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European Journal of Cancer 38 (2002) 2070–2078

European Journal of Cancer

www.ejconline.com

CT colonography (virtual colonoscopy) for the detection of colorectal polyps and neoplasms: current status and future developments

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Received 10 September 2001; accepted 10 December 2001

Abstract

Computed tomography colonography (CTC) is a new, rapidly developing non-invasive CT technique used to detect colonic polyps and cancers. It employs two- (2D) and three-dimensional (3D) images of the colon in order to display neoplastic lesions. Clinical trials demonstrate promising results for the detection of polyps and cancers greater than or equal to 10 mm in size. Our purpose is to describe the technique of CT colonography, review recent published trials of CT colonography, and elucidate current clinical applications. Continuing technical innovations such as multidetector CT, computer-aided diagnosis, new image display techniques and faecal tagging promise to improve the performance and patient acceptance of CT colonography in the future.

Keywords: Colon neoplasms; Diagnosis; Computed tomography (CT); Computer programs; Image processing; Three-dimensional (3D)

1. Introduction

Colorectal cancer is the third most common cancer in the United States and the second most common cause of cancer death, accounting for approximately 56 000 deaths per year in the United States [1]. As most colorectal cancers arise from pre-existing polyps, detection and removal of precursor adenomatous polyps results in a decrease in the incidence of colorectal cancer as well as in reduced cancer-related mortality [2–4]. Several methods for colorectal screening are available, such as colonoscopy, sigmoidoscopy, barium enema and faecal occult blood testing. However, each method has limitations [5,6], and there continues to be an ongoing search for a non-invasive, rapid and well-tolerated exam that is highly acceptable to patients.

Computer tomographic colonography (CTC), also called virtual colonoscopy, is a rapidly developing technique that is gaining increased scientific and public awareness. CTC is simply the acquisition and review of the three-dimensional (3D) CT dataset created from scanning an air-distended colon with helical CT.CTC software permits the examination of the entire 3D (or volumetric) dataset in axial and oblique planes, as well as the creation of endoluminal 3D images. These 3D images are usually perspective, volume renderings, and display CT data so that it resembles the optical view from an endoscope (thus the term 'virtual colonoscopy'). 2D and 3D views are complementary for the visualisation and interpretation of the data sets, as well as comparison of the colon in the supine and prone positions. In addition to the colon, extracolonic abnormalities are also noted [7]. The purpose of this article is to describe the appearance of colorectal neoplasia using CTC, to review current clinical indications and the results of published trials, to elucidate the advantages and limitations of the technique, and to describe future directions for innovation and research.

2. The CTC exam

Patients currently prepare for CTC the evening before by undergoing routine bowel purgation cleansing using a variety of existing commercial regimens. Once patients enter the CT suite the following day, an enema tube is

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0959-8049/02/$ - see front matter © 2002 Published by Elsevier Science Ltd.
PII: S0959-8049(02)00384-2

inserted into the rectum, and the colorectum is inflated with air or carbon dioxide to patient tolerance. The patient is then placed in the supine or prone position, and a CT scanogram is performed to ensure adequate colonic inflation. A helical scan is subsequently performed using a narrow collimation and reconstruction interval, in order to achieve the spatial resolution needed to detect small cancers and polyps. The scan is generally performed using a low-dose technique to minimise radiation exposure to the patient, as low-dose exams do not compromise the conspicuity of polyps and cancers [8]. The patient is then rolled 180° into the complementary position, and additional air is insufflated into the colon, again according to patient tolerance. The CT scanogram and helical scan are then repeated. Using a standard low-dose technique of 70 mAs for a single detector helical CT scanner or 50 mAs for a multidetector CT scanner, the radiation dose is roughly equal to that obtained during a double-contrast barium enema [9]. The entire time required for the examination ('door-to-door time'), including the positioning of the patient, is between 15 and 20 min. The obtained data are then reconstructed with specialised software, usually installed on an off-line computer workstation.

