasible in clinical practice, and be neither harmful nor too expensive. The test should be cost-effective where the potential benefits must outweigh the costs.

Multiple screening options are available because no single test offers an unequivocal superiority (WINAWER et al. 2003). Until today conventional colonoscopy (CC) is the most accurate technique, because it offers a high sensitivity for polyp detection. Although the CC has the possibility for polyp removal, this might not be taken into account in a screening setting since polyp removal will only be performed in the second therapeutic session. Further, the majority of lesions are not advanced adenomas and can be left in place if not detected.

On the other hand, optical colonoscopy has some disadvantages, especially the laxative bowel preparation which is experienced as an unpleasant procedure since it causes a lot of patient discomfort, and the rather high cost. Although there is a risk of bowel perforation, in particular in case of polyp removal, this might not be taken into account in case of a screening programme, since polyp removal will only be performed in the second therapeutic session.

In addition, the participation rate for CRC screening programmes is rather low, be it \( \pm 30\% \) for flexible sigmoidoscopy and \( \pm 57\% \) for FOBT (SEEFF et al. 2004). In general, the majority of US population remains unscreened. Information regarding this topic is lacking for Belgium, since there are no organized screening programmes yet. A pilot project on CRC screening supported by the Flemish Community will start soon.

This low prevalence may be due to the lack of awareness, an inadequate provider counselling, the fact that patients had to make an appointment by themselves (GOLDER et al. 2007), and seems to be related to the number of primary care office visits (ZIMMERMAN et al. 2006). Although the degree of participation remains higher in men (MEISSNER et al. 2006), women with up-to-date mammography and cervical cancer screening were more likely to be up to date concerning CRC screening (CARLOS et al. 2005). A positive family history of CRC (HLAVATY et al. 2005), the knowledge of a sibling’s illness (GILI et al. 2006), a tailored telephone outreach (BASCH et al. 2006), or a patient navigator system (JANDORF et al. 2005) are likely to increase the participation rate.

### 2.2 CT Colonography

Since its introduction in 1994 (VINING and GELFAND 1994) many papers on CTC technique and its reliability have been published in both radiology and gastroenterology-related journals. CTC did just recently become an accepted screening tool according to the guidelines of the American Cancer Society (LEVIN et al. 2008a, b).

Besides the detection and characterisation of polyps, one of the advantages of CTC is that the technique is also able to measure polyps. This allows risk stratification of patients according to polyp size, since the main determinant of the risk for CRC is believed to be polyp size. The success of the patient’s risk stratification by CTC can be judged using the criteria as proposed by the Working Group on Virtual Colonoscopy (ZALIS et al. 2005a).
Further, CTC offers the possibility to evaluate not only the colonic lumen and mucosal surface, but also the colonic wall and the extracolonic structures, allowing, for example, the staging of disease in case of a colonic malignant tumour in one session.

To become acceptable and be able to compete with the CC, CTC should be sufficiently accurate, i.e. be able to detect at least significant polyps. Although there is no consensus on what should be the targets, guidelines recommend to target on the advanced adenomas, whereas the importance of lesions 6–9 mm remains controversial (Winawer et al. 2003). This topic, especially, gives rise to a lot of controversy. One study, examining a large patient population resembling the target population for a screening programme, proved that CTC with the use of a 3D approach is an accurate screening method in an average risk population and compared favourably with optical colonoscopy, with a sensitivity for lesions >10 mm that was >90% (Pickhardt et al. 2003). Another study stated that the sensitivity for lesions >10 mm was only 55% and that the accuracy varied considerably between centres, leading to the conclusion that CTC by these methods is not yet ready for widespread use, and that techniques and training need to be improved (Cotton et al. 2004; Rockey et al. 2005).

Two recent publications (Kim et al. 2007; Johnson et al. 2008) are more optimistic, indicating that primary screening strategies with CTC and CC resulted in similar detection rates for advanced neoplasias.

An explanation for these different conclusions might be found in the fact that the above mentioned Pickhardt-study was performed under optimal conditions with a standardized CTC technique and reading conditions, whereas the other studies grouped different centres, different CTC techniques and readers’ experiences, very close to what might be found in daily practice.

