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Virtual Colonoscopy

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9.1 INTRODUCTION

In modern radiology, image acquisition techniques such as X-ray computer tomography (CT) and magnetic resonance imaging (MRI) provide multiple cross sections of parts of the body. Images of multiple slices may be combined to volume information that can be presented in many ways. By segmentation and volume rendering techniques, surfaces of specific organs can automatically be presented to the user in any desired viewing angle. These image processing steps make it possible to present the image information in a manner which better corresponds with the way the body is observed by the clinician than with cross-sectional information.

Virtual colonoscopy is an example of such an image processing approach. In this approach, the CT or MRI image information is presented in a way similar to normal optical colonoscopy. This presentation technique therefore corresponds with the way an endoscopist is used to inspect the colon and this makes this technique suitable as a follow-up to conventional optical endoscopy. In addition, the technique is more patient-friendly, more time-efficient, and yields a better surface visibility than conventional colonoscopy.

Colon cancer is the second leading cause of cancer death in the Western world. Virtual colonoscopy is a modern technique to inspect the bowel in a

noninvasive, virtual manner. It is widely studied for colorectal cancer surveillance and screening.

Colorectal polyps are considered important precursors of colon cancer (Vogelstein, Fearon, & Hamilton, 1988). Typically, such a benign tumor presents a sphere extending from the colon wall, like a mushroom. Generally, only polyps larger than 5 mm are considered important because smaller ones are known to rarely contain malignant tissue (Waye, Lewis, Frankel, & Geller, 1988). Early detection and removal of polyps has proven to lead to a decrease in incidence of colon cancer (Toribrara & Sleisenger, 1995). The interval before polyps develop into a malignancy is estimated to be on the order of 5 years (Potter, Slattery, & Bostick, 1993). Hence, screening seems an attractive possibility for prevention. Clearly, to enable large-scale screening programs, an effective procedure to detect polyps is needed.

Until recently, barium enema and optical colonoscopy were the two procedures available for examining the colon (Dodd, 1998; Rex, Cutler, & Lemmel, 1997). In "double contrast barium enema," several planar X-ray images of the abdomen are acquired by rotating the camera around the patient. Immediately before image acquisition, a barium solution followed by air is injected into the bowel via the anus. The radio-opaque barium sticking to the colon wall enables the visualization of the surface as a white structure on a dark background. In conventional colonoscopy, an endoscopic camera is transanally guided through the colon. By manipulating the tip of the probe, the physician inspects the inner surface for abnormalities. A drawback of the barium enema is the radiation burden of the X-rays. Moreover, the sensitivity is rather poor (50–80%, for polyps of 0.5–1 cm in diameter; Dodd, 1998). Colonoscopy requires intravenous sedation, whereas the colon ascendens often cannot be accessed by the endoscope (Rex et al., 1997). The sensitivity is estimated to be in the order of 80 to 82% for polyps of 0.5 to 1 cm.

People eligible for screening often avoid the examinations because of the associated discomfort (Winawer, Fletcher, & Miller, 1997). In the past few years, virtual colonoscopy has been developed as a patient-friendly alternative (Hong, Muraki, Kaufman, & He, 1997). First, the patient's colon is cleansed and transanally inflated with air. Subsequently, a 3D image volume of the abdomen is acquired by CT. Image acquisition by MRI is currently still in an experimental stage, because the lower resolution and signal-to-noise ratio strongly limit the applicability of virtual colonoscopy. Finally, the interior bowel surface is extracted and visualized, after which the physician virtually navigates through the colon and examines the surface for abnormalities (Fig. 9.1). Radiologists have immediately recognized the importance of this new technology. Currently, virtual colonoscopy is already clinically used in a few institutions (Fenlon & Ferucci, 1999).

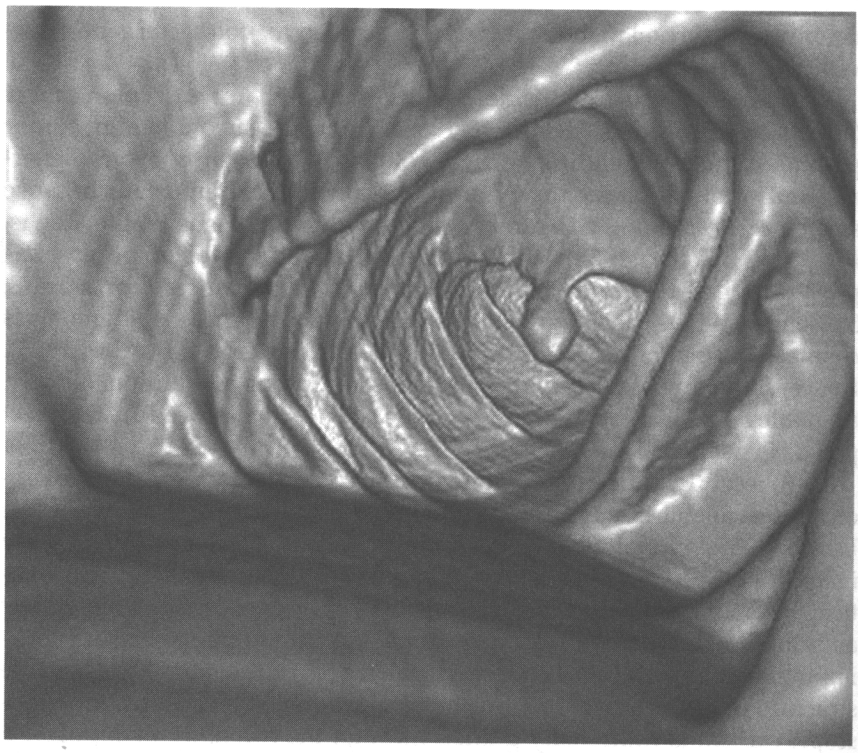

FIG. 9.1. Shown is a virtual endoscopic view of a protruding polyp (from Vos et al., 2001, reprinted by permission of the Radiological Society of North America).

To overcome current limitations of virtual colonoscopy, a display method was developed that renders six planar projections ("6P," cubic projection) at 90° viewing angles from points on the central path (Serlie, Vos, & Gelder, 2001). Unfolding such a cube shows the complete field of view at a path position. The image sequence of unfolded cubes aims to facilitate rapid exploration of the entire colon wall.

The conventional 3D visualization for CT virtual colonoscopy is compared with the new method regarding time efficiency and surface visibility. For more detailed information, see also Vos et al. (2001, 2003).

