Computed tomography colonography

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Computed tomography colonography (virtual colonoscopy) is an exciting technique that continues to evolve but promises to be a valuable tool for diagnosis of and screening for colorectal neoplasia.

Computed tomography colonography (CTC) refers in this review to the examination of the colon by spiral computed tomography (CT) after bowel cleansing and distension of the lumen with gas. Strictly, the term 'virtual colonoscopy' (VC) should be reserved for the process of examining three-dimensional (3-D) endoluminal images (simulated colonoscopic images) with the associated capability to navigate, using appropriate software, through the bowel.

VC was first described by Vining and Gelfand (1994) and the first clinical publication, by Hara et al, appeared in 1996.

If CTC/VC is shown to be acceptable to patients, safe, affordable and accurate, it has enormous potential as a diagnostic and screening tool for colorectal neoplasia.

TECHNIQUE

Bowel cleansing is performed preferably using low-volume barium enema preparations rather than high-volume colonoscopy preparations, because fluid residues can be a major impediment to polyp detection by CTC/VC.

The colon is insufflated with room air or CO_2 by a rectal catheter to the level of patient tolerance, usually 2–4 litres. CO_2 may cause less post-procedural discomfort. The use of intravenous hyoscine butylbromide improves patient tolerance and reduces bowel spasm. No sedation is used.

Image acquisition

The degree of bowel distension is assessed on an initial CT scout view and more gas introduced if necessary. Scans are acquired in supine and prone positions (dual position scanning).

Some authors advocate standard X-ray dosage scans to optimize detection of extra-colonic pathologies (Kay et al, 2000; Pescatore et al, 2000; Spinzi et al, 2001). However, most use low-dosage regimens since, even with 70 mAs (milliamperes sec) scans, the ability to detect colorectal polyps is preserved (Hara et al, 1997a) and it is possible to detect many important incidental lesions, such as aortic aneurysms, renal and ovarian tumours (Hara et al, 2000; Edwards et al, 2001a).

The images are acquired in one breath hold whenever possible, which may be facilitated by pre-oxygenation of the patient. For a single-array spiral CT scanner, the breath hold required is about 30–45 seconds.

Image reconstruction and interpretation

The images are transferred to a workstation computer for reading. Various software packages are available for the examination of the images.

The software enables multiplanar reconstructions from the volume data set acquired, as well as 3-D endoluminal reconstructions using surface-shading or volume-rendering techniques (virtual colonoscopy) (*Figure 1*). The optimal method of examining images has not been fully clarified. Examination of two-dimensional axial images only is performed by scrolling through the images, examining each image serially from rectum to caecum. Alternatively, examination of axial and reformatted coronal and sagittal images and routine examination of 3-D endoluminal reconstructions can be undertaken, but this is very time-consuming. The authors, as do others (Macari et al, 2000), examine axial images and selectively use multiplanar and 3-D reformats for problem-solving. Nearly all lesions larger than 10 mm detected by CTC are visible on axial images.

Window settings, approximating lung windows, are suitable for polyp detection on two-dimensional images. Soft-tissue windowing is used to detect bowel wall thickening (*Figure 2*), for clarification of intraluminal filling defects (gas content, heterogeneity) and for extra-colonic pathology.

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RESULTS OF CT COLONOGRAPHY

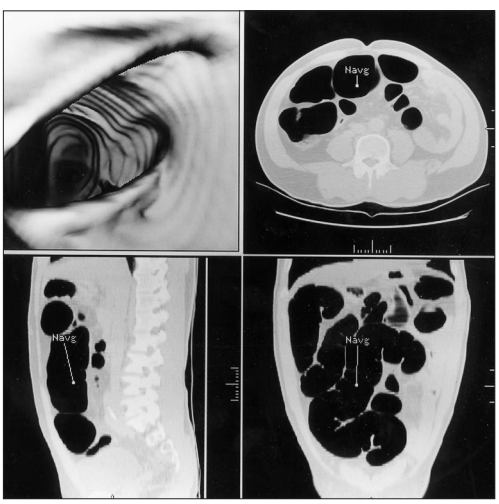
There is a significant learning curve for reading CTC/VC (Spinzi et al, 2001). The number of examinations required for proficiency is unknown, but the authors' experience suggests that this is up to 50 examinations.