Today, the CTC examination promises to be sufficiently sensitive and specific for the detection of large and medium sized polyps and symptomatic cancers (Halligan et al. 2005). It shows a similar detection rate for advanced neoplasias, i.e. adenocarcinoma and advanced adenoma, as that of CC (Kim et al. 2007), and is a valuable tool for tumour staging and detecting polyps and cancers in case of suspicion of colorectal cancer (Chung et al. 2005). Since the sensitivity and negative predictive value for 8 mm lesions is as high as 94 and 99% using four or eight channel multidetector CT scanners and double dose oral colon cleansing, CTC should even replace the double contrast barium enema for screening purposes.

### 2.3 Our Experience

The basic principles of the CTC technique have been described in detail in many publications. These include the necessary bowel preparation with laxatives and tagging, the bowel relaxation, the bowel distension with room air or carbon dioxide, the image acquisition in both supine and prone patient positions, the use of high resolution CT scan protocols, and the evaluation of the images in 2D as well as in 3D endoscopic view in both a colon window (e.g. 1,700/−500 HU) and soft tissue window (e.g. 450/50 HU).

All these different steps can be subject to personal interpretation and implementation by the radiologist, making the technique prone to variations and subsequently variable results.

#### 2.3.1 Patient Acceptance

While the feasibility of reduced preparation with faecal tagging and/or rigorous dietary restrictions (Zalis et al. 2000; Callstrom et al. 2001; Gryspeerdt et al., 2002; Lefere et al. 2002; Thomeer et al. 2002; Bielen et al. 2003) has been described, our own study evaluated the effect of different preparation regimens on patient acceptance (Bielen 2008). The bowel preparation regimens contained a decreasing proportion of laxatives, with the intention to reduce patient discomfort i.e. diarrhoea. We evaluated the combination of moderate dietary restrictions, laxatives and faecal tagging preparation vs. a tagging-only preparation, i.e. without the use of any laxatives.

All participants were invited to complete a questionnaire on their pre-test expectation, their assessment of the two different CTC preparation regimens, their post-test experience, i.e. immediately and after 24–48 h, and their future preference in case a new colonic exam would be necessary: CTC, CC or no difference.

According to the pre-test expectation questionnaire, in which patients had to answer the question as to whether they expected CTC or CC to be least pleasant, more patients expected CC to be least comfortable compared to CTC. These findings were not related to the preparation regimen or a previous CC.

The rating of the CTC preparation, the CTC and the CC exams was scored using a visual assessment scale, with 0/9 being uncomfortable and 10/9 being highly comfortable.
The mean score for the preparation with the combination of laxatives and tagging was 5.4 whereas the mean score for the tagging-only preparation was 6.7, indicating that the patients preferred the preparation without laxatives to the preparation with laxatives and this difference was statistically significant. Although even the use of the water-soluble iodinated contrast medium for tagging purposes might induce some laxation, only one patient mentioned a mild diarrhoea, which might be due to the tagging.

The mean score for the CTC exam was 6.7 whereas the mean score for the CC exam was 5.8, indicating that the CTC exams were preferred to the CC. This was the case for both preparation regimens. The mean score for the CC exam was significantly higher in case of a previous CC while this was not the case for the mean CTC score.

The CTC exams were experienced as least comfortable by a minority of patients, whereas this was the case in half of the CC exams, after completion of both exams and after 24–48 h. The same outcome is reflected in the future preference in case a new colonic exam would be necessary. More than 50% would prefer CTC compared to 15% who would choose CC. Neither post-test experience nor future choice was influenced by preparation regimen or previous CC.

Given the fact that reduced preparation for CTC seems to improve patient acceptance for undergoing a colonic exam, that a minority experiences CTC as least comfortable, and that a majority would prefer a CTC in case a new colonic exam would be necessary, CTC might become a more acceptable alternative for, or complement to, the CC in screening programmes, considering that the polyp detection would not be hampered by the use of a tagging-only preparation. Concerning the answers given after completion of the CC, it has been reported that these answers could be affected by the sedation used for the CC, especially for reasons of the retrograde amnesiac characteristics of midazolam (Svensson et al. 2002). However, the above does not impair the results of our survey, since the CTC procedure was chosen over the CC exam, irrespective of the side effects of sedation. Other parameters that might influence the results of such a questionnaire are the phrasing of the questions, the age and the education of the patients.