9.2 THE CURRENT STATE OF VIRTUAL COLONOSCOPY

The virtual colonoscopy examination can be modeled to comprise four stages: patient preparation, image acquisition, visualization, and diagnostic examination.

9.2.1 Patient Preparation

For optimal visualization, proper patient preparation is required prior to scanning. Conventionally, the procedure consists of the following steps (Fletcher & Luboldt, 2000; Helen & Ferucci, 1999; Serlie et al., 2001):

- On the day before the examination, the patient is asked to drink 4 to 5 L of a laxative fluid. Such a regime is necessary because remaining faeces may easily be interpreted as polyps (Fenlon, 1998; Lakare, Wan, Sato, & Kaufman, 2000).
- Immediately before data acquisition, a bowel relaxant may be administered intravenously. Although the beneficial effect has been disputed (Yee, Hung, Akerkar, & Wall, 1999), it is widely used to prevent movement artifacts due to peristalsis and to improve the distension (Fletcher & Luboldt, 2000).
- For distension and to introduce contrast, 1.5 to 2.0 L of carbon dioxide or room air is transanally brought into the colon (Rogalla, Schmidt, Korves, & Hamm, 1999). Fluid gadolinium solutions are generally applied in MRI (Luboldt, Bauerfeind, Wildermuth, & Debatin, 1999).

9.2.2 Image Acquisition

Advances in image acquisition technology (MRI and CT) have given a strong impetus to virtual endoscopy (Fig. 9.2). In CT imaging, the development of spiral multidetector scanners enabled acquisition within a breathhold at a

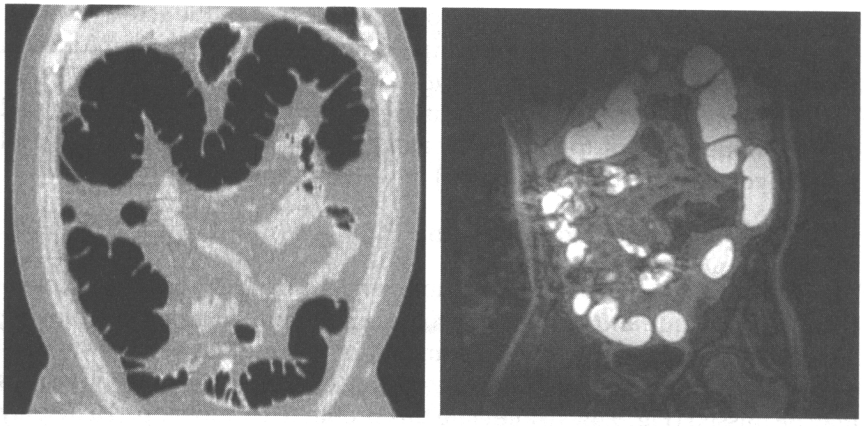

FIG. 9.2. Shown are images acquired with CT (left) and MRI (right; from Vos et al., 2001, reprinted by permission of the Radiological Society of North America).

high resolution (Halligan & Fenlon, 1999). MR colonoscopy has come within reach with the development of increasingly faster gradients.

Both prone and supine scanning remain essential with CT as well as MRI to enhance distension and to resolve possible ambiguities due to stool rests (Chen, Lu, Hecht, & Kadell, 1999). Stool rests may closely resemble a true polyp. By moving the patient, mobile fecal rests may be distinguished by not remaining stationary. However, such an approach goes at the expense of a doubled radiation dose with CT. On the other hand, suboptimal contrast and resolution still obstruct a large-scale application of MRI (Fletcher & Luboldt, 2000).

9.2.3 3D Visualization

For 3D visualization of CT or MRI volume data, there are two techniques available: surface fitting and direct volume rendering (Shahidi, 1996). Surface fitting is a preprocessing step to extract iso-valued surfaces from the data volume. Conventionally, 3D graphics hardware can be used for fast visualization. The number of generated polygons, however, grows proportionally with volume size, expressed in number of voxels. For high-resolution data, this number is typically between 10^5 and 10^6 triangles. Thus, interactive viewing is only possible using powerful graphics accelerators, or after a reduction of the mesh size (Garland & Heckbert, 1997), which is at the expense of loss in accuracy and fine details (Hopper, Lyriboz, & Kasales, 2003).

Information on the local signal values is lost in surface extraction. Direct volume rendering (DVR) preserves such information by projecting an image of the 3D data volume on the screen (Kaufman, 1991; Levoy, 1988). An example of DVR is volume ray casting (Fig. 9.3). The image is generated by casting a ray from the viewpoint through each pixel on the screen into the data volume. Next, the volume is sampled along the ray. A transfer function associates the data values with values for color (RGB) and opacity (0–1). The color of each image pixel is determined by "compositing" the color and opacity values in front-to-back order along the ray. Both surface fitting and DVR have been successfully applied in virtual colonoscopy.

9.2.4 3D Diagnostic Examination

The conventional 3D display method renders images similar to colonoscopy. Antegrade and retrograde movies are generated offline, displaying forward and backward viewing planes ("2P"; Fenlon et al., 1999). However, haustral folds may occlude the wall, as a consequence of which lesions may be missed (Fig. 9.4). To alleviate this problem, we developed a display method based on so-called unfolded cubes (Serlie et al., 2001). In the next sections, we evaluate the usefulness of our method by comparison with the

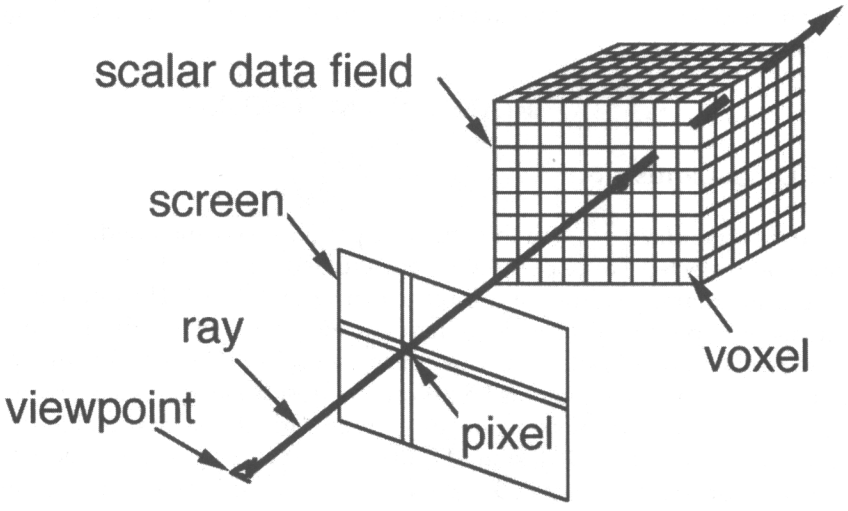

FIG. 9.3. Shown is the principle of volume ray casting (from Vos et al., 2001, reprinted by permission of the Radiological Society of North America).

