

Virtual colonoscopy and colorectal cancer screening

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Abstract

Colorectal cancer (CRC) is the leading cause of cancer related death in the United States. Virtual colonoscopy is a new method for imaging the colon and has produced promising early results for polyp and cancer detection. The challenge remains to reproduce these favorable results in clinical practice and to evaluate the use of virtual colonoscopy in a purely screening population. Virtual colonoscopy may dramatically improve population participation in screening programs and play a major role in minimizing the impact of CRC.

Key words: Colonoscopy—Tomography, X-ray computed—Magnetic resonance imaging—Colonic polyps—Colorectal neoplasms.

Colorectal cancer (CRC) is a leading cause of cancer-related death in the United States [1]. In 1999, approximately 140,000 cases of CRC were diagnosed in the United States, and 60,000 patients died of the disease. Colon cancer can be prevented if precursor polyps are discovered and removed early in their course [2–6]. Nevertheless, individuals at greatest risk of developing colorectal cancer remain largely underscreened, in part because of poor public awareness, acceptance of current screening techniques, and continuing controversy among health care professionals as to the best method for screening.

There are currently four Medicare-reimbursable tests for colon cancer screening: the fecal occult blood test, sigmoidoscopy, the double-contrast barium enema, and colonoscopy. Fecal occult blood testing detects only 30–40% of colorectal cancers and 10% of adenomas [7, 8]. Sigmoidoscopy fails to detect lesions in the proximal colon (40% of all cancers) and misses 10–15% of sigmoid colon neoplasms. Barium enema and colonoscopy permit visualization of the entire colon, with an increase

in overall detection rate compared with fecal occult blood test or sigmoidoscopy. However, the sensibility of barium enema is far from optimal (about 70% for polypoid lesions >7 mm) and is uncomfortable for both patient and examiner.

Colonoscopy is associated with increased risk and cost. It fails to demonstrate the entire colon in up to 10% of cases, misses 10–20% of colorectal neoplasms, results in colonic perforation in one in 1500 patients, and incurs a cost triple that of barium enema [9, 10]. The introduction of a safe, noninvasive, and effective method of detecting colorectal polyps and cancers has obvious appeal.

Virtual colonoscopy is a new method for imaging the colon and has produced promising early results for polyp and cancer detection. Favorable attributes of virtual colonoscopy include its safety, high patient acceptance, and ability to provide a full structural evaluation of the entire colon [11].

Technique

Although a variety of scanning techniques have been described for virtual colonoscopy, the same basic imaging principles apply: cleaning the patient's bowel with a standard barium enema or colonoscopy bowel preparation, colonic insufflation with room air or carbon dioxide, supine and prone thin-section helical computed tomography (CT) of the abdomen and pelvis, followed by offline computerized manipulation of the CT dataset to facilitate inspection of the colonic wall.

Recommended scanning parameters include a collimation of ≤ 5 mm, a table speed of 6.25 mm/s (pitch 1.25), 110 mA, 110 kVp, and a 512×512 matrix. A single acquisition of the abdomen and pelvis is obtained with the patient breath-holding for the first 15–20 s of the scan (to cover the upper abdomen), and the remainder of the data is acquired during gentle respiration. After the supine scan, helical CT is routinely repeated with the patient prone. Use of both supine and prone helical CT datasets helps differentiate mobile stool (Fig. 1) from