3. The appearance of colorectal neoplasia using CTC

The colonic polyps displayed by CTC have an appearance that is analogous to their appearance with other imaging modalities such as barium enema or conventional colonoscopy. For example, polyps can be sessile, pedunculated or flat. Sessile polyps appear as round filling defects protruding into the colon lumen; pedunculated polyps have a stalk; and flat lesions are broader than they are high. However, the volumetric CT dataset makes analysis with CTC unique in some respects. Neoplasia is of soft-tissue density if it is of sufficient size. Lipomas will possess fat density, and stool generally possesses a heterogeneous density and may contain internal locules of air [10] (Fig. 1). Additionally, the margins of colorectal neoplasia can be displayed on both 2D and 3D images. Sessile polyps can be differentiated from haustral folds because they possess polypoid morphology on 2D and 3D images (Fig. 2). Pedunculated polyps are best displayed using axial or 2D images, as 3D endoluminal images may not discriminate between the lesion and the adjacent colonic wall (in the case of pedunculated lesions) [10] (Fig. 3). 3D endoluminal images also cannot distinguish inadequate distention from luminal narrowing due to cancer

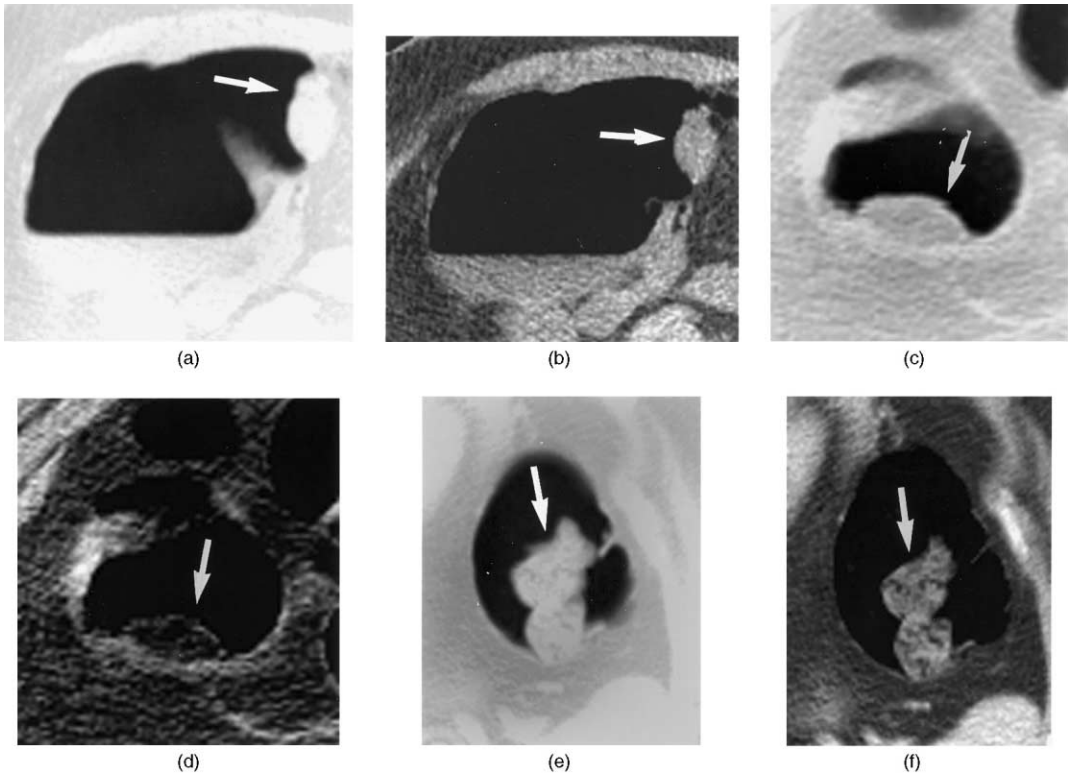

Fig. 1. Three filling defects at computed tomography colonography (CTC) displayed using lung and soft-tissue windowing. Adenomas demonstrate homogeneous soft-tissue attenuation if they are of sufficient size (a and b, arrows). Lipomas, the most common submucosal tumour of the colon, show internal fatty attenuation similar to surrounding mesenteric fat (c and d, arrows). Stool usually possesses an heterogeneous internal attenuation, and may contain small locules of internal air (e and f, arrows) (used with permission from the Mayo Foundation for Medical Education and Research).

(Fig. 4). Cancers of soft-tissue attenuation may be annular and constrict the lumen of the colon, or may be focal, smaller lesions indistinguishable from sessile or flat polyps. The comparison of supine and prone CT datasets is also important. The use of additional prone images improves the sensitivity of CTC for colorectal polyps by approximately 15% [11], primarily by improving distention in the rectosigmoid colon, and making some lesions more conspicuous (Fig. 5).