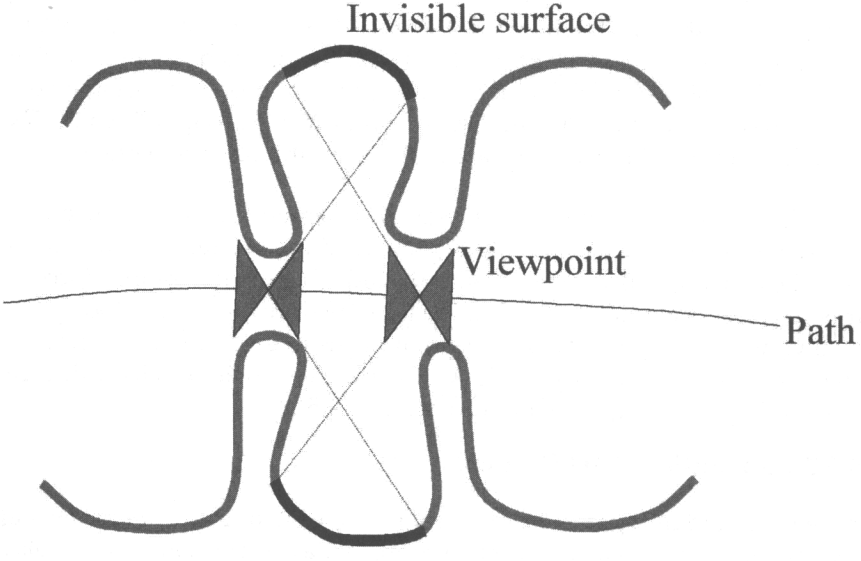

FIG. 9.4. The areas in black are missed in a 2P view (from Vos et al., 2003, reprinted by permission of the Radiological Society of North America)

conventional technique. More detailed information can be found in Vos et al. (2003).

9.3 MATERIALS AND METHODS

9.3.1 Data Acquisition

Patient Population. For this study, 30 patients were included. The patients were selected from a population at increased risk for colorectal cancer (a medical or family history of colorectal cancer or polyps). The number of patients with polyps was representative for the prevalence in this surveillance population; 27 out of 50 was reported earlier (Gelder, Venema, & Serlie, 2002). The selection was based on the presence of polyps, irrespective of the location. At colonoscopy, 16 of the 30 patients had at least 1 polyp of any size with a total of 78 lesions. Eight of thirty patients harbored polyps larger than or equal to 5 mm in diameter amounting to nine such findings in total. The patients were informed a priori by letter as well as verbally of the study's purpose and gave written consent.

CT Virtual Colonoscopy. Starting on the day before the examination, each patient drank 4 to 6 L of a laxative fluid for bowel preparation. Directly before image acquisition, a bowel relaxant was administered intravenously to reduce peristalsis. The colon was distended by approximately 2 L of CO_2 enriched air. The adequacy of the distension was gauged via a scout view image. Multislice spiral CT scans were acquired in prone and supine positions. The effective slice thickness was 3.2 mm at an overlap of 1.6 mm. The insufflation procedure was repeated after repositioning the patient.

Colonoscopy. Colonoscopy was performed by an experienced gastroenterologist. A research fellow recorded the examination on videotape. Lesion size was estimated with the aid of an opened biopsy forceps. Its shape was characterized as flat, sessile, or pedunculated. The location of a polyp was considered by classification in one of the following segments: coecum, ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon, sigmoid and rectum (Fig. 9.5).

9.3.2 Conventional 3D Display

Antegrade and retrograde cine loops were evaluated from both prone and supine positions of each patient to represent a conventional 3D display method. The images were volume rendered at positions 4 mm apart on the central colon path (the sampling rate is clarified later). The method from Truyen, Lefere, Gryspeerdt, and Deschamps (2000) was applied for path generation. The viewing angle was set to 120° to compromise between im-

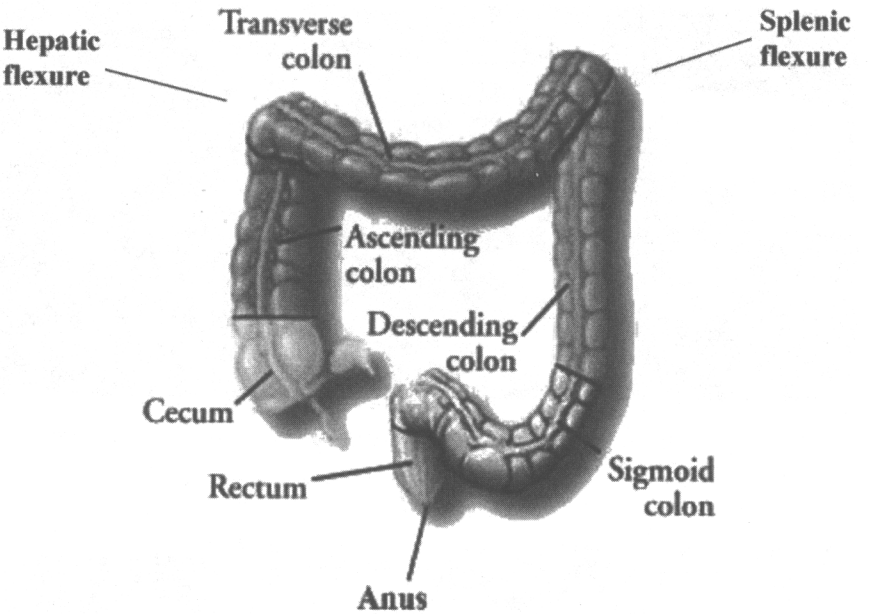

FIG. 9.5. Shown are the colonic segments.

age distortion and surface visibility. Frame rate was fixed at one image per sec. Multiplanar reformatted images in any direction were available from the original CT to verify potential lesions.