### 2.3.2 Polyp Detection

In our own study we evaluated the feasibility of polyp detection using three different preparation regimens with a decreasing proportion of laxatives, in order to reduce patient’s discomfort. The goal was the correct referral to CC, based on the referral criteria of the Working Group on Virtual Colonoscopy (Zalis et al. 2005a). Therefore, we evaluated the accuracy of the CTC using both manual lesion size measurements as well as the use of an automated measurement tool delivering on the patient’s risk stratification.

All patients underwent, besides dietary restrictions, one of three different bowel preparation regimens for which they received recommendations. Preparations contained a decreasing proportion of laxatives, with the intention to reduce patient discomfort, i.e. diarrhoea.

To evaluate the effect of a standard laxative bowel preparation, patients in “Group 1”, the laxative-only group had to drink 4–5 L electrolyte solution on the morning of the colonoscopy (Na⁺ 141 mEq, K⁺ 10 mEq, Cl⁻ 121 mEq, HCO₃⁻ 30 mEq/L water).

To evaluate the effect of tagging, patients in “Group 2”, the laxative-and-tagging group, had to drink a low volume laxative preparation with two doses (45 mL each) sodium phosphate (Fleet Phospho Soda®, Wolfs, Belgium) on the afternoon and evening prior to the colonoscopy.

For tagging purposes, patients had to drink 100 mL of a water-soluble iodinated contrast medium (meglmine ioxitalamate 3% – Telebrix Gastro® Guerbet/Codali Belgium): 10 mL diluted in a standard glass of water (250 mL) together with the three principal meals (breakfast, lunch, dinner) the day prior to the exam, 25 mL diluted in a standard glass of water together with each dose of the laxative and 20 mL diluted in a standard glass of water on the morning of the exam. The use of the contrast material is intended to enhance the density of possible residual stool (“faecal tagging”) (Bielen et al. 2003) allowing discrimination between non-contrast containing polyps and contrast containing stool.

To evaluate the effects of a minimal preparation, patients in “Group 3”, the tagging-only group, received a minimal preparation of “faecal tagging” only. The same tagging scheme as used in Group 2 was applied, but patients had to drink 25 mL of contrast medium diluted in a standard glass of water (250 mL) in the afternoon and in the evening, i.e. without the laxatives.

Considering the lesions 6–9, ≥10 mm and tumours (Figs. 2.1–2.4), the per patient sensitivity and negative predictive value were 62.5 and 96.7% respectively for Group 1 using the laxative only preparation, 90.0 and 99.1% respectively for Group 2 using the laxative with tagging preparation, and 100.0 and 100.0%...
respectively for Group 3 using the tagging-only preparation. For the three groups together, the per patient sensitivity and negative predictive value were 81.8 and 98.53% respectively. These results are in line with recently presented studies (JOHNSON et al. 2008).

Considering the diminutive lesions, i.e. lesions measuring £5 mm, the results are far less beneficial. The same is true for the flat lesions, which remain easily overlooked, both on CTC and CC. According to literature, less than 50% of flat lesions could be visualized, unless they were 2 mm or greater in height, 7 mm or larger in diameter. Contrast enhancement, location on a haustral fold, and abnormal 2D and 3D morphology contributed to lesion conspicuity (PARK et al. 2006).
This is remarkable since current CT scanners offer high spatial resolution that should make the detection of these lesions feasible. On the other hand, these lesions might be obscured due to the uncontrollable stretching or overstretching of the bowel wall as a consequence of the insufflation, whereas insufflation in CC can be controlled easily. The 3D evaluation software we used for problem solving did not present the lesions in a colour different to the surrounding normal bowel wall lining and so discrimination of lesions was not always clear, not even in 3D.