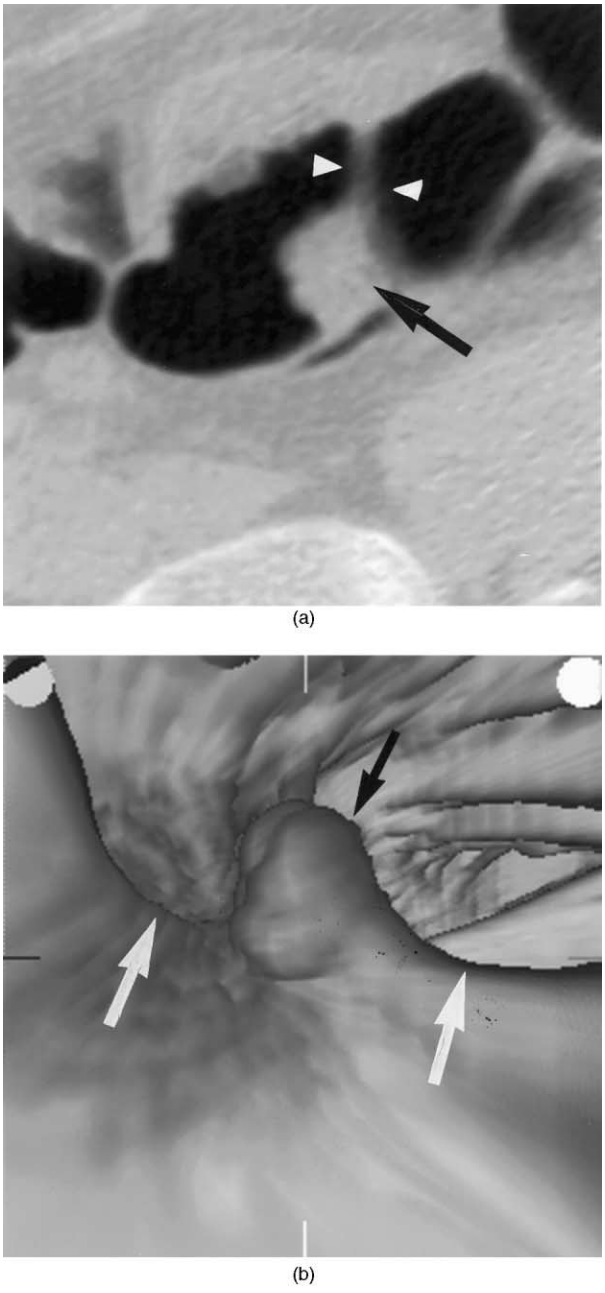

Fig. 2. Sessile polyp in the transverse colon. Two-dimensional multiplanar reformatted (a) and three-dimensional endoluminal images (b) demonstrate a filling defect of soft-tissue attenuation (black arrow) located along a haustral fold (white arrowheads) in the transverse colon. Colonoscopy confirmed the presence of a 7-mm hyperplastic polyp in this location.

Additionally, sessile lesions do not change their position in the colon between the supine and prone positions, while pedunculated polyps and stool characteristically do change position between the supine and prone dataset (Fig. 3). Finally, intravenous contrast is beginning to be used both on a routine basis and for problem-solving, to enhance visualisation of colonic neoplasia [12,13]. Morrin and colleagues recently demonstrated that intravenous contrast improves the detection of medium-sized polyps, particularly if stool or excess fluid is present [13].

Currently, most radiologists rely upon enlarged axial images for the primary interpretation of the dataset, and the detection of suspicious abnormalities. Suspicious filling defects are then investigated with oblique 2D reformatted images and 3D endoluminal renderings. These additional images are particularly helpful in discriminating polyps from haustral folds, and investigating complex anatomical regions such as the colonic flexures and the region about the ileocaecal valve.

4. Current clinical indications and results of published trials

One of the prime, current clinical applications of CTC is the investigation of the colon after an incomplete colonoscopy. Barium enema can evaluate the entire colon in only 42–60% of the patients with obstructing colorectal cancers [14–16]. Additionally, patients often need to repeat the bowel preparation in order to obtain a double-contrast barium enema study after incomplete colonoscopy. In contrast, CTC can be performed the same day after incomplete endoscopy without an additional bowel preparation. The cause of endoscopic failure can be ascertained in just over 70% of patients but, more importantly, the entire colon can be evaluated in over 90% of these patients [17]. When incomplete endoscopy is due to an obstructing colorectal cancer, CTC can complete the structural exam of the colon to identify synchronous polyps or cancers that can be treated at the time of primary resection. Fenlon and colleagues examined 29 patients with obstructing colorectal cancer and identified two synchronous cancers and 24 synchronous polyps in the proximal colon using CTC [18].