Sensitivity

Sensitivity on a polyp-by-polyp basis depends on polyp size. Literature analysis is difficult; several studies report the use of supine only (Hara et al, 1997b; Pescatore et al, 2000) or prone only (Kay et al, 2000) scans, whereas dual-position scanning increases sensitivity and specificity (Chen et al, 1999; Fletcher et al, 2000). In several studies, patients have been preselected to yield a high proportion of positive results (Hara et al, 1997b; Fenlon et al, 1999a; Mendelson et al, 2000; Pescatore et al, 2000), some include the operators' learning curve (Mendelson et al, 2000; Pescatore et al, 2000; Spinzi et al, 2001), and some use standard rather than low mA regimens (Kay et al, 2000; Pescatore et al, 2000; Spinzi et al, 2001).

Published studies using dual-position scans show sensitivities for polyp detection (on a polyp-by-polyp basis) of 73–91% and 22–82% for polyps of more than 10 mm and intermediate size polyps respectively (Fenlon et al, 1999a; Fletcher et al, 2000; Mendelson et al, 2000; Yee et al, 2001). Sensitivity for polyps of less than 5 mm is poor in most series. Fenlon et al (1999a) reported sensitivities of 91%, 82% and 55% for polyps with a diameter of 10 mm or more, 6–9 mm and 5 mm or less respectively. The three cancers in this series were detected.

Figure 1. Workstation display from 'Navigator' software (GE, Milwaukee) showing (clockwise from top right) axial source images, coronal and sagittal reformats and endoluminal three-dimensional reconstructions (virtual colonoscopy).



Attempts to improve sensitivity of polyp detection by administering an oral contrast agent with the bowel preparation has not yet gained wide acceptance.

Studies using dual-position scanning quoting the sensitivity on a per patient basis (that is the ability to identify patients with polyps) suggest sensitivities for polyps >10 mm of 85–96%, with positive and negative predictive values of 81–96% and 85–97% respectively (Fenlon et al, 1999a; Fletcher et al, 2000; Yee et al, 2001).

Relatively little has been published on the sensitivity for the detection of carcinomas, and in most published series the numbers of such lesions have been too small for meaningful analysis.

Specificity

False positive results of CTC/VC arise particularly from the misinterpretation of faecal residue. Specificities reported on a per patient basis, using colonoscopy as a gold standard, range from 74–96% (Fenlon et al, 1999a; Fletcher et al, 2000; Kay et al, 2000; Pescatore et al, 2000); the better of these results comes from studies using dual positioning. The use of 3-D imaging for problem-solving increases specificity.

Sources of error

The main sources of errors and artefacts and potential solutions are related to:

- Breath hold misregistration owing to mismatching of the data set at the site of adjacent breath hold acquisitions. This may be mitigated by the use of a single breath hold
- Faecal residue leading to false-positives for polypoid lesions. Faeces may be distinguished from polyps by movement of the filling defect within the lumen to the dependent wall of the bowel in both supine and prone projections (*Figure 3*), gas content within the faeces or heterogeneity of attenuation (*Figure 3*). The

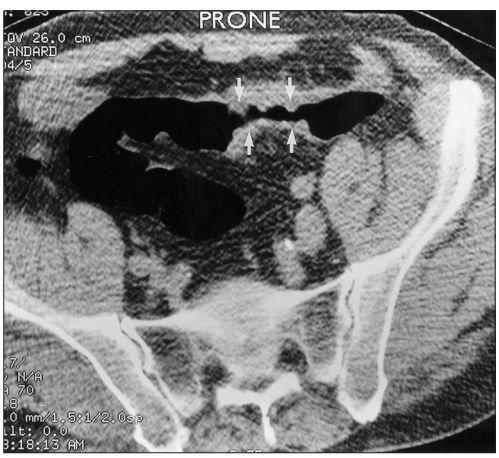


Figure 2. Axial image, soft tissue windows showing concentric thickening of sigmoid colon caused by carcinoma (indicated).