These shortcomings of the CTC technique will certainly be the subject of debate with the gastroenterology community, since especially the flat lesions constitute nearly 25% of colorectal polyps and harbour an increased malignant potential (Parrablanco et al. 2006). The prevalence of flat lesions in our own study was significantly lower, i.e. only three flat lesions in 296 patients. Further, the National Polyp Study did not show a higher risk for high-grade dysplasia in flat lesions (O’Brien et al. 2004). On the other hand, a recently published study revealed a rather high prevalence of flat lesions in a group of veteran patients, and that these lesions had a greater association with carcinoma compared with polyoid lesions (Soetikno et al. 2008). There are differences in prevalence of flat lesions in our study patients compared to other populations, but it remains unclear whether this is due to differences in the population or in the possibilities to detect these lesions by CC and CTC. These findings might lead to the discussion on the necessity for the search of these lesions.

Even on CC using white light, these flat lesions are overlooked easily. More advanced techniques, e.g. magnification chromo-colonoscopy, autofluorescence endoscopy and narrow-band imaging approve detection of adenoma, but necessitate a longer endoscopic procedure (Helbig 2006; Lapalus et al. 2006).

2.3.3
Referral to Optical Colonoscopy

Although there is evidence for the use of the referral criteria from the Working Group on Virtual Colonoscopy (Zalis et al. 2005a), other thresholds and referral criteria might be considered.

Selection criteria using a simple 8 mm threshold for referral to CC by CTC led to a per patient sensitivity and negative predictive value of 60.0 and 95.6% respectively for Group 1, 71.4 and 96.2% respectively for Group 2 and 83.3 and 98.5% respectively for Group 3. For the three groups together, the per patient sensitivity and negative predictive value were 70.0 and 96.6%, respectively.

Compared to the standard referral criteria, the use of a simple 8 mm threshold for polyp detection and patient’s risk stratification resulted overall in slightly worse results for every individual group as well as for the three groups together.

It is clear that polyp detection and accordingly patient’s risk stratification by CTC using a laxative preparation without tagging resulted in a significant number of failed referrals, using either the standard referral criteria or the simple 8 mm threshold. The main reason for this could be the amount of residual fluid and the lack of contrast difference between the low-density residual fluid covering the polyps of which the density is in the same range.

Sensitivity and NPV were clearly higher in both Group 2 and Group 3, which solely might be related to the use of tagging, since one preparation regimen was with, and the other without, the use of laxatives. In these groups, the polyp detection is enhanced, resulting in an improved patient’s risk stratification compared to the preparation without tagging. This improvement is true for both sensitivity and NPV. However, most remarkable is the fact that the best
results were found in Group 3, i.e. the group with the tagging-only preparation, findings which one would not expect in these setting, given this minimal preparation without any laxatives.

On the other hand, one should ask the question whether the improvement of these results are related to the preparation regimen only or are influenced by the improvement of the reader’s skill as a consequence of a learning curve, since the three groups were examined in consecutive order.

For these reasons, a data sample of 60 patients, composed of patients from the three study groups with a mix of lesion types, was evaluated by three other readers: one with no CTC experience, one with limited CTC experience and one experienced reader. The purpose was to try to eliminate the possible effect of a learning curve by analyzing a new randomly composed study group.

As was the case with the initial reader, the sensitivity and NPV improved by adding tagging to the laxative preparation in Group 2 for the reader with no experience, the reader with limited experience as well as for the experienced reader.

There was no further improvement of the results in Group 3 for the reader with no CTC experience or for the reader with limited CTC experience. For the initial reader, who evaluated Group 3 at the end of the study, i.e. after having read at least 200 CTC examinations with endoscopic feedback, as well as for the experienced external reader, there was a further improvement of the results.

Besides improvement of the results as a consequence of more experience, one can expect that the reading time for an experienced reader might be far less than that for a non experienced reader, with consequences on the final cost of the CTC procedure.

Given these results, we can recommend CTC with a laxative and tagging preparation in case the reader has no or limited experience, allowing adequate polyp detection. In case the reader is experienced in reading CTC, the patient’s bowel preparation can be simplified i.e. using a tagging-only preparation without laxatives, resulting in less patients’ discomfort, without compromising the CTC results.

2.3.4 Interpretation

It remains unclear whether to use a primary 2D or 3D approach for evaluation of the CTC data. Some studies recommend the primary 3D approach for the detection of polyps, with 2D views used chiefly for correlation (Pickhardt et al. 2003). Other advocate using 2D axial images only, since this approach results in a very low rate of unnecessary referral for colonoscopy (Bruzzi et al. 2004), or since 2D and 3D show similar diagnostic performance (McFarland et al. 2001; van Gelder et al. 2007) (Fig. 2.5).