Most studies evaluating CTC have been conducted in patients at high risk for colorectal cancer (i.e. personal or family history of polyps, surveillance after prior resection of colorectal cancer or polyps), or symptomatic patients (i.e. melena, anaemia). A summary of published studies of CTC including over 10 adenomatous polyps or cancers in the study population is given in Table 1. The first study estimating the sensitivity of CT colonography in humans was published by Hara and colleagues from the Mayo Clinic. It was based on

70 patients who underwent CTC and conventional colonoscopy. Half of the patients had positive findings for polyps in sigmoidoscopy and barium enema. This study demonstrated an sensitivity of 70% for polyps greater than 10 mm in size, and a per-patient specificity of 90% [8]. Subsequently, the Mayo Clinic group demonstrated in a larger series of 180 patients at high risk for colorectal neoplasia that the sensitivity for polyps greater than or equal to 1 cm was 75%. The sensitivity for patients with polyps greater than or equal to 1 cm in size (i.e. those patients who should undergo subsequent therapeutic colonoscopy) was 85% per polyp with a specificity of 93% per patient. This study further demonstrated that the sensitivity for the detection of polyps greater than 10 mm was improved from 64 to 75%, when prone scans were performed in addition to supine scanning [11]. A more recent study from Boston University was based on 100 patients at high risk for colorectal neoplasia. In this study, all three carcinomas and 20 of 22 polyps greater or equal to 10 mm were detected using supine and prone CTC, yielding a sensitivity of 91% for polyps and neoplasia greater or equal to 1 cm [19]. The specificity on a per patient basis (for those with lesions greater than or equal to 1 cm) was 96%. The most recent large series was published by Yee and colleagues of the University of San Francisco [20]. This study included 300 patients who were either symptomatic or referred to colonoscopy for screening purposes. All eight carcinomas were detected. 90% of polyps greater or equal to 10 mm in size were detected, with a sensitivity of 80% for polyps between 6 to 9 mm in size. The specificity for polyps of all sizes