use of intravenous contrast media has been suggested by some authors to increase accuracy; the polyps should enhance, whereas faecal material does not (Morrin et al, 2000). However, this increases the costs and risks of the procedure without, as yet confirmed, major benefits. The use of faecal-tagging techniques and subsequent digital subtraction of faeces from the image is under investigation

- Fluid residue can hide even large lesions, but the problem is minimized by dual-position scanning (*Figure 4*) and by use of a low-volume lavage preparation
- Poor distension. The degree of distension achieved is dictated by patient tolerance, and this is optimized by the use of spasmolytics. Supine and prone scans are complementary in rendering dependent collapsed loops on one scan position to be non-dependent and distended on the other.

SAFETY OF CT COLONOGRAPHY

Risks associated with CTC/VC are those of the bowel preparation, drugs used (hyoscine butylbromide), perforation by the rectal tube or by insufflation, and radiation dosage.

The potential for bowel perforation, albeit small, must be recognized, although the authors are unaware of any reported case. The 'low-dose' technique described above results in effective whole body doses of about 5 mSv (milliSievert) with the authors' scanner (CTi, GE, Milwaukee, USA; Mendelson et al, 2000). A dosage of 5 mSv gives a lifetime risk of fatal cancer induction of about 1 in 4000–5000.

PATIENT ACCEPTANCE

In the authors' series, CTC/VC was highly acceptable to patients (Forbes and Mendelson, 2000). Although there was significantly more discomfort from unsedated CTC/VC than sedated

Figure 4. Fluid residue. a. Supine axial image demonstrating fluid-filled sigmoid loop with resultant poor visualization of dependent mucosal surface. b. Prone image, photographed inverted, at the same level shows the fluid has moved. Supine and prone views combined are complementary, with good visualization of sigmoid.

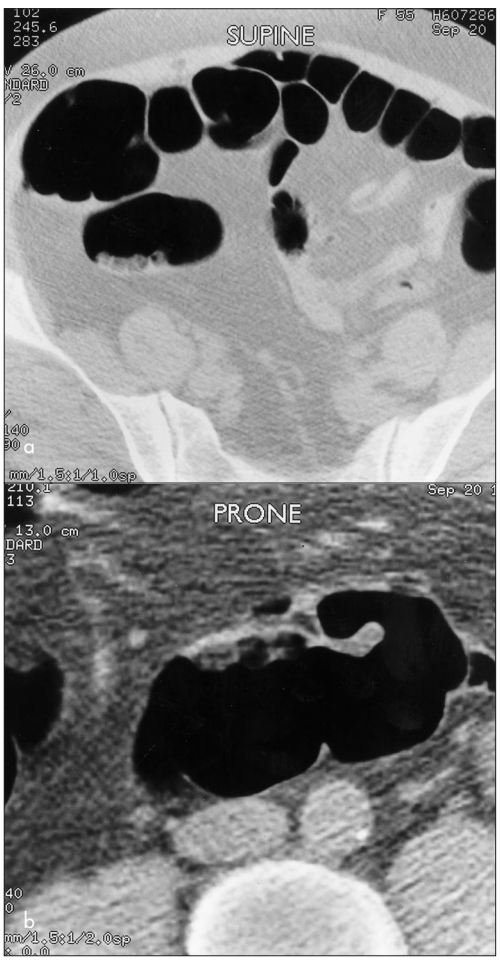
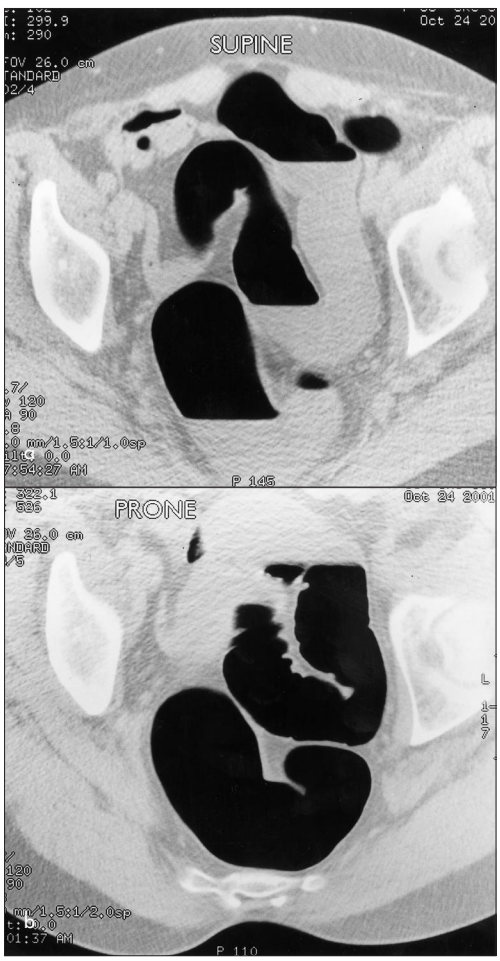