More important than this controversy on the 2D or 3D approach is the level of competency needed for CTC interpretation. Where on the one hand competence cannot be assumed even after directed training via 50 cases (Taylor et al. 2004), others recommend a specific training during hands-on courses with 40–50 cases under supervision or during mini fellowships (Soto et al. 2005). Reader errors are most of the time due to failure of detection rather than failure of lesion characterisation (Slater et al. 2006). Untrained reader performance is generally poor, so basic training should focus on lesion detection. Also the interpretation time depends on the reader’s experience: the more the experience, the lesser the time needed for the image evaluation (Burling et al. 2006a). Less interpretation time is needed for normal cases. Compared to radiologists, technologists read CTC exams more slowly but more accurately.

It is clear from our study that a 2D approach is feasible, but a minimal level of experience is needed (Bienen 2008). Since we strive to a limited bowel preparation in the frame work of a screening programme, we should recommend that, in case such a low preparation CTC examination would be implemented, reading of these examinations should be done only by an experienced radiologist. In case the radiologist has little or no experience in reading CTC examinations, we should recommend doing the CTC examinations with a laxative and tagging preparation, favourable only in a clinical diagnostic setting, where a less stringent preparation can be used.

2.3.5 CAD

Another aspect regarding CTC is that it is unclear whether CTC might benefit from the use of computer aided detection (CAD). In the area of medical imaging, first CAD experiments involved the identification and classification of micro calcifications in mammography (Freer and Ulissey 2001). Positive results encouraged the development of algorithms to identify lung nodules on chest radiographs (Giger et al. 1988) and helical CT images (Kaneko et al.
Whereas the idea behind CAD in CTC is quite simple – “Look for polyps and present them to the radiologist” – CAD is a multi step procedure typically consisting of (1) segmentation of the colonic wall, (2) generation of intermediate polyp candidates, (3) classification for detection of final candidates and (4) presentation of the polyp candidates.

In our study, we evaluated the added value of an experimental homemade CAD programme as a second reader for the three different bowel preparation regimens (Bielen 2008). The detection of polyps in this CAD software was based on sphere fitting and surface normals (Kiss et al. 2006). To judge the accuracy of our CAD technique, the same criteria for patient’s risk stratification, as proposed by the Working Group on Virtual Colonoscopy (Zalis et al. 2005a) based on the size of the largest lesion detected, were used.

To evaluate the added value of the CAD on patient referral, the results from the radiologist and the CAD were combined: failed CTC referral became a correct referral in case of a correct CAD referral, unnecessary CTC referral was eliminated in case CAD decided a lesion not eligible for referral.

Based on the referral criteria of the Working Group on Virtual Colonoscopy (Zalis et al. 2005a), per patient sensitivity and negative predictive value were 87.5 and 98.9% respectively for Group 1 using the laxative only preparation, 90.0 and 99.1% respectively for Group 2 using the laxative with tagging preparation, and 100.0 and 100.0% respectively for Group 3 using the tagging-only preparation. For the three groups together, the per patient sensitivity and negative predictive value were 90.9 and 99.3% respectively.

By changing the selection criteria using a simple 8 mm threshold referral per patient sensitivity and negative predictive value were 80 and 97.8% respectively for Group 1, 71.4 and 96.4% respectively for Group 2 and 83.3 and 98.5% respectively for Group 3. For the three groups together, the per patient sensitivity and negative predictive value were 76.7 and 97.4% respectively.

The use of CAD alone shows only a slightly higher per patient sensitivity and NPV than CTC in Group 1 when using the referral criteria of the Working Group on Virtual Colonoscopy as well as the simple 8 mm threshold. The combined use of the CTC and CAD findings resulted in an improved risk stratification in Group 1 and for all three groups together, for the standard referral criteria of the Working Group on Virtual Colonoscopy as well as the simple 8 mm threshold. In the latter case, only the NPV in both Group 2 and Group 3 was slightly improved.
2.3.6 Polyp Measurements