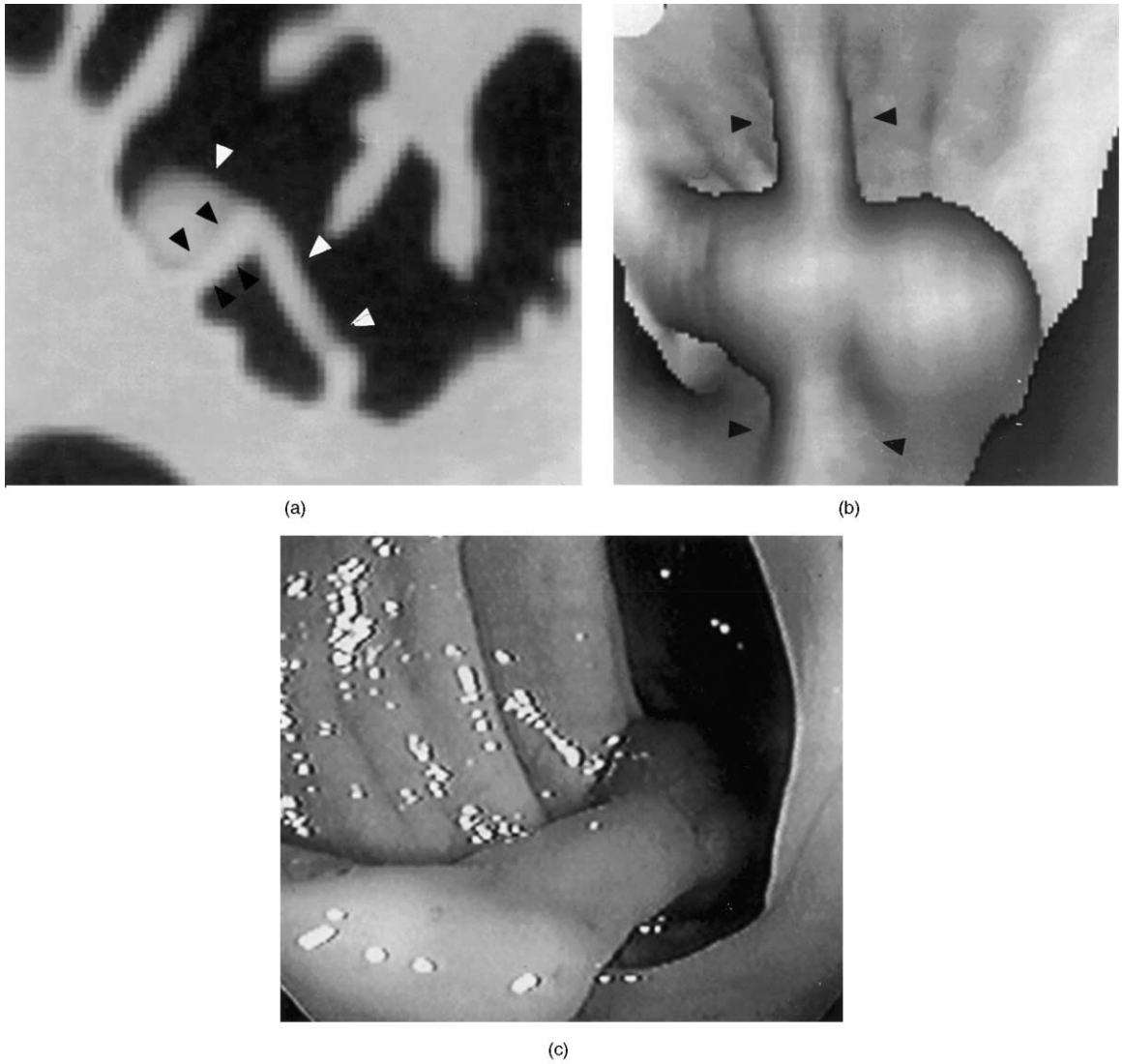

Fig. 3. Pedunculated polyp. Axial computed tomography colonography (CTC) image shows a pedunculated polyp (white arrowheads) draped over a haustral fold (a, black arrowhead). The corresponding 3D endoluminal view demonstrates the polyp, but the rendering does not show that the polyp is separate from the haustral fold (b, black arrowheads). The endoscopic view of the polyp (c) resembles the 3D endoluminal rendering (reprinted by permission from the *American Journal of Roentgenology*).

was 72%. Importantly, this study did not show any difference in polyp detection when comparing the subgroups of lesions in asymptomatic (or screening) and symptomatic patients.

Not all results regarding the performance of CTC have been promising. One study, based on 50 patients evaluated by two observer groups, demonstrated sensitivities of only 38% and 63% for lesions greater than or equal to 1 cm in size, with a specificity of 74% [21]. In this series, data evaluation was based principally on 3D data sets and data acquisition was performed only in supine position. The same group performed a subsequent follow-up study with another 50 patients, and showed an improved sensitivity and specificity of 75 and 88%, respectively, for polyps of significant size. They attributed their improved performance to increased reliance upon 2D images for the detection of neoplasia, greater experience in interpreting CT images, supine and prone imaging, and the use of multidetector CT [22]. Spinzi and colleagues also demonstrated that there is a significant learning curve for radiologists interpreting CTC exams in their study of 99 patients [23]: the detection rate for polyps of all sizes increased from 32% for the first 25 patients to 91% among the last 20 patients. Thus, the initial lack of experience is surely an important contributing factor to the relatively low sensitivity in many early series.

Another potential factor affecting the performance of CTC is the spatial resolution and artifacts affecting the axial reconstructed images. It is important to note from Table 1 that CTC appears to perform suboptimally when the collimation or slice thickness is wide (above 5 mm). Additionally, new generation multidetector CT scanners, which employ multiple X-ray detectors, promise to greatly improve the performance of CTC by scanning patients much faster with slice thicknesses of only 1–2.5 mm. For example, the whole abdomen can now be examined with a slice thickness of only 1 mm in 20–30 s. The improved spatial resolution appears to improve the depiction of medium-sized polyps [24]. Whereas scanning was often performed using multiple breath-holds using single-detector scanners, multidetector scanners allow for complete scanning of the abdomen and pelvis in a single breath-hold. The decreased scan time possible with multidetector CT scanner results in fewer motion artifacts and improved colonic distention [25].