Figure 3. Faecal residue. a. Supine axial image showing filling defects on dependent wall of sigmoid colon. Note that one of these contains a small bubble of gas. b. Soft tissue windows. Prone axial image photographed inverted (i.e. as if patient is supine). Filling defects have moved to a dependent surface and are of heterogeneous attenuation, containing gas.



colonoscopy, the discomfort was still at an acceptable level. No significant differences between CTC/VC and colonoscopy were observed for how well the procedure was tolerated, satisfaction with the procedure or embarrassment. CTC/VC was preferred by 27%, colonoscopy was preferred by 23% and in 49% there was no preference. The vast majority would have either examination repeated if necessary.

In an ongoing feasibility study of CTC/VC for colorectal cancer (CRC) screening of asymptomatic average risk individuals, acceptance of the technique was very good, with the vast majority of subjects willing to repeat the examination in the future if required (Edwards et al, 2001b).

ROLES OF CT COLONOGRAPHY

Diagnosis of colorectal neoplasia in symptomatic patients

CTC/VC in future may be considered as a replacement for double-contrast barium enema (DCBE) in symptomatic patients (*Figures 5–7*). There is accumulating evidence that the technique is as accurate as DCBE for this indication, although no direct comparative studies have been performed. CTC/VC is likely to be better tolerated than DCBE; it is quicker for the patient and requires less change in patient position during the procedure.

It is stressed that CTC/VC is not a suitable technique for the detection of mucosal disease, such as inflammatory bowel disease and angiodysplasia. However, diverticula are easily detected.

In some patients, CTC/VC may in future also replace diagnostic colonoscopy. Symptomatic patients are likely to be selected to undergo either CTC/VC or colonoscopy in a similar way to that in which patients are currently selected for either colonoscopy or DCBE. Often the decision is based on availability (especially regarding open-access colonoscopy), cost, local expertise and local referral patterns. In practice, the determination is also subject to the degree of clinical suspicion of CRC and/or to the age of the patient – those patients with a higher pre-test probability of CRC being initially referred for colonoscopy and those with a lower probability being referred for DCBE. It is for these latter patients that CTC/VC is likely to replace DCBE, with the added bonus that CTC/VC may be able to identify some extracolonic pathologies.

In addition, in those patients in whom there is a contraindication to colonoscopy or previous examinations have been difficult, CTC/VC can provide an alternative to diagnostic colonoscopy.

Incomplete colonoscopy

In patients in whom colonoscopy has been incomplete, it is desirable to proceed to an alternative examination immediately while the bowel remains prepared. The advantage of CTC/VC over DCBE is that residual air from colonoscopy is an aid rather than a hindrance to examination. Patients tolerate CTC/VC better than DCBE in this context, and the examination is complete in the vast majority of cases (Morrin et al, 1999).

A further indication for CTC/VC is in the patient with a stricturing lesion that is non-traversable by conventional colonoscopy. In most cases, CTC/VC can be utilized to exclude significant neoplasms proximal to the known lesion (Fenlon et al, 1999b).