9.3.3 Unfolded Cubic Projection

To avoid extreme deformations while showing the full visible field around a position, we introduced a series of "unfolded cubic renderings" (Serlie et al., 2001). A cube was virtually placed in each path-point and on the faces, 90° views from the center were projected (Fig. 9.6 illustrates the principle). Folding the six images out onto a single plane (a 6P view) rendered the complete field of view as a movie. Reformatted views of the original CT data became accessible by clicking in the displayed images. Then, the movie was stopped and the physician could manipulate the reformatted images for closer inspection of suspicious areas. Real-time rendering of the corresponding wall part also facilitated local inspection of the surface by adapting the virtual camera position and orientation. The parameters of volume rendering transfer function, sampling, and frame rate were identical to 2P inspection. Figure 9.7 shows the graphical user interface.

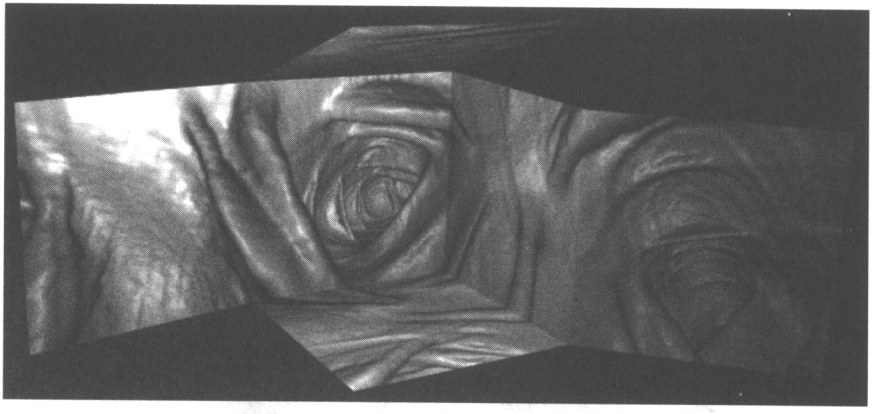

FIG. 9.6. Shown is the cubic rendering (from Vos et al., 2003, reprinted by permission of the Radiological Society of North America).

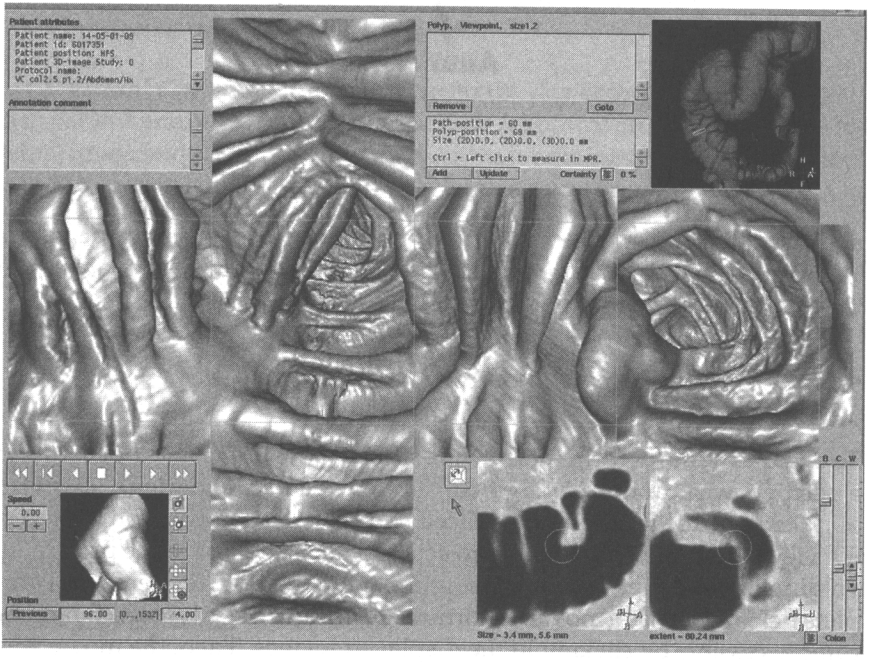

FIG. 9.7. A sequence of outfolded cubes is presented in a graphical user interface (from Vos et al., 2003, reprinted by permission of the Radiological Society of North America).

9.3.4 Evaluation

An abdominal radiologist (Observer 1) and a research fellow (Observer 2) independently evaluated the data by means of both display methods. The observers had a previous experience from more than 50 CT virtual colonoscopy examinations at the start of the study. They were unaware of the prevalence of polyps. The evaluations using a 6P display preceded those with 2P display. The cases were presented in random order. Each surmised polyp was scored with respect to size, morphology, and location.

9.3.5 Outcome Parameters and Statistical Analysis

Evaluation Time. The evaluation time per patient was recorded for both observers and display modes. The outcome was stratified according to the presence of colonoscopically proven polyps. The classes were compared using a paired t test. Differences were considered significant at $p < 0.05$. The initialization time for generating the 2P and 6P sequences was disregarded in the analysis.

Surface Visibility. The surface visibility was defined as the percentage of colon surface voxels coming into view (Paik, Beaulieu, Jeffrey, Karadi, & Napal, 2000). To measure the visibility, the colon's interior volume was obtained by thresholding. Subsequently, the surface voxels were identified by their adjacency to the interior. A surface voxel was defined as visible if a line could be drawn to a position on the central path that was not obstructed by another surface voxel. Wilcoxon's signed rank test was used to compare differences in 6P and 2P surface visibility.

Sensitivity and Specificity and User Agreement. A polyp detected via CT virtual colonoscopy was considered true positive if it matched a colonoscopy finding with regard to size, shape, location (i.e., colon segment), and anatomic interrelation to haustral folds. A deviation in size by at most 5 mm was accepted to accommodate with the inherent inaccuracy of colonoscopic size measurement. A false negative finding was defined as a polyp detected during colonoscopy that was not found at CT virtual colonoscopy. A patient was correctly identified to harbor polyps if there was at least one true positive finding. Absence of lesions during CT virtual colonoscopy was considered true negative if lesions were also absent at colonoscopy.

The sensitivity of both display methods was determined on a per patient and on a per polyp basis. The specificity of both display methods was determined per patient. Lesions detected during colonoscopy were divided in two categories: "medium to large" for lesions equal to or larger than 5 mm,

and "small" for polyps less than 5 mm in diameter. The analysis was stratified according to polyp size.

Differences in sensitivity per patient between the methods were tested by a McNemar test. Differences in sensitivity per polyp between the display methods were assessed via logistic regression with random effects (i.e., a generalized version of a McNemar test for clustered data). Logistic regression was used to adjust for clustering of polyps withing patients. A McNemar test was also applied to compare the specificities of the display methods. The agreement between the observers was measured on a per segment basis for all detected lesions by the kappa statistic. The kappa values were interpreted according to the next qualification: < .20: poor; 0.21 to 0.40: fair; 0.41 to 0.60: moderate; 0.61 to 0.80: good; 0.81 to 1.0: very good.