Currently, several large studies are under way evaluating CTC for screening asymptomatic patients for polyps, but no results have yet been published. Two small studies have evaluated the performance of CTC in asymptomatic screening populations, but arrived at

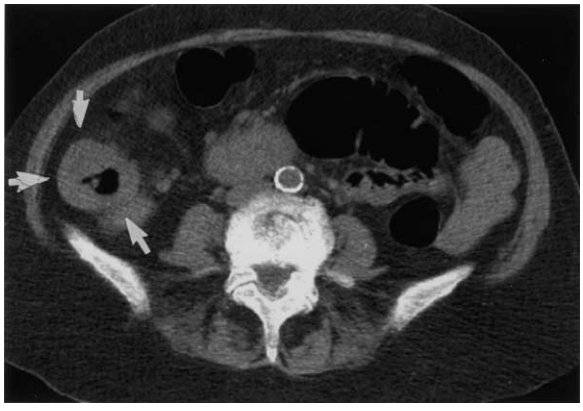

Fig. 4. Annular cancer of the ascending colon. Axial computed tomography colonography (CTC) image demonstrates marked mural and circumferential wall thickening in the ascending colon (arrows), the typical appearance of an annular carcinoma at CTC. Surgical resection demonstrated an invasive mucinous adenocarcinoma (used with permission from the Mayo Foundation for Medical Education and Research).

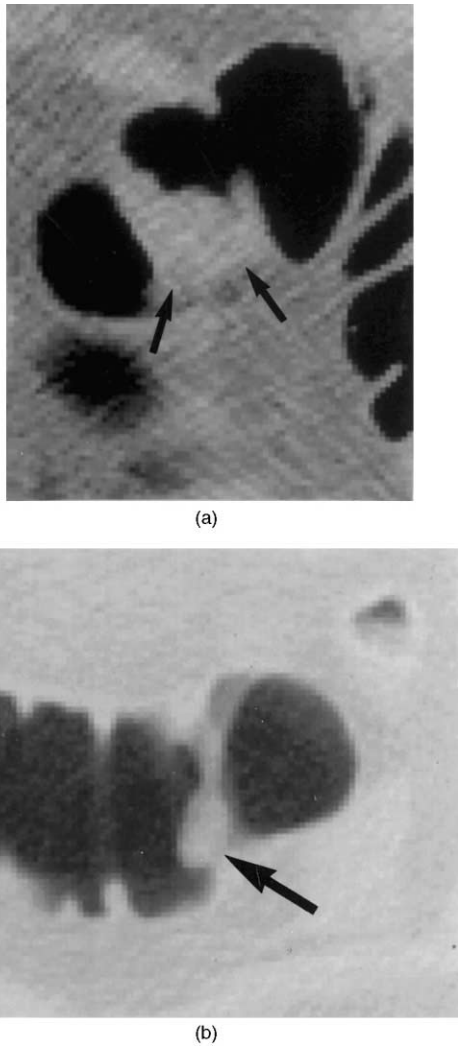

Fig. 5. Utility of supine and prone positioning at computed tomography colonography (CTC). Supine axial image demonstrates suspicious soft tissue adjacent to a fold, which could represent a polyp or stool (a, arrows). Corresponding prone axial image increases the conspicuity of the lesion, showing that the suspicious filling defect on the supine image is a small pedunculated polyp (b, arrow).

disparate results [26,27]. We currently offer CTC at our institution for patients who are unwilling to undergo barium enema or screening colonoscopy. Patients remain fasting until their exams are interpreted, so if positive, therapeutic endoscopy can be performed the same day.

There are other applications outside of screening and incomplete colonoscopy for CTC. Harvey and colleagues reported an accuracy of 96% for distinguishing between colorectal cancer and benign diverticular strictures in 52 patients with the use of contrast-enhanced CTC [28]. CTC can also be performed in patients with a prior history of invasive colorectal carcinoma undergoing surveillance for recurrent disease. These patients are at increased risk for metachronous disease, in addition to local recurrence and liver, lung and peritoneal metastases. CTC in these patients is performed with intravenous contrast and normal dose settings to permit optimal evaluation of the liver and peritoneum. The use of intravenous contrast increases the sensitivity of CTC for medium-sized polyps 6–9 mm in size [12], and should aid in the depiction of metachronous lesions. Colonoscopy is a poor method for evaluating local recurrence in these patients, as the majority of local recurrences are predominantly extraluminal [29,30]. Carbone and colleagues recently detected one local recurrence, one metachronous polyp, and five liver metastases in patients undergoing surveillance for recurrent tumour using contrast-enhanced CTC [31]. We recently examined 50 patients undergoing surveillance for recurrent colorectal cancer, and used CTC to identify two local recurrences, one large metachronous tubulovillous adenoma, and 5 patients with metastatic disease [32]. Importantly, one local recurrence and the metachronous tubulovillous adenoma in our study were endoscopically occult.