Besides the detection of polyps, CTC has the inherent advantage to measure polyps. The measurements are performed with a calliper, either in the native transversal CT images, or in the multiplanar reformatted images (MPR), and in a coronal, sagittal or manually adjusted MPR plane along the longest axes of the polyp (BURLING et al. 2006c). Alternatively, the measurements may be carried out manually in 3D view or by using semi- or fully automated tools allowing either linear or volume measurements (BURLING et al. 2003, 2005; PICKHARDT et al. 2005, 2006). It is recommended for routine CTC examinations that polyps should be measured on 2D axial or MPR images using lung window settings (e.g. WW 1,500 HU and WL between −200 and −600 HU) or using dedicated 3D visualization software (YOUNG et al. 2007).

While CTC measurements in one study underestimated all polyps (BURLING et al. 2006b) and manual measurement techniques in another study either over- or underestimated polyp size, there is a wide variety among the observers, with CTC diameters less than the endoscopic reference measurements (BURLING et al. 2006b). The variations in the measurements of polyp diameters are related to the reader’s experience and the viewing display used. Although the 3D display is commonly used for the detection of polyps, its use should not be recommended for polyp measurement (BURLING et al. 2006); this recommendation is not supported by other publications mentioning that linear polyp measurements in 3D are more accurate than measurements in 2D (PICKHARDT et al. 2005) and correlate better with the CC measurements (YESHWANT et al. 2006). The use of volume measurements instead of linear measurements allows better detection of small incremental polyp size changes in CTC (PICKHARDT et al. 2006).

Automated size measurements are technically feasible, resulting in an increased inter and intra reader agreement (BURLING et al. 2005). The automated size measurements are more precise than manual measurements, but the reader has to control the automated measurements, especially in case of small and flat polyps and lesions located on folds (FLETCHER et al. 2007). For lesions <10 mm, the measurement differences are within expected ranges of inter- and intra reader agreement for the manual 2D, the manual 3D and the automated measurement technique (TAYLOR et al. 2007).

In our own study (BIelen 2008) some polyps were also over- or underestimated, with consequences of risk stratification. It remains unclear whether this distribution is related to the use of different WW/WL settings in the referred studies.

This distribution can also be explained by the use of the open biopsy forceps technique in all studies for the measurements, although this is the least accurate technique (GOPALSAMY et al. 1997). The use of a linear probe measurement immediately after resection agrees best with polyp size. Alternatively, measurements can be done after polyp fixation or by the pathologist (SCHOEN et al. 1997). These uncertainties and the fact that endoscopic measurements may be operator dependent pose the question whether or not endoscopy is the gold standard for reference size estimation (FENNERTY et al. 1993; WAVE 1993).

The automated tool for polyp size measurement used in our study determined the longest dimension of polyps with high accuracy and reproducibility in the phantom study, even for low mAs values and irrespective of WW/WL settings. This also seems to be the case for the patient study, since differences between manual, endoscopic and automated measurements were not statistically significant, as long as we carried out the manual measurements using WW/WL setting of 1,700/−300 HU. The automated measurement tool provides an advantage over manual measuring since only one click on a lesion was necessary to measure it, avoiding time-consuming reconstruction, tilt and spin of MPRs along the axes of the polyp. Although the automated size measurement categorized the patients to the correct size groups without any significant difference to the radiologist, it slightly improved patient risk stratification by reducing failed and unnecessary colonoscopy referral using the referral criteria as described by the Working Group on Virtual Colonoscopy (ZALIS et al. 2005a) as well as the simple 8 mm threshold. However, it is not clear why fewer polyps were assigned to the correct size group by reader 2.

Further, it should be evaluated whether maximum linear dimension or polyp volume is the best indicator for cancer risk in polyps, and the best parameter to determine if patients are eligible for future surveillance or routine screening. In addition, the combined use of the automated tool with computer-assisted detection of polyps might be subject to future investigation.