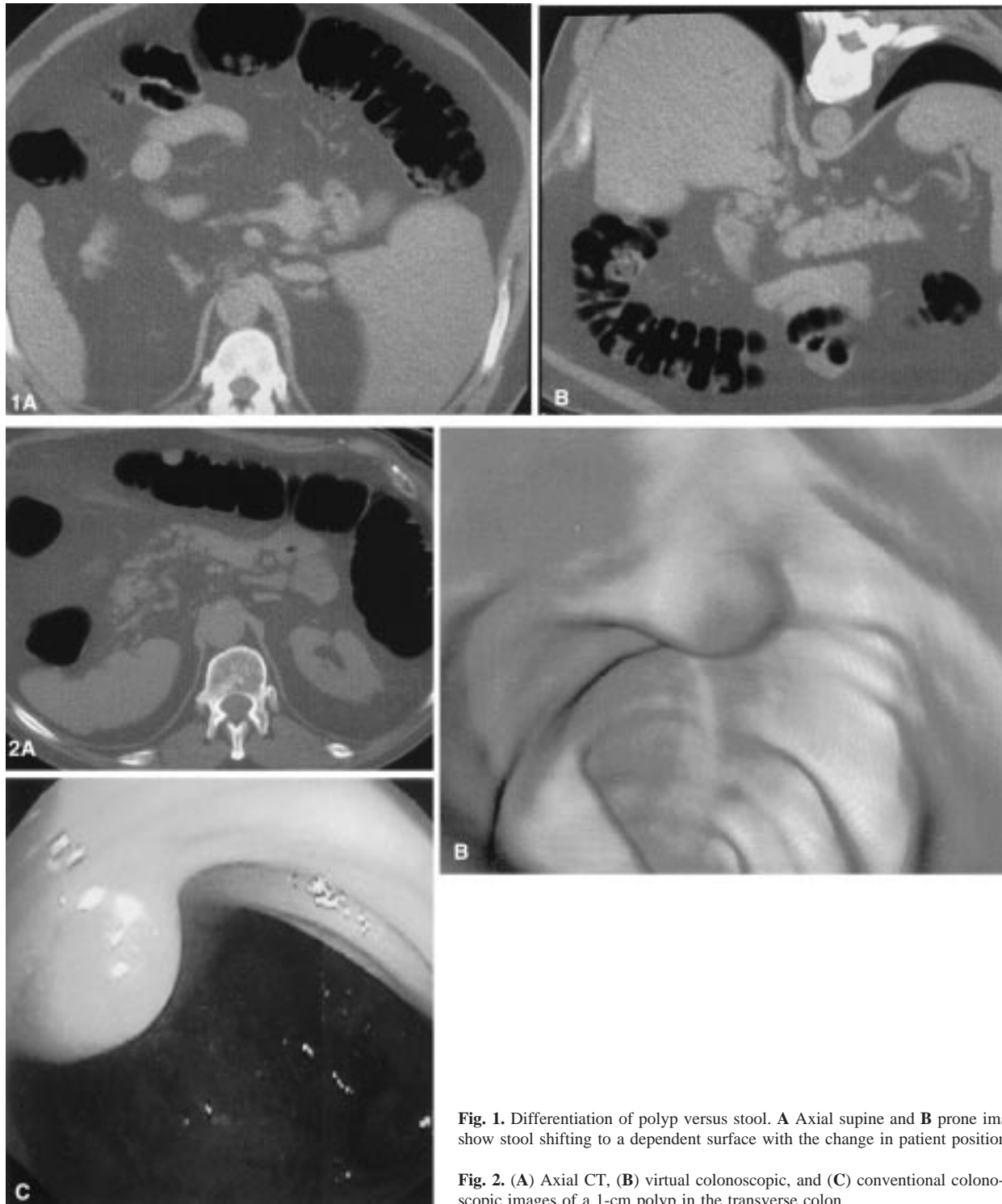


Fig. 1. Differentiation of polyp versus stool. **A** Axial supine and **B** prone images show stool shifting to a dependent surface with the change in patient position.

Fig. 2. (A) Axial CT, (B) virtual colonoscopic, and (C) conventional colonoscopic images of a 1-cm polyp in the transverse colon.

fixed pathology such as cancers and polyps (Fig. 2), allows more even distention of the colon, and improves visualization of segments of colon obscured by intraluminal fluid. Some investigators have questioned the routine use of a muscle relaxant, and others have advocated

the addition of intravenous contrast to improve the conspicuity of both colonic and extracolonic lesions.