5. Limitations and advantages of CTC

CTC offers several advantages over other screening alternatives: it is a full structural exam, is non-invasive, and does not require sedation. Patients can return to work the same day following the exam. The entire exam requires only 20 min of the patient's time. CTC also appears to be highly acceptable to the patient. In our experience, CTC was clearly preferred over other full structural examinations such as conventional colonoscopy and double-contrast barium enema [33]. Two groups of patients were asked about their experiences and discomfort during full structural screening examinations. One group of 696 patients underwent both CTC and conventional colonoscopy, and 73% of patients preferred CTC over conventional colonoscopy. A second group of 617 patients underwent CTC and double contrast barium enema, and 97% of patients preferred CTC over the conventional radiological exam. It remains to be seen if a greater patient acceptance will translate into a higher compliance, which would increase the cost-effectiveness of CTC.

In contrast to other full structural colonic examinations, CTC can also detect important extracolonic findings [9]. In one series of 264 patients, 9 patients had a previously unknown renal lesion, including 2 patients with an unknown renal cell carcinoma. 3 patients had a large asymptomatic abdominal aortic aneurysm. In total, 6 of 264 patients (2.3%) of patients underwent surgery for significant extracolonic findings detected on their CTC exams. Investigators noted that follow-up examinations for extracolonic findings were infrequent (only 6.8% of patients), and extra imaging and procedures incurred consequent to positive CT exams resulted in an additional cost of only $28 per patient.

Table 1
Overview of published studies of CTC including at least 10 adenomatous polyps in the study population

Study [Ref.]	Modality	Positioning	Protocol	No of patients	Per patient performance (%)		Per polyp sensitivity (%)	
			Collimation/ re-construction interval		⩾1 cm Sensitivity	⩾1 cm Specificity	6–9 mm	⩾10 mm
Hara [8]	Single Detector	Supine	5.0/3.0	70	75	91	–	70
Yee [20]	Single Detector	Supine/prone	3.0/1.5	300	100	–	80	90
Fenlon [19]	Single Detector	Supine/prone	5.0/2.0	100	96	96	82	91
Fletcher [11]	Single Detector	Supine/prone	5.0/3.0	180	85	93	47	75
Morrin [12]	Single Detector + Multi Detector	Supine/prone	2.5–3/1.25–1.5	81	87	100	65	90
Kay [45]	Picker PQ 500	Supine/prone	5.0/2.0	38	90	82	38	91
Miao [46]	Single Detector	Supine±prone	8.0/4.0	201	–	94	16	73
Pescatore [21]	Single Detector	Supine	5.0/2.5	50	38–63	74	–	–
Spinzi [23]	Single Detector	Supine/prone	5.0/2.5	99	–	100	–	62
Rex [26]	Multi Detector	Supine/prone	5.0/2.0	46	80	89	43	50
Mendelson [47]	Single Detector	Supine±prone	5.0/1.0–2.0	100	–	94	22	73

CTC, computed tomography colonography.

CTC does have some disadvantages. We have previously alluded to the significant learning curve required for skilful interpretation of the CT dataset. Additionally, poor bowel preparation can result in erroneous conclusions: retained stool can mask colon polyps (i.e. false-negative results) or can mimic polyps or masses (i.e. false-positive results) [10]. Excess fluid remaining from the bowel preparation can also be the cause of false-negative exams, since lesions can be submerged beneath dependent fluid. Attempts to minimise the deleterious effects of residual stool and fluid can be undertaken by scanning in different positions (to move stool and fluid) or by injecting intravenous contrast (to enhance true colonic lesions) [11,12]. Inadequate bowel distention can also result in false-negative exams, but can generally be avoided by dual position scanning and monitoring of CT examinations by the radiologist. Finally, as with all radiographic techniques, the detection of flat lesions remains problematic [34]. Flat lesions run an increased risk of early colorectal cancer [35], and may be subtle at CTC [36]. We discourage the use of CTC in patients who may be prone to the development of flat cancers (e.g. patients with ulcerative colitis).

6. Future developments in CTC

Apart from further clinical studies, CTC is undergoing continued technical improvement. Multidetector row helical CT results in improved spatial resolution, increased colonic distention, and fewer artifacts [25], all of which promise to improve the sensitivity and specificity of the test by displaying smaller lesions and improving the assessment of internal attenuation characteristics. However, the improved spatial resolution possible with multidetector row CT scans can result in an increased amount of data that must be evaluated. For example, a dataset of the abdomen and pelvis obtained with a slice thickness of 1 mm contains 700–800 slices, compared with approximately 250 images in a study obtained with a slice thickness of 5 mm. The increased number of images increases the time necessary for data transfer as well as storage requirements for computer workstations. The increased number of images may also increase interpretation time. Even using routine low-dose techniques, radiation dose may increase by 50–100%, depending upon the imaging parameters used, but new algorithms which correct for image noise may allow further reductions in dose.