Colorectal cancer screening

Most authorities agree that subjects with an above-average risk of CRC should ideally undergo colonoscopy for screening. Therefore, this discussion will be limited to individuals with an average risk of CRC.

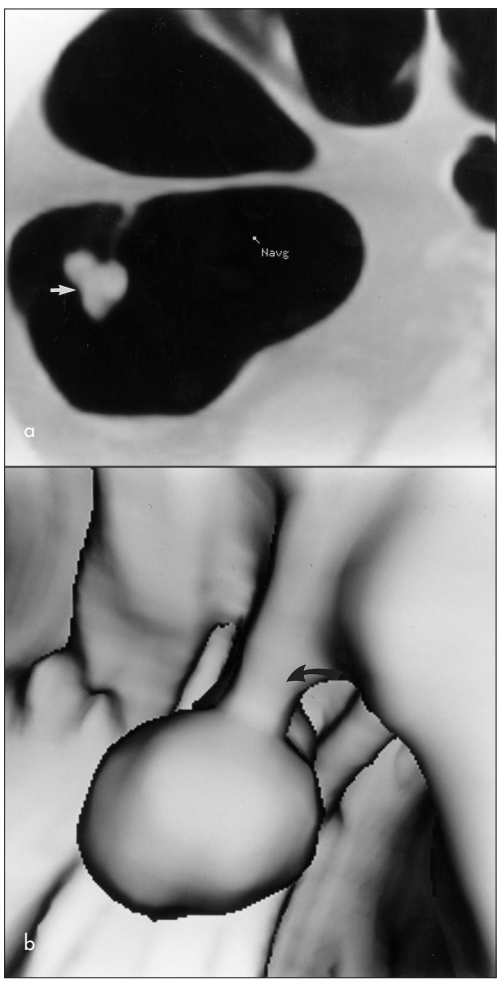
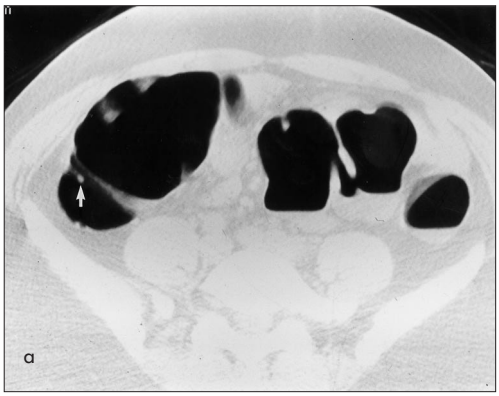


Figure 5. a. Pedunculated polyp in ascending colon (indicated), approximately 15 mm in diameter, on magnified axial image. b. Endoluminal three-dimensional image of same polyp showing stalk (curved arrow) and head of polyp (straight arrow).



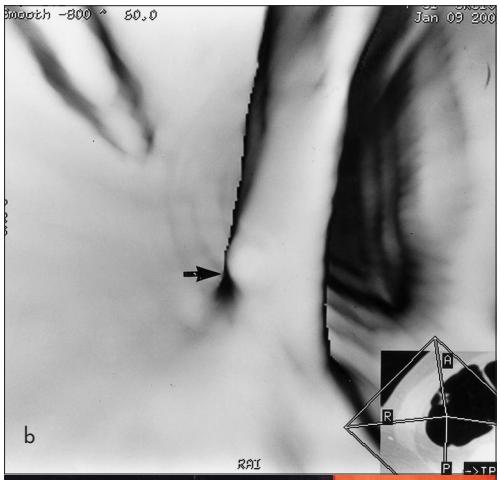
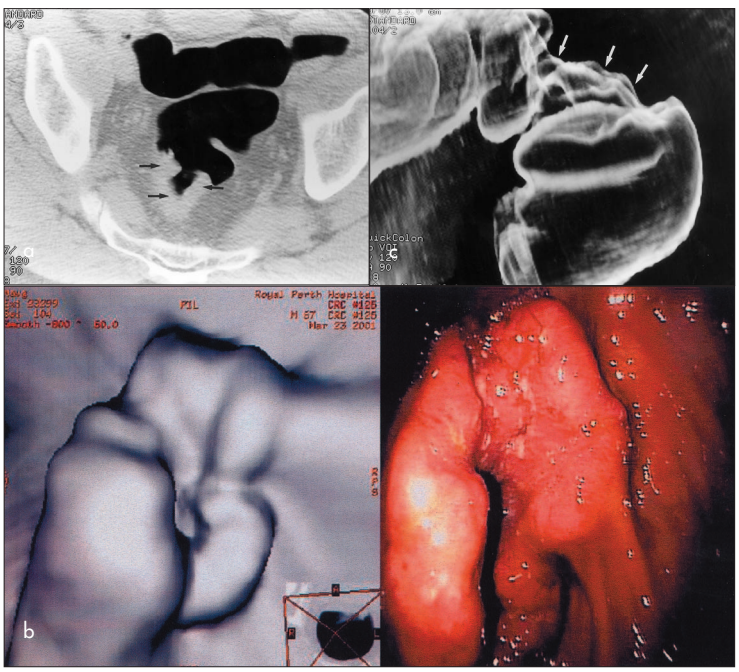