9.4 RESULTS

Evaluation Time

The average evaluation using 2P display (observer 1: 36.49 min; observer 2: 35.05 min) was significantly slower than by 6P display (observer 1: 19.33 min; observer 2: 20.09 min). The presence of polyps did not lead to significantly longer evaluation time with either technique. Also, the time differences between the observers were not significant. Table 9.1 collates the

TABLE 9.1
Mean Evaluation Time (and Standard Deviation) Per Patient for the Conventional 3d (2P) and Unfolded Cube (6P) Display Stratified by the Presence of Polyps Detected by Colonoscopy

Colonoscopy Outcome:	*2P*		*6P*		*Paired Difference*	
	Observer 1	*Observer 2*	*Observer 1*	*Observer 2*	*Observer 1*	*Observer 2*
Proven polyps: Mean	38′22″	38′55″	21′32″	21′55″	16′50″	17′00″
SD	(09′21″)	(17′38″)	(07′42″)	(07′34″)	(09′36″)	(13′36″)
No proven polyps: Mean	35′01″	30′41″	17′16″	18′08″	17′44″	12′33″
SD	0′30″)	(10′10″)	(04′30″)	(04′18″)	(10′46″)	(09′02″)
Any: Mean	36′49″	35′05″	19′33″	20′09″	17′15″	14′55″
SD	9′51″)	(14′59″)	(06′40″)	(06′27″)	(09′58″)	(11′43″)

Note. 2P = 2 Plane; 6P = 6 Plane. This was adapted from Vos et al., 2003. Reprinted by permission of the Radiological Society of North America.

mean evaluation time and standard deviation per observer for the 2P and 6P displays stratified by the presence of polyps.

Surface Visibility

Using an antegrade view only, on average 73% of the colon surface came into view. The 2P display (using ante and retrograde views) resulted in 93.8% visibility. The 6P display visualized 99.5% of the bowel surface. All differences were significant ($p < 0.05$).

A typical outcome showing the invisible voxels is given in Fig. 9.8 (the "unseen" elements are marked in black). The example bowel wall consisted of 387.225 voxels. Using the 2P display, 25.833 elements remained invisible, the largest cluster of which contained 10.685 voxels (the next cluster contained 2,070 elements; the average cluster size equaled 190). This is considerably more than the surface of a polyp, which is approximately 500 voxels (modeling it by a sphere of 5 mm in diameter at a voxel size of $0.6^2 \times 1.6$ mm). The 6P figure shows one relatively large patch (consisting of 3,077 voxels) in the rectum where the path had an open end and the tube with the balloon occluded the wall. Excepting these elements, the next largest cluster contained only 316 voxels (the average cluster size is 69).

Figure 9.9 shows, for one data set, the relation between the surface visibility and the sampling rate along the central path. The surface area coming into view asymptotically approximates 99.8% for 6P display. The figure illustrates that a sampling rate of once every 4 mm yields optimal visibility for the 6P method. The graphs were similar for other data sets.

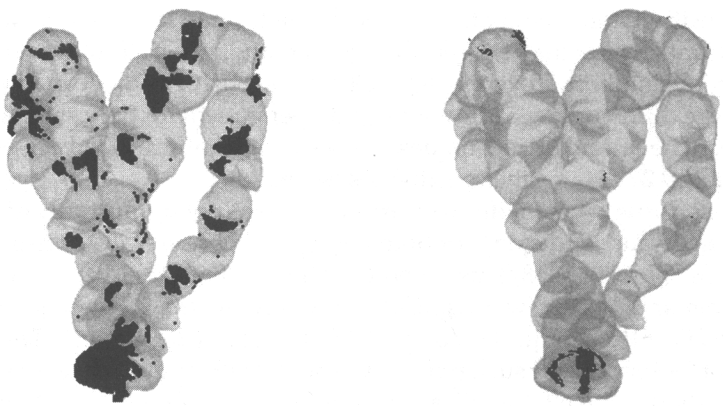

FIG. 9.8. Indicated in black are the parts missed in 2P display (left) and 6P display (right; from Vos et al., 2003, reprinted by permission of the Radiological Society of North America).

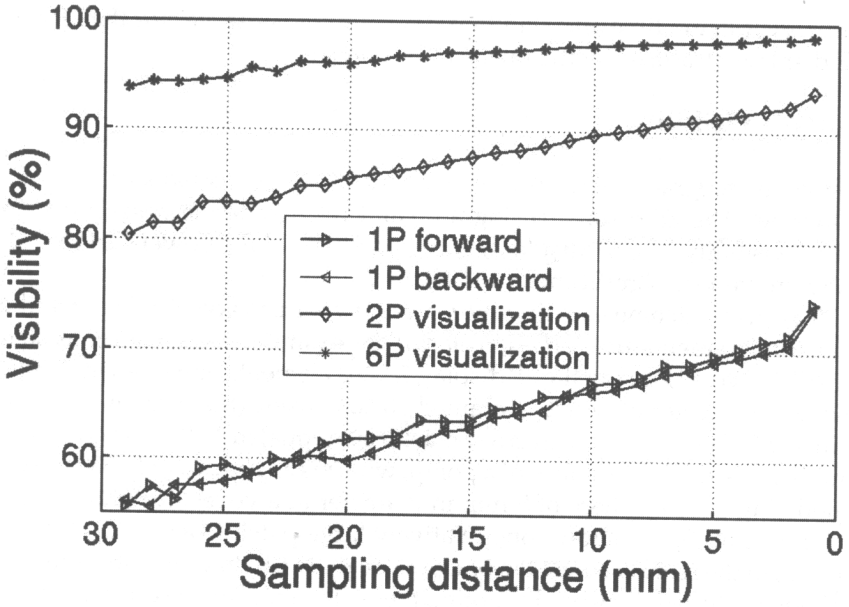

FIG. 9.9. Shown is the relation between the surface visibility and the sampling rate along the central path for one dataset. The surface area coming into view asymptotically approximates 99.8% for 6P display only (from Vos et al., 2003, reprinted by permission of the Radiological Society of North America).

Sensitivity and Specificity

The sensitivity on a per patient basis for medium to large polyps was not significantly different between the two methods for both observers (Observer 1 using both methods, 8/8; Observer 2 using 2P 7/8 and with 6P 8/8). The difference regarding sensitivity per patient for only small polyps between the 2P and 6P techniques was also not significant for both observers. Table 9.2 contains the sensitivities per patient.