The total patient time required for the study is approximately 20 min. Because sedation is not required, patients are immediately discharged from the CT suite without the

need for observation or recovery. After image acquisition, the CT data can then be viewed by using a variety of software techniques: one can choose to view the axial two-dimensional (2D) CT images displayed at lung window settings alone or use a variety of visualization techniques including three-dimensional (3D) endoluminal images (simulating conventional endoscopy images), multiplanar reconstructions, and mathematically straightened views of the colon, or “unraveled” views of the colon (virtual gross pathology). The former reformatting unfolds the colon as a straight tube, eliminating all physiologic curves. The latter reformatting is a way to visualize the colon similarly to gross pathology in which the colon is opened along its longitudinal axis and is inspected in a flat rather than a tubular form. Most investigators agree that some form of 3D postprocessing is required to help differentiate polyps from normal haustral folds, which have a similar appearance when viewed in profile using the axial images alone (Fig. 3).

Preliminary results of virtual colonoscopy

Preliminary results indicate that the accuracy of virtual colonoscopy for polyp detection exceeds that of barium enema and approaches that of conventional colonoscopy. Hara et al. of the Mayo Clinic evaluated 30 endoscopically proven polyps in 10 patients and detected 100% of all polyps larger than 1 cm in diameter, 71% of polyps between 0.5 and 0.9 cm, and up to 28% of polyps smaller than 0.5 cm [12]. In a subsequent study, the same group evaluated 70 consecutive patients and reported a sensitivity and specificity of 75% and 90% for patients with adenomatous polyps larger than 10 mm, 66% and 63% for patients with adenomatous polyps larger than 5 mm, and 45% and 80% for patients with adenomatous polyps smaller than 5 mm, respectively [13]. Dachman et al. of the University of Chicago, using combined axial 2D CT images with limited 3D endoluminal reconstructions for problem solving in 44 patients with 22 proven polyps, reported a sensitivity of 83% and a specificity of 100% for polyps 8 mm or larger.

Royster et al. of Boston University compared the diagnostic accuracy of axial 2D CT images of the air-distended colon, 3D endoscopic reconstructions, and conventional colonoscopy in 20 patients with suspected colon cancer [14]. Using 2D axial images alone, all 20 carcinomas and 12 of 13 polyps (all <1 cm) were successfully detected. Comparable results were obtained with axial CT images and 3D endoscopic reconstructions for colon cancer detection, but the specificity of the 3D endoscopic images in patients with subcentimeter polyps was greater than that of axial 2D images alone. Another study from Boston University evaluated the performance of virtual colonoscopy in 38 patients with 38 pathologically proven colorectal cancers and 23 adenomatous polyps. On virtual