The goal of computer workstations and display techniques in CTC is to reduce perceptive errors by demonstrating data in a fashion that facilitates the interpretation for the observers, and that reduces interpretation time. Furthermore, new and elaborate algorithms and software will likely also prove helpful. As mentioned before, most radiologists primarily utilise 2D images to detect suspicious filling defects, and 2D reformatted images and 3D renderings to characterise these abnormalities. Several investigations for algorithms to improve the detection of lesions in 2D have been performed and continue [37,38]. In panoramic endoscopy, the circular structure of the inner surface of the colon is presented as one single, flattened view [39]. Another possibility is to create hybrid 2D and 3D images, inserting 3D renderings of the luminal surface into the air-filled lumen of 2D axial and multiplanar reformatted images [38].

Computer-aided detection of colonic neoplasia also promises to improve the sensitivity of CTC [40,41]. Polyp characteristics can be mathematically and geometrically described, with such algorithms detecting potential polyps along the surface of the colon. Potential lesions are then evaluated by an interpreting radiologist. Preliminary data provide encouraging results and show the feasibility of this technique, but existing morphological algorithms are highly dependent on the colonic distention and preparation [41]. In the future, morphological characteristics may be combined with perfusion information to detect neoplasia, as colonic polyps are enhanced with intravenous contrast [13].

As already mentioned, though colonic preparation is a crucial factor in current CT techniques, rigorous bowel purgation cleansing is one of the main deterrents to higher patient compliance. In one survey performed, approximately half of all patients rated the bowel preparations as causing moderate, severe or extreme discomfort. A higher percentage (78–81%) of patients found the preparation to be somewhat (37–60%) or very (21%) inconvenient [33]. Clearly, methods that would reduce discomfort, inconvenience or totally eliminate the need for preparation would address a very important obstacle for widespread colorectal cancer screening [33]. Ideally, bowel preparation could be avoided altogether in order to maximally reduce the patient's discomfort. 'Virtual bowel preparation' or 'prepless CTC' seeks to alter the X-ray attenuation of stool, so that it can be distinguished from neoplasia. Rather than a bowel preparation, the patient is asked to ingest multiple doses of oral contrast agent over 1 or 2 days prior to the CT exam. The contrast agents are designed to mix with enteric contents and homogeneously intermix with faecal material in the colon. The soft-tissue attenuation of polyps can be distinguished from the high attenuation of the labelled stool. In one feasibility study, dilute barium sulphate, administered over a period of 48 h in seven doses of 225 ml, efficiently labelled stool particles [42]. The observers had a sensitivity of 80–100% for lesions greater and equal to 1 cm. The specificity per patient varied and was 67% when stool tagging was optimised. Lefere and colleagues adopted a combined regimen of oral contrast, low-residue diet, and mild bowel cleansing in the day

preceding CT examination, and achieved a sensitivity of 85% in a feasibility study of 50 patients [43]. In the future, automated techniques promise to digitally subtract labelled stool, so that interpretation will be similar to that in the prepared colon [44].

7. Conclusions

CTC is a new and rapidly developing technique. It has demonstrated good sensitivity and specificity for significant polyps and masses of the colon in patients at high risk for colorectal cancer. However, these promising results have not yet been extended to a large screening population with a low incidence of colonic lesions. Technical improvements such as the introduction of multidetector helical CT, new and improved methods of image analysis, and the potential use of intravenous contrast material promise to improve the test further. The high patient acceptance of CTC among patients is encouraging. Future developments such as faecal tagging, or 'virtual bowel preparation', may negate the need for conventional bowel purgation cleansing and further improve compliance. Unlike other full structural screening examinations of the colon, CTC also serves as a survey of extracolonic structures within the abdomen. Currently, CTC is indicated after incomplete endoscopy, as a problem-solving tool for patients with colonic abnormalities at endoscopy or barium enema, and for patients who are reticent to undergo alternative full structural screening examinations. It may be an adjunctive tool for the surveillance of patients with prior colorectal carcinoma. Larger clinical trials are warranted for the further evaluation of CTC for widespread screening and surveillance.

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