The sensitivity per medium to large polyp was not significantly different between 2P and 6P display for both observers (Observer 1, 9/9 using both methods; Observer 2, 8/9 using both methods). For Observer 1, the sensitivity per small polyp was significantly worse via the 2P method (16/69) than via the 6P technique (27/69; $p < 0.003$ by logistic regression). The sensitivity of Observer 2 for such polyps was not significantly different between the methods (26/69 for 2P and 24/69 for 6P). Table 9.3 collates the sensitivities per polyp.

Specificity regarding the correct identification of patients without medium to large polyps for Observer 1 was 16 of 22 patients with conventional

TABLE 9.2
Sensitivity on a "Per Patient" Basis for Conventional 3D (2P) and Unfolded Cube Display (6P)

Polyp Size	*2P*		*6P*		*Colonoscopy*
	Observer 1	*Observer 2*	*Observer 1*	*Observer 2*	
Any	14 (87%)	12 (75%)	13 (81%)	13 (81%)	16
< 5 mm	6 (75%)	5 (62%)	5 (62%)	5 (62%)	8
≥ 5 mm	8 (100%)	7 (87%)	8 (100%)	8 (100%)	8

Note. 2P = 2 Plane; 6P = 6 Plane. This was adapted from Vos et al., 2003. Reprinted by permission of the Radiological Society of North America.

TABLE 9.3
Sensitivity on a "Per Polyp" Basis for Conventional 3D (2P) and Unfolded Cube Display (6P)

Polyp Size	*2P*		*6P*		*Colonoscopy*
	Observer 1	*Observer 2*	*Observer 1*	*Observer 2*	
Any	25 (32%)	34 (44%)	36 (46%)	32 (41%)	78
< 5 mm	16 (23%)	26 (38%)	27 (69%)	24 (35%)	69
>= 5 mm	9 (100%)	8 (89%)	9 (100%)	8 (89%)	9

Note. 2P = 2 Plane; 6P = 6 Plane. This was adapted from Vos et al., 2003. Reprinted by permission of the Radiological Society of North America.

display and 15 of 22 patients with unfolded cube display. For Observer 2, these findings were 16 of 22 patients with conventional 3D display and 19 of 22 patients with unfolded cube display. The differences between the display methods were not significant for both observers. Also, the specificity for any polyp size was not significantly different between the methods for both observers. Table 9.4 summarizes the outcome regarding specificity.

On a per segment basis, the agreement between the observers was $k = 0.605$ (SE = 0.052) for 2P and $k = 0.692$ (SE = 0.048) for 6P display. Both kappa values indicate "good" agreement. The difference in kappa value between the methods was not significant.

9.5 DISCUSSION

Our study shows that CT virtual colonoscopy using the 6P display method enables time efficient inspection (about 15–20 min per patient) and compre-

TABLE 9.4
Specificity on a "Per Patient" Basis for Conventional 3D (2P) and Unfolded Cube Display (6P)

Patients Without Polyps	*2P*		*6P*		*Colonoscopy*
	Observer 1	*Observer 2*	*Observer 1*	*Observer 2*	
Any	7 (50%)	4 (29%)	3 (21%)	5 (36%)	14
³ 5 mm	16 (73%)	16 (73%)	15 (68%)	19 (86%)	22

Note. 2P = 2 Plane; 6P = 6 Plane. This was adapted from Vos et al., 2003. Reprinted by permission of the Radiological Society of North America.

hensive visibility (99.5%) superior to conventional 2P display. The sensitivity and specificity of the technique is high when a cutoff value of 5 mm is taken (this is a commonly applied threshold to distinguish relevant polyps).

Various alternative display techniques were introduced to evaluate CT virtual colonoscopy data. Initially, the complementary use of 2D and 3D images was reported to provide the best sensitivity (Hara, Johnson, Reed, Ehman, & Ilstrup, 1996; Royster, Fenlon, Clarke, Nunes, & Ferucci, 1997). Later, evidence was given that mere (reformatted) 2D images can be just as effective as a 3D fly-through approach (Dachman, Kuniyoshi, & Boyle, 1998; Macari, Milano, Lavelle, Berman, & Megibow, 2000). We opted for a 3D method because significantly better sensitivity was found for the 3D modes after correction for lesion visibility (Beaulieu, Jeffrey, Karadi, Paik, & Napel, 1999).

Evaluation times per patient reported in previous articles are 20 to 26 min with axially reformatted images only (Dachman et al., 1998; Royster et al., 1997), 15 min just using 3D image sequences (Royster et al., 1997), and 16 to 35 min in a combined approach (primarily 2D and a 3D display for problem solving; Dachman et al., 1998; Macari et al., 2000).

The presented outcome per patient is in the same range for the 6P evaluation (17–22 min) and significantly slower regarding the 2P display (31–39 min). The evaluation time could reduce at a larger fixed frame rate or at a user controlled speed. However, this will probably not change the relative time difference between the display methods (the same frame rate was used for both techniques). We opted for a "save" frame rate of one image per sec at 4 mm intervals to yield optimal surface visibility and to endorse a sure detection of lesions.

The initialization time such as the generation of movies was disregarded, because it was performed offline in batch mode. It is justified to exclude the movie generation time from the analysis as this is done in the background. On average, it took us 35 min per patient to render the 6P

views on a UltraSparc 10. The 2P sequences were generated in approximately 12 min (one third of 35 min). A reduced resolution will speed up sequence generation. However, it may go at the expense perhaps of the sensitivity. Other initialization times, such as for image loading and path tracking, are on the order of a few minutes.

The results on surface visibility confirm earlier findings (using nine data sets). Paik et al. (2000) reported approximately 75% visibility applying either "forward" or "reverse" viewing only, 95% using both, and 98% visibility through a so-called Mercator projection. Clearly, visibility is important for its direct influence on the sensitivity. Beaulieu et al. (1999) showed that the sensitivity improves significantly after correction for lesion visibility.

Several methods have been explored that aim to optimize the amount of colon surface coming into view. The viewing angle may simply be increased, but this is at the expense of severe deformation toward the edges of the image. A so-called flattening method attempts to "straighten" the colon mathematically (Dave et al., 1999). Thus, images of large surface parts of the colon are generated similar to gross pathology specimens. Unfortunately, such an approach may yield severe distortion, causing lesions to appear more than once in different patches (Dave et al., 1999; Paik et al., 2000). Such repeated appearances are reported to arise whenever the central path makes a sharp turn.