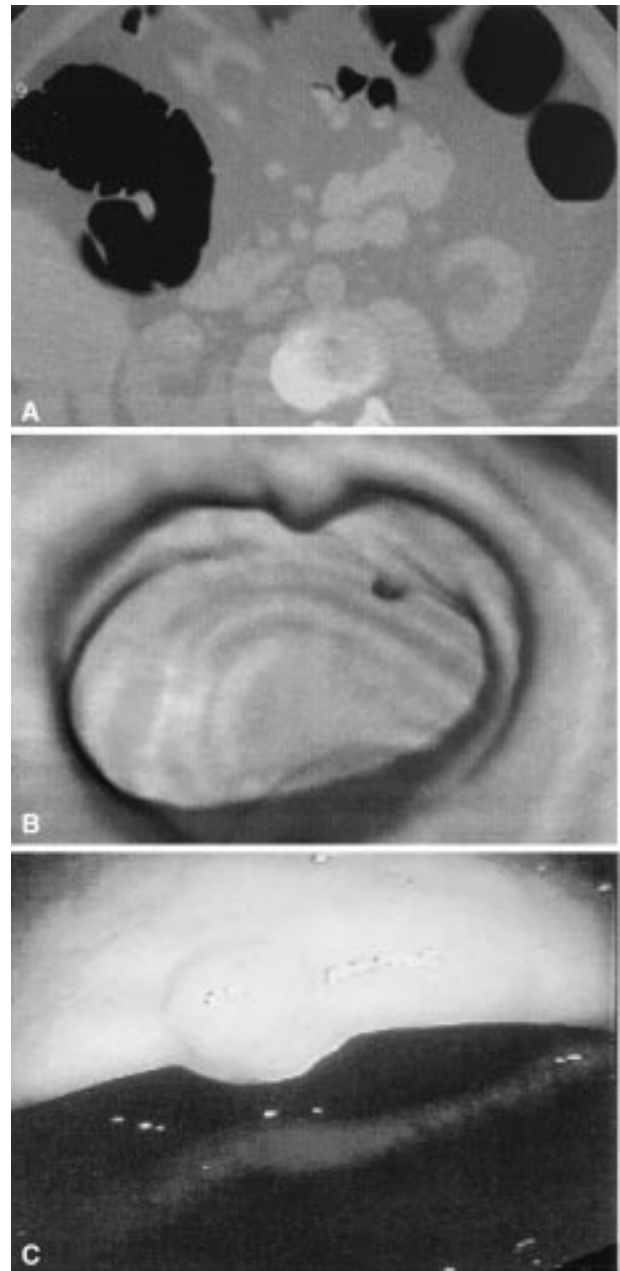


Fig. 3. Polyp versus fold: contribution of three-dimensional virtual colonoscopic images. **A** Axial image shows a questionable polyp versus a prominent fold. **B** Virtual colonoscopy and **C** conventional colonoscopy confirms the presence of a polyp on a fold.

colonoscopy, all cancers and all polyps larger than 6 mm were identified, and there were two false-positive reports of polyps. Virtual colonoscopy enabled visualization of the entire colon in 35 patients; conventional colonoscopy was incomplete in 14 patients. Virtual colonoscopy correctly localized all 38 cancers, compared with 32 cancers that were correctly localized with conventional colonoscopy.