Figure 6. a. Axial image showing small polyp (about 5mm) in ascending colon (indicated). b. Three-dimensional endoluminal image of same lesion. c. Real colonoscopy image for correlation.

CRC is a disease that ideally lends itself to screening: it is common, prognosis is poor if it is detected late but excellent if early disease is treated, and there is a premalignant phase (the adenoma) which has a long dwell time during which it can be detected and treated relatively safely. Unfortunately, the tools currently available for screening are imperfect.

Faecal occult blood testing (FOBT) is cheap, safe, able to be administered by the general practitioner and is most widely advocated as the only test to have been shown to reduce mortality from CRC (by 15–33%) when applied to mass population screening (Australian Health Technology Advisory Committee, 1997). Accuracy depends on the type of FOBT used and the frequency of testing, but on an individual basis FOBT misses 21–63% of cancers and most adenomas and has a false positive rate of 2–13% (Allison et al, 1996).

Figure 7. Carcinoma of the rectum. a. Axial image showing mass in rectum (indicated). b. Endoluminal view (right) of the same stricturing lesion and colonoscopic image (left) for correlation. c. Volume rendered computed tomography image, reformatted to resemble barium enema, showing annular constricting nature of the lesion.



Flexible sigmoidoscopy (FS) is being assessed in Australia (Collett et al, 2000) and elsewhere as a tool for population screening. The rationale is that most neoplasms occur within reach of FS and that distal adenomas may be predictors of proximal lesions. However, 25% of subjects only have adenomas proximal to the splenic flexure and therefore beyond reach of FS (Nicholson et al, 2000).

These factors have prompted calls for whole-colon screening techniques. These include

DCBE, colonoscopy and CTC/VC. While accuracy is important, other issues that must be assessed include acceptability, compliance, availability, safety and cost. Both DCBE and colonoscopy have drawbacks which make it unlikely that they will gain widespread acceptance as tools for mass screening. DCBE has its advocates, but it is probably not of adequate accuracy without concomitant FS (Mendelson, 1998), which would increase costs and almost certainly decrease compliance. There have been no formal studies of DCBE in this context, and there is a significant radiation dose.

Colonoscopy has been supported by some authorities, but taking into account the need for sedation, consequent bed fees and cost of time off work, it is relatively expensive and not without risk. In addition, completion rates to the caecum outside specialist centres may be 80–90% (Freeman et al, 1993; Thiis-Evensen et al, 1999) or less. For these reasons, VC has been suggested as a contender for use as a screening tool. Currently, it is more accurate than FOBT and can compete with FS with regard to accuracy for detecting medium- and large-sized polyps, but more importantly it examines the whole large bowel.