The sensitivity per patient is in the high range compared to values from the literature (65%–94% for polyps larger than 5 mm and 25%–57% for any size). The sensitivity per polyp over 5 mm previously was reported in the range of 46%–90%. The numbers from our observers are in the upper range. The sensitivities for smaller polyps are in concordance with the literature (15%–55%) and confirm the poor results of CT virtual colonoscopy for such (perhaps not relevant) lesions. The specificities for both observers are low in comparison to values reported earlier (being 62%–91% considering all and 74%–96% for polyps > 5 mm only; Beaulieu et al., 1999; Dachman et al., 1998; Fenlon et al., 1999; Fletcher, Johnson, & Welch, 2000; Hara, Johnson, & Reed, 1997; Macari et al., 2000; McFarland, Brink, & Pilgram, 2001; Pescatore, Glucker, & Delarive, 2000; Rex, Vining, & Kopecky, 1999; Spinzi et al., 2001; Yee et al., 2001).

The relatively low specificity may result from the rather strict definitions of true and false positive findings that we used. CT colonographic findings were compared with the colonoscopy video with regard to anatomic interrelation to haustral folds, anatomic segment, size, and morphology. In most studies, a less strict criterion concerning location is employed: a finding is considered to be true positive if the lesion is found in the same colon segment with both colonoscopy and CT virtual colonoscopy. Because a colon segment is between 15 and 40 cm long, this may cause an erroneous interpretation of CT colonographic findings to be true positive, whereas they are

actually false positive, because they match with other lesions in the colon segment or are in fact residual stool. Thus, in our opinion, this strategy may overestimate the number of true positive results and underestimate the number of false positive results of CT virtual colonoscopy.

Another explanation for the high rate of false positive findings is the fact that 27% of small polyps (< 5 mm) are missed by colonoscopy (Rex et al., 1997). Therefore, some small lesions detected during CT virtual colonoscopy may in fact be true positive findings. Anyhow, the benefit of the detection of lesions smaller than 5 mm in a screening setting is dubious because very small polyps are known to rarely contain malignant tissue (Waye et al., 1988).

The 2P and 6P display methods both yielded good interobserver agreement. Several previous studies were performed with more than one independent observer (Beaulieu et al., 1999; Dachman et al., 1998; Hara et al., 1996; McFarland et al., 2001; Paik et al., 2000; Pescatore et al., 2000) using the same evaluation method. However, the agreement between the observers via kappa statistics was reported only by McFarland et al. (2001; $k = 0.53–1.0$), and Pescatore et al. (2000; $k = 0.56–0.72$). The kappa values in this study are in the same range.

The future role of CT virtual colonoscopy in cancer screening depends on the improvement on issues such as the efficiency, the patient acceptance, and the effective radiation dose. One of the main drawbacks of CT virtual colonoscopy is the long evaluation time. Computer aided diagnosis is an important development that could support the practical use of CT colonography. Although positive early results were reported on automatic polyp detection, further research is warranted. We foresee a scheme in which potential lesion sites, suggested by the computer algorithm, are checked by a human observer. A primary 3D display method to do so may be superior to a primary 2D technique (as several studies indicate). The 6P display method may contribute to such an evaluation strategy. Consequently, it could facilitate the implementation of CT virtual colonoscopy in colorectal cancer screening.

9.6 CONCLUSION

The unfolded cube (6P) display is an alternative method to evaluate CT virtual colonoscopy data. The evaluation time measures 19.5 to 20 minutes during which 99.5% of the colon wall is inspected. The method is more time efficient and yields better surface visibility than a conventional technique. The sensitivity is 8 out of 8 for medium to large polyps at a specificity of 15 to 19 out of 22. The method facilitates good agreement among different observers ($k = 0.692$). The 6P display successfully combines time efficiency and high accuracy. Thus, it improves the 3D display for CT virtual colonoscopy.

REFERENCES

Beaulieu, C. F., Jeffrey, R. B., Karadi, C. A., Paik, D. S., & Napel, S. (1999). Display modes for CT colonography: Part II blinded comparison of axial CT and virtual endoscopic and panoramic endoscopic volume-rendered studies. *Radiology, 212,* 203–212.

Chen, S. C., Lu, D. S. K., Hecht, J. R., & Kadell, B. M. (1999). CT colonography: Value of scanning in both the supine and prone positions. *American Journal of Roentgenology, 172,* 595–599.

Dachman, A. H., Kuniyoshi, J. K., & Boyle, C. M. (1998). CT colonography with three dimensional problem solving for detection of colonic polyps. *American Journal of Roentgenology, 171,* 959–989.

Dave, S. B., Wang, G., Brown, B. P., McFarland, E. G., Zhan, Z., & Vannier, M. W. (1999). Straightening the colon with curved cross sections: An approach to CT colonography. *Academic Radiology, 6,* 398–410.

Dodd, G. D. (1998). Colon cancer and polyps imaging perspectives. *Proceedings of the First International Symposium on Virtual Colonoscopy,* 15–17.

Fenlon, H. M. (1998). Artefacts on virtual colonoscopy. *Proceedings of the First International Symposium on Virtual Colonoscopy,* 40–41.

Fenlon, H. M., Nunes, D. P., Schroy, P. C., Barish, M. A., Clarke, P. D., & Ferucci, J. T. (1999). A comparison of virtual and conventional colonoscopy for the detection of colorectal polyps. *New England Journal of Medicine, 341,* 1496–1503.

Fenlon, M., & Ferucci, J. T. (1999). Virtual endoscopy becomes viable option. *Gastroenterology, 114,* 57–68.

Fletcher, F. G., Johnson, C. D. J., & Welch, T. J. (2000). Optimization of CT colonography technique: Prospective trial in 180 patients. *Radiology, 216,* 704–711.

Fletcher, J. G., & Luboldt, W. (2000). CT colonography and MR colonography: Current status, research directions and comparison. *European Radiology, 10,* 786–801.

Garland, M., & Heckbert, P. S. (1997). Surface simplification using quadratic error metrics. *Proceedings of the 24th Annual Conference Association for Computing Machinery Special Interest Group on Computer Graphics,* 209–216.

Gelder, R. E. v., Venema, H. W., & Serlie, I. W. O. (2002). CT colonography at different radiation dose levels: Feasibility of dose reduction. *Radiology, 224,* 25–33.

Halligan, S., & Fenlon, H. M. (1999). Science, medicine, and future—Colonography. *British Medical Journal, 219,* 1249–1252.

Hara, A. K., Johnson, C. D., & Reed, J. E. (1997). Detection of colorectal polyps with CT colography: Initial assessment of sensitivity and specificity. *Radiology, 205,* 59–65.