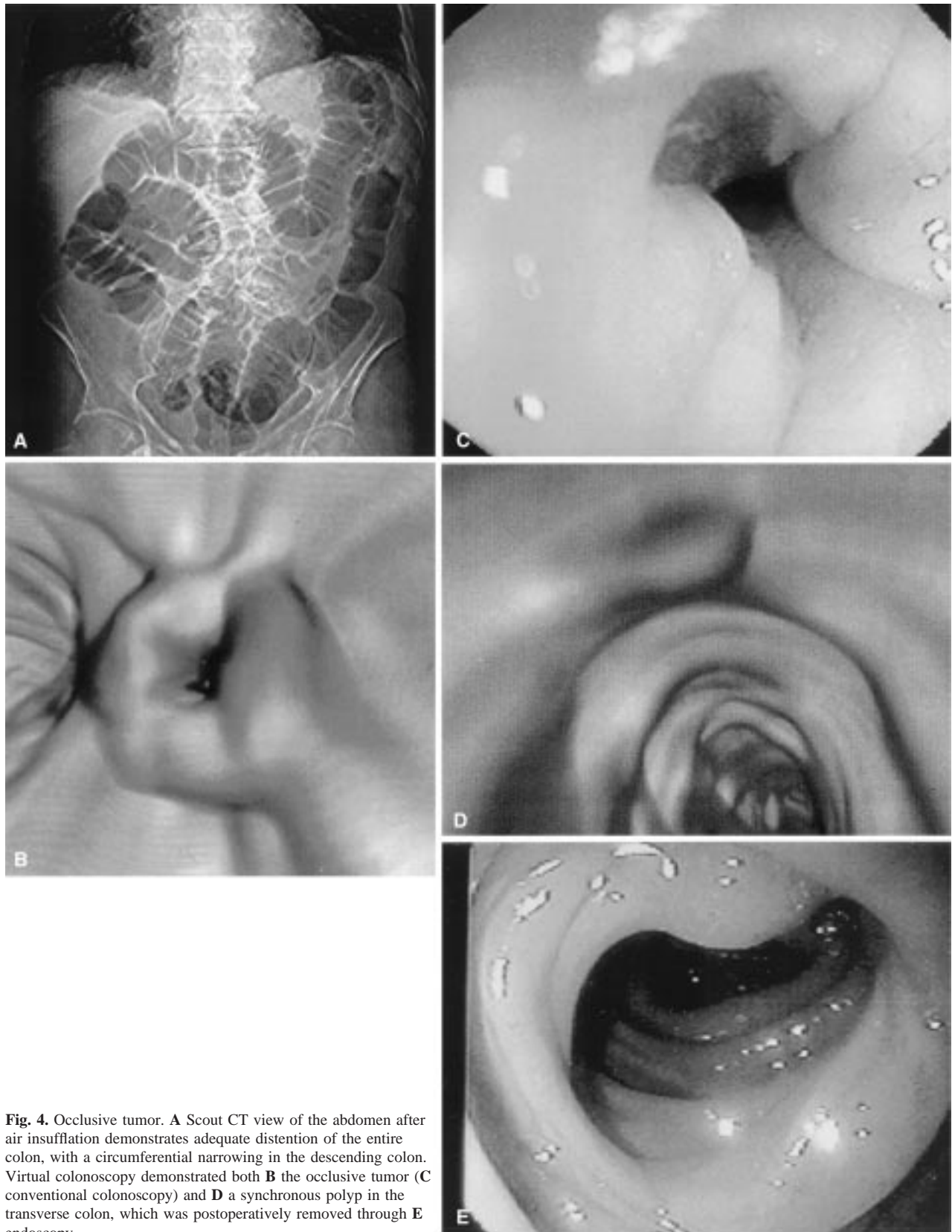


Fig. 4. Occlusive tumor. **A** Scout CT view of the abdomen after air insufflation demonstrates adequate distention of the entire colon, with a circumferential narrowing in the descending colon. Virtual colonoscopy demonstrated both **B** the occlusive tumor (**C** conventional colonoscopy) and **D** a synchronous polyp in the transverse colon, which was postoperatively removed through **E** endoscopy.

Table 1. Preliminary results of virtual colonoscopy for colorectal polyps >1 cm

	No. patients	No. polyps ≥1 cm	% Sensitivity for polyps ≥1 cm	% Sensitivity for patients with polyps ≥1 cm
Mayo Clinic	70	15	73	75
Bowman Gray/Indiana University	46	14	50	75
Medical University of South Carolina	38	11	91	—
Univ. of Chicago	21	5	100	100
Boston University ^a	77	14	100	92

^a Unpublished results

Another application of virtual colonoscopy, the preoperative assessment of the colon proximal to an occlusive cancer (defined as a tumor that cannot be traversed endoscopically), was recently reported by Fenlon et al. [15]. In 29 patients with occlusive carcinomas, virtual colonoscopy identified all 29 occlusive cancers (Fig. 4) and demonstrated two cancers and 24 polyps in the proximal colon. Both of the synchronous cancers were confirmed intraoperatively and resected. Virtual colonoscopy successfully demonstrated the proximal colon in 26 of 29 patients studied compared with preoperative barium enema, which failed to adequately demonstrate the proximal colon in any patient studied. In three patients, retained stools proximal to an occlusive tumor prevented a complete virtual colonoscopic evaluation.

When the results of these preliminary studies are combined, the sensitivity of virtual colonoscopy for detecting polyps larger than 10 mm exceeds 85–90% and that for polyps 5–9 mm is 70–80%, with an overall specificity exceeding 80% (Table 1). Furthermore, virtual colonoscopy has proven useful for evaluating patients after incomplete colonoscopy, for accurate preoperative tumor localization, and for evaluating the colon proximal to occlusive carcinomas before surgery.