Potential advantages include its minimal invasiveness and speed – the scan takes only a few minutes, no sedation is required and initial studies have shown it is highly acceptable to asymptomatic subjects in a screening context (Edwards et al, 2001a). Its high-tech profile makes it potentially attractive to the lay public. Radiation dosages for CTC/VC, when low dosage protocols are used, are considerably less than conventional DCBE. There is also the potential to detect incidental extracolonic pathology, such as asymptomatic aortic aneurysms and renal carcinoma.

The lack of sensitivity of CTC/VC for the detection of polyps of 5 mm or less has been cited as a limitation. In the context of a screening programme, this probably does not matter. The probability of a 5 mm lesion being malignant at discovery is negligible. In fact, only about 50% of diminutive polyps are adenomatous, the rest being hyperplastic and therefore having no malignant potential. Although most cancers develop from adenomatous polyps, the dwell time for a polyp to turn to cancer is estimated at about 10 years for a polyp of more than 1 cm in size (Winawer et al, 1997), allowing an enlarging lesion to be picked up on subsequent screening examinations. There is also evidence that some small polyps may undergo spontaneous regression (Hoff et al, 1996).

THE FUTURE OF VIRTUAL COLONOSCOPY

CTC/VC is a technique in evolution. There are a number of areas which require further work, as detailed below.

Technical developments that require further assessment include:

- The effect on accuracy for polyp detection of multi-slice helical scanners. Potential benefits include shortening of scan acquisition time and detection of smaller polyps. Large clinical studies are yet to be published, although initial reports are encouraging (Hara et al, 2001). However, the question of whether it is necessary or desirable to detect diminutive polyps in the context of a screening programme needs to be resolved
- Patients undergoing CTC/VC, colonoscopy or DCBE find the bowel preparation the most uncomfortable part of the procedure. The use of faecal tagging agents and subsequent digital subtraction techniques of faeces (virtual preparation), after minimal or no bowel preparation, is currently under investigation (Callstrom et al, 2001; Zalis and Hahn, 2001)
- Computer-aided polyp detection software that will allow a semi-automated reading of examinations. Early clinical reports show that this is feasible (Summers et al, 2001)
- Assessment of the optimal rendering process for 3-D reconstructions and of innovative projections that allow the maximum mucosal surface to be examined in the shortest time
- Magnetic resonance imaging-based VC. This has been shown to be feasible and has the advantage of a lack of ionizing radiation (Debatin et al, 1999). However, in the foreseeable future, availability of suitable scanners is likely to be a problem.

The clinical aspects of CTC/VC that require clarification include:

- The role in screening of average-risk asymptomatic subjects for colorectal neoplasia. Only one study has been published (Rex et al, 1999), the conclusion of which was that CTC/VC was insufficiently sensitive in this context. However, the sensitivities in this study were among the lowest reported and the results of further feasibility studies are awaited
- In symptomatic patients, the potential for CTC/VC to replace DCBE and some diagnostic colonoscopies in the investigation of suspected CRC
- Issues of accreditation and training in interpretation of CTC/VC

- The trade-off between increased sensitivity for extra-colonic pathology that might result from using standard abdominal CT dose parameters and the increased radiation dosage. The use of low-dose parameters is likely to remain prevalent in the screening context.

CONCLUSIONS

CTC/VC is a technique in evolution that has great potential as a diagnostic tool for colorectal neoplasia in symptomatic patients and as a screening tool in average-risk asymptomatic subjects. With hardware and software developments and increased operators' experience, there will undoubtedly be advances in the performance characteristics of the test. Many issues, both technical and clinical, remain unresolved and are the subject of continuing research. HM

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KEY POINTS

- Computed tomography colonography/virtual colonoscopy (CTC/VC) is a technique for examining the whole large bowel which continues to evolve technically and has high patient acceptability.
- Sensitivity for larger polyps and cancer is good.
- Potential important roles include diagnosis of colorectal cancer in symptomatic patients, screening for colorectal neoplasms in average-risk individuals and use in patients in whom colonoscopy is incomplete or contraindicated.
- At present, there is no role for CTC/VC in the diagnosis of inflammatory bowel disease.
- CTC/VC is able to detect a variety of extracolonic pathology