Hara, A. K., Johnson, C. D., Reed, J. E., Ehman, R. L., & Ilstrup, D. M. (1996). Colorectal polyp detection with CT colography: Two versus three dimensional techniques. *Radiology, 200,* 49–54.

Helen, M., & Ferucci, J. T. (1999). Virtual endoscopy becomes viable option. *Gastroenterology, 114,* 57–68.

Hong, L., Muraki, S., Kaufman, A., & He, T. (1997). Virtual voyage: Interactive navigation in the human colon. *Proceedings of the 24th Annual Conference Association for Computing Machinery Special Interest Group on Computer Graphics,* 27–34.

Hopper, K. D., Lyriboz, A. T., & Kasales, C. J. (2003). Mucosal detail at CT virtual reality: Surface versus volume rendering. *Radiology, 214,* 517–522.

Kaufman, A. (1991). *Volume visualization.* Los Alamitos, CA: IEEE Computer Society Press.

Lakare, S., Wan, M., Sato, M., & Kaufman, A. (2000). 3D digital cleansing using segmentation rays. *Proc IEEE Visualization,* 37–44.

Levoy, M. (1988). Display of surface from volume data. *IEEE Computer Graphics and Applications, 8,* 29–37.

Luboldt, W., Bauerfeind, W., Wildermuth, S., & Debatin, J. F. (1999). Contrast optimization for assessment of the colonic wall and lumen in MR colonography. *Journal of Magnetic Resonance Imaging, 9,* 745–750.

Macari, M., Milano, A., Lavelle, M., Berman, P., & Megibow, A. J. (2000). Comparison of time efficient colonography with two and three-dimensional colonic evaluation for detecting colorectal polyps. *American Journal of Roentgenology, 174,* 1543–1549.

McFarland, E. G., Brink, J., & Pilgram, T. (2001). Spiral ct colonography: Reader agreement and diagnostic performance with two- and three-dimensional image-display techniques. *Radiology, 218,* 375–383.

Paik, D. S., Beaulieu, C. F., Jeffrey, R. B., Karadi, C. A., & Napal, S. (2000). Visualization modes for CT colonography using cylindrical and planar map projections. *Journal of Computer Assisted Tomography, 24,* 179–188.

Pescatore, P., Glucker, T., & Delarive, J. (2000). Diagnostic accuracy and interobserver agreement of CT colonography (virtual colonoscopy). *Gut, 47,* 126–130.

Potter, J. D., Slattery, M. L., & Bostick, R. M. (1993). Colon cancer: A review of the epidemiology. *Epidemiologic Reviews, 15,* 499–545.

Rex, D. K., Cutler, C. S., & Lemmel, G. T. (1997). Colonoscopy misrates of adenomas determined by back-to-back colonoscopies. *Gastroenterology, 112,* 24–28.

Rex, D. K., Vining, D., & Kopecky, K. K. (1999). An initial experience with screening for colon polyps using spiral CT with and without CT colography (virtual colonoscopy). *Gastrointestinal Endoscopy, 50,* 309–313.

Rogalla, P., Schmidt, E., Korves, M., & Hamm, B. K. (1999). Optimal colon distention for virtual colonoscopy: Room air versus CO2 insufflation. *Radiology, 213,* 342.

Royster, A. P., Fenlon, H. M., Clarke, P. D., Nunes, D. P., & Ferucci, J. T. (1997). CT colonoscopy of colorectal neoplasms: Two-dimensional and three-dimensional virtual-reality techniques with colonoscopic correlation. *American Journal of Roentgenology, 169,* 1237–1242.

Serlie, I. W. O., Vos, F. M., & Gelder, R. E. v. (2001). Improved visualisation in virtual colonoscopy using image-based rendering. In D. Ebert, J. M. Favre, & R. Peikert (Eds.), *Proceedings of the Joint Eurographics–IEEE TCVG Symposium on Visualization, Ascona, Switzerland,* 137–146.

Shahidi, R. (1996). Surface rendering versus volume rendering in medical imaging: Techniques and applications. *Proc IEEE Visualization Conf ACM Press,* 439–440.

Spinzi, G., Belloni, G., Martegani, A., Sangiovanni, A., Del Favero, C., & Minoli, G. (2001). Computed tomographic colonography and conventional colonoscopy for colon diseases: A prospective, blinded study. *American Journal of Gastroenterology, 96,* 394–400.

Toribrara, N. W., & Sleisenger, M. H. (1995). Screening for colorectal cancer. *New England Journal of Medicine, 332,* 861–867.

Truyen, R., Lefere, P., Gryspeerdt, S., & Deschamps, T. (2000). Speed and robustness of (semi-) automatic path tracking. *Proceedings of the Second International Symposium on Virtual Colonoscopy,* 102.

Vogelstein, B., Fearon, E. R., & Hamilton, S. R. (1988). Genetic alterations during colorectal tumour development. *New England Journal of Medicine,* 319, 525–532.

Vos, F. M., Gelder v., R. E., Serlie, I. W. O., Florie, J., Nio, Y., Glas, A. S., et al. (2003). Comparison of two three-dimensional display modes for CT colonography: Conventional virtual colonscopy versus the unfolded cubic projection. *Radiology, 228,* 878–885

Vos, F. M. Serlie, I. W. O., Gelder, R. E. v., Stoker, J., Vrooman, H. A., & Post, F. H. (2001). A review of technical advances in virtual colonoscopy. In V. L. Patel, R. Rogers, & R. Haux (Eds.), MEDINFO 2001, Proceedings the 10th World Congress on Medical Informatics (pp. 938–942). Ohmsha, Amsterdam: IOS Press.

Waye, J. D., Lewis, B. S., Frankel, A., & Geller, S. A. (1988). Small colon polyps. *American Journal of Gastroenterology, 83,* 120–122.

Winawer, S. J., Fletcher, R. H., & Miller, L. (1997). Colorectal cancer screening: Clinical guidelines and rationale. *Gastroenterology, 112,* 594–642.

Yee, J., Akerkar, G. A., Hung, R. K., Steinauer-Gebauer, A. M., Wall, S. D., & McQuaid, K. R. (2001). Colorectal neoplasia: Performance characteristics of CT colonography for detection in 300 patients. *Radiology, 219,* 685–692.

Yee, J., Hung, R. K., Akerkar, G. A., & Wall, S. D. (1999). The usefulness of glucagon hydrochloride for colonic distention in CT colonography. *American Journal of Roentgenology, 173,* 169–172.