2.3.7 The Issue of Radiation

There is an increased awareness of the possible adverse effects of the ionizing radiation of CTC, even at low
dose. Although the dose used in CTC is lower than
the dose in a diagnostic abdominal CT, we have to
strive to use a CTC technique with a dose as low as
reasonably achievable, according to the ALARA prin-
ciple, with respect to both image quality and accu-

The effective dose (E) is currently believed to be the
best available dose descriptor for quantifying risks in
diagnostic radiology (McCulloch and Schueler
2000; Huda and Vance 2007). In an attempt to estimate
E, we recorded in our own study (Bielen 2008) for all
acquisitions the effective mAs, and the for CT exams
specifically DLP in mGy.cm and the CTDIvol in mGy.E
reflects the equivalent whole-body dose that results in a
stochastic risk, equivalent to the stochastic risk from
the absorbed dose to those tissues irradiated in a non-
uniform irradiation as CTC exams (International
Commission on Radiological Protection 1991;
McCulloch and Schueler 2000; Bushberg et al.
2001).

Per individual, the calculated E ranged from
0.80 mSv for the prone acquisition with 140 kV,
15 mAs and CARE dose4D to 5.30 mSv for the supine
acquisition with 120 kV, 55 mAs and CARE dose4D.
These measured E is far below the calculated theoreti-
cal E for a routine abdominal CT examination acqui-
sition with 120 kV, 200 mAs and CARE dose4D, or
for CTC examinations in a diagnostic setting, this
dose would be around 11 mSv for a man and 15 mSv
for a woman (Liedenbaum et al. 2008).

To estimate the risk of an additional fatal cancer,
we used the risk for a working population, of which
the age is close to the age of the screening target
group, i.e. 50–70 years.

We studied the assessment of image quality and
the feasibility of polyp detection using the original
data sets and simulated low dose data sets in a sample
of 30 patients.

The calculated E for this study sample ranged
from 0.40 mSv for the prone acquisition with 100 kV,
15 mAs and CARE dose to 3.0 mSv for the supine
acquisition with 120 kV, 55 mAs and CARE dose.
Related to the natural background radiation dose in
Belgium, this would result in a multiplication factor
of 0.002 for the prone acquisition with 100 kV,
15 mAs and CARE dose and up to 1.15 for the supine
acquisition with 120 kV, 55 mAs and CARE dose.
The theoretical risk of the induction of a fatal can-
cer would be 1/50,000 for the prone acquisition with
100 kV, 15 mAs and CARE dose and 1/6,667 for
the supine acquisition with 120 kV, 55 mAs and
CARE dose.

Besides having sufficient image quality for inter-
pretation, the feasibility of polyp detection in the low
dose scans should be as accurate as in high dose set-
tings. All five radiologists detected the tumour, the
lesions ≥10 mm and the two lesions 6–9 mm in all
patients in both the high and the low dose series.
This resulted in correct referral to CC in all four
patients by all five readers. These findings corre-
csponded to a per patient sensitivity and negative pre-
ddictive value of 100%. Unfortunately, one reader
erroneously detected three lesions 6–9 mm in the low
dose series leading to unnecessary referral. Another
reader erroneously referred two patients to CC in
both the high and the low dose series, and a third
reader erroneously referred one patient to CC in both
the high and the low dose series, and two different
patients in either the high or the low dose series.
These three readers had knowledge in reading CTC
examinations but were not experienced. While these
findings had no influence on the per-patient sensitiv-
ity and negative predictive value, it led to a lower
specificity.

2.4 Conclusion

In conclusion, polyp detection by means of CTC is
feasible. Besides the implementation of CTC in a
screening programme, the radiologists should offer
this examination in a clinical diagnostic setting in
case a CC is not possible, or in case patients are not
able or willing to undergo a CC.

References

to increase colorectal cancer screening in an urban minor-

Bielen D (2008) Screening for colorectal cancer with CT colonog-
raphy: facing the challenges. Leuven University Press, Leuven

Bielen D, Thomeer M, Vanbeeckvoort D et al (2003) Dry prepa-
ration for virtual CT colonography with fecal tagging using
water-soluble contrast medium: initial results. Eur Radiol
13:453–458

study of colonoscopy practice in the UK today: are we ade-
quately prepared for national colorectal cancer screening
tomorrow? Gut 53:277–283

using CT colonography: agreement with colonoscopy and
effect of viewing conditions on interobserver and intraobserver agreement. AJR Am J Roentgenol 186:1597–1604
Johnson CD (2007) Results of the ACRIN Colonography Trial. In: RSNA annual meeting, Chicago, pp VG21-14