Technical developments and controversies

There are many unanswered questions relating to the technique of virtual colonoscopy. These include issues of bowel preparation, room air versus carbon dioxide insufflation, routine use of smooth muscle relaxants, the need for both prone and supine acquisitions, relative contribution of 2D images and 3D renderings, and the optimal method for 3D postprocessing of the acquired dataset. Most researchers agree that both prone and supine scans should be routinely acquired to differentiate true pathologic lesions from stool and intraluminal fluid. At this time, a full colon preparation is required to achieve acceptable results. Orally administered barium contrast products to mark or tag fecal residue are under investigation, but neither specific formulations nor results are available. The incentive behind the development of such

Table 2. Range of visualization techniques that may be used for virtual colonoscopy

Axial 2D CT images
Multiplanar reconstructions (MPR)
Perspective surface rendered endoscopic images
Perspective volume rendered endoscopic images
Mathematically straightened views of the colon
Digital unravelling techniques (virtual) gross pathology
Oblique tomograms
Panoramic endoscopy
Map projections

products is to minimize bowel preparation requirements and increase patient compliance, but the efficacy of these agents remains unproven. Expected improvements in CT data acquisition (multidetector systems) are likely to improve test performance in the future as a result of shorter acquisition time, fewer image artifacts, and superior z-axis image resolution.

There are many techniques in use for postprocessing and interpreting the acquired CT datasets (Table 2). These range from simple evaluation of the axial CT images at lung window settings, reformatted two-dimensional CT images at cross-sectional and orthogonal angles to the long axis of the colon, 3D extraluminal and endoluminal renderings, mathematically straightened views of the colon, and “fly-through” intraluminal visualizations. Which of these methods will prove to be the best in terms of speed and accuracy is as yet unclear.

Virtual endoscopy based on 3D magnetic resonance imaging is feasible and may also be an alternative to CT. The colon is filled with a preparation of 1500–2000 mL of dilute Gd-DTPA in water. Three-dimensional gradient echo sequences are used to visualize the colon. Three-dimensional datasets can be acquired in the prone and supine positions. Image analysis is based on a combination of multiplanar reconstructions (MPR) and 3D extraluminal and endoluminal renderings. Luboldt et al. reported sensitivities and specificities of 100% for polyps larger than 10 mm and of 40% and 75%, respectively, for polyps 5–10 mm with magnetic resonance imaging techniques (magnetic resonance colonography) [16].

The lack of ionizing radiation is an advantage, although the use of a contrast enema is a less appealing feature. Air may prove to be a more tolerable alternative, if technical challenges can be overcome.

The development of virtual colonoscopy has stimulated great interest among endoscopists. Although some see virtual colonoscopy as a potential threat, many are eager to participate in its development. Some regard virtual colonoscopy as a technique within the domain of the endoscopist, and issues of professional “turf” have already surfaced. Terminology has also become an issue of considerable controversy, with a variety of terms in use including virtual colonoscopy, CT colonography, CT colonoscopy, and CT colography. Although each term has merit and uniformity is undoubtedly required, it seems premature to rigidly enforce a single term to a technology that lacks any form of standardization with regard to technical performance.

Virtual colonoscopy and colon cancer screening

If the promising results of virtual colonoscopy achieved in these studies are reproducible in clinical practice, what will be its place in the colon cancer screening process? Adenomatous polyps are common, being present in 30–50% of persons older than 50 years. Most measure less than 1 cm, and within this subset, the probability of malignancy is extremely low and the likelihood of any lesion progressing to malignancy is extremely small. Many non-neoplastic polyps also measure less than 1 cm. Because many small polyps have no malignant potential, it may be possible to target only polyps above a certain size threshold (6 mm or even 1 cm) for colon cancer screening and removal and by doing so achieve comparable benefits to universal polypectomy, with considerable savings in cost and risk. Although provocative, a decision to ignore polyps below a certain size threshold has important implications for virtual colonoscopy because of its limited sensitivity (approximately 50%) for polyps smaller than 5 mm.

Furthermore, the American Cancer Society has recently revised its recommendations for colon cancer screening. Emphasis is now placed on the need to evaluate the entire colon (the so-called total colon examination) because up to 45% of neoplasms occur proximal to the splenic flexure. Colonoscopy, barium enema, and virtual colonoscopy are the only techniques capable of providing a full structural examination of the colon. Virtual colonoscopy is safer than colonoscopy and is likely to be more acceptable than barium enema to patients.

Decision processes regarding suitability of a test for screening are complex and involve estimates of performance characteristics (sensitivity, specificity, and predictive values), long-term outcomes, cost, patient acceptability, compliance, and availability. The true diagnostic

performance of virtual colonoscopy in a purely screening population has not yet been established. Furthermore, the ability to reproduce acceptable results outside of a research protocol has not been established and may be difficult to prove because such information from the non-academic environment rarely becomes apparent. The time required to process and interpret studies will undoubtedly decrease considerably in the future, and the issues of cost and reimbursement will need to be addressed.

Based on initial results, the strength of virtual colonoscopy appears to be the ability to separate patients with normal colons and colons containing only subcentimeter insignificant polyps from patients with clinically significant polyps, the latter of which require therapeutic colonoscopy for polypectomy. Because only 3–10% of average-risk persons age 50 years or older have a polyp 1 cm or larger, a test that could reliably and accurately identify this group would result in a dramatic reduction in the number of purely diagnostic colonoscopies performed, freeing up endoscopy services for those patients requiring therapeutic intervention.

In this regard, virtual colonoscopy is in direct competition with barium enema because both provide only the ability to diagnose polyps without the ability to perform therapy. In the only direct comparison to date, virtual colonoscopy proved more sensitive than single-contrast barium enema for polyp detection. There are no published screening studies of double-contrast barium enema (DCBE), but in a screening population of 738 average-risk asymptomatic persons, DCBE detected adenomas in only 2% of the population [17], well below that population's expected prevalence of 20–40% [18]. Results surpassing these are likely achievable with virtual colonoscopy. Furthermore, results of DCBE are highly operator dependent, and as referral numbers continue to decrease, training, skill, and enthusiasm among younger radiologists decline. As automated navigation techniques and “intelligent” software develop for virtual colonoscopy, operator input and interoperator variability may reduce substantially in the future. Although virtual colonoscopy cannot compete with therapeutic colonoscopy, it may be a useful adjunct as a first-line primary screening technique to help cope with the number of patients requiring CRC screening. With the emergence of a more “patient-friendly” screening approach, some gastroenterologists envision an increase in colonoscopy demand and welcome a more targeted population for therapeutic intervention.

Cost-analysis assessments of virtual colonoscopy will have a major impact on its potential use for CRC screening. Such assessments are complex and must include analysis of basic costs for equipment, running costs, personnel training, staffing, technical and professional fees, estimates of performance characteristics (in particular the test's specificity), patient compliance rates, selected intervals for screening, cost of cancer treatment, and long-

term outcomes. To be competitive, virtual colonoscopy will have to be provided at a cost only slightly greater than DCBE and well below that of conventional colonoscopy. The reason for this is that virtual colonoscopy and DCBE are diagnosis-only strategies and a proportion of patients will require subsequent colonoscopy to evaluate and treat lesions detected by CT. A low specificity (high rate of false-positive findings) may make the cost of virtual colonoscopy prohibitive because of an excessive number of unnecessary follow-up colonoscopy examinations. At this time, no data are available for reimbursement of virtual colonoscopy. Unpublished data from a number of centers, however, suggest that CRC strategies incorporating virtual colonoscopy can be more effective than currently recommended screening strategies when virtual colonoscopy is used at 3–5-year intervals. Further analysis is clearly required in this respect.

Conclusions

Preliminary research results of virtual colonoscopy are extremely encouraging, and performance characteristics will improve with technical innovations and experience of the radiologists. Software techniques designed to improve the speed, accuracy, and reproducibility of results are rapidly emerging. The challenge remains to reproduce these favorable results in clinical practice and to evaluate the use of virtual colonoscopy in a purely screening population. If virtual colonoscopy proves to be an accurate, reliable, and cost-effective method for detecting polyps and early cancers, it may dramatically improve population participation in screening programs and play a major role in minimizing the impact of CRC.

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