CT Colonography (Virtual Colonoscopy)

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Abstract

CT colonography (CTC), also known as virtual colonoscopy, is a recent radiologic technique enabling the detection of tumoral lesions in the colon. Double contrast barium enema, has lost most of its adherents, and CTC constitutes a real opportunity for radiologists to play a preponderant role in the diagnosis and treatment of colorectal cancer and adenoma. CTC has dramatically evolved through the refinement of existing techniques as well as the introduction of new techniques such as fecal tagging, the use of carbon dioxide to inflate the colon, multi-detector row CT scanners, the use of ultra-low dose scan protocols, and computer-aided detection systems. These technical improvements have helped both the radiologists and the patients. The successful performance of CTC is dependent on several technical factors; fecal tagging, which improves patients’ compliance by allowing reduced bowel preparation and facilitates the differentiation of true polyps from residual feces, resulting in the improvement of diagnostic accuracy, automated \( CO_2 \) insufflation, which is more efficient and safer in colonic distention compared to manual room air insufflation, and the performance of CTC using a thin collimation of \( \leq 3 \) mm with a reconstruction increment of \( \leq 3 \) mm and a low radiation dose of 30 mAs to 50 mAs. There are two strategies to interpret CTC datasets; primary 2D versus 3D interpretation. There is not any one correct method for interpretation of CTC; therefore, readers should be well-trained with both interpretation methods. Finally, radiologists should also be familiar with potential dangers in reaching a final correct diagnosis, that is, false positives and false negatives. In experienced hands, CTC seems to be ripe for prime-time colorectal cancer screening. However, it is not yet ready for widespread application of screening until several obstacles can be overcome. Therefore, considerable effort should be undertaken to take CTC to the next level, as a widely accepted screening method for colorectal cancer.

Introduction

Colorectal cancer is the third or fourth leading cause of cancer death with approximately 6–10% of the population developing colorectal cancer in their lifetime in the United States and in Korea, respectively.\(^1\)\(^2\) Globally, there are an estimated 1 million new cases and 50,000 deaths per year.\(^3\) The adenoma-carcinoma sequence refers to the process of transformation of small adenomas into large adenomas, then into noninvasive carcinomas, and finally into invasive carcinomas. This process occurs slowly and therefore, colorectal cancer is highly suited to screening due to its long preclinical phase during which it can be detected and cured.\(^4\) The American Cancer Society has recommended several screening methods, ranging from occult stool blood tests to invasive procedures, such as colonoscopy.\(^5\) Unfortunately however, screening programs for colorectal cancer have been only partly successful, owing largely to poor patient compliance to screening recommendations.\(^6\)\(^7\) Recent studies indicate compliance rates of only 25–40%.\(^8\)\(^9\) Major obstacles to patient acceptance of colorectal cancer screening with colonoscopy are the requirements for a rigorous bowel preparation, the invasiveness of the procedure and the need for sedation.

CT colonography (CTC), also known as virtual colonoscopy, has been introduced as a non-invasive technique that uses data generated from CT imaging of the fully prepared and gas-distended colon to create two-dimensional (2D) and three-dimensional (3D) images of the colon.\(^10\)\(^11\) This article reviews the current indications, techniques, imaging findings, pitfalls, and computer-aided diagnosis (CAD) of CTC.

Indications of CT Colonography

In addition to the potential as a screening option for colorectal polyps and cancer, which is still controversial, CTC has increasingly established clinical indications, inclu-
Techniques

1. Colon Preparation

Bowel preparation for CTC determines the adequacy of an examination, and may affect diagnostic performance for the detection of colonic polyps. There are two types of bowel preparation, dry and wet preparation. Sodium phosphate and magnesium citrate are known as dry preparation regimens since they leave little fluid in the colon. Polyethylene glycol (PEG) is known as a wet preparation regimen since it leaves a large amount of fluid. In the preparation of CTC, unlike conventional colonoscopy, too much residual fluid could potentially obscure a clinically important lesion, i.e., a polyp or cancer, despite examining both supine and prone positions. In addition, patient compliance for 4 liters of PEG is much less than that for dry preparation regimens. Therefore, “dry preparation” with sodium phosphate or magnesium citrate, with or without bisacodyl tablets the night before CTC is recommended as a preparation protocol by most CTC experts. Sodium phosphate, however, is absolutely contraindicated in patients who have renal insufficiency or congestive heart failure and is relatively contraindicated in patients who have large ascites or ileus because of potentially large amount of fluid and electrolyte shifts or induction of renal failure. Magnesium citrate has been a useful alternative in such patients.

The use of a bisacodyl suppository in the morning of CTC is controversial. According to Yoon et al., remnants of the bisacodyl suppository can be a problematic source of false-positives in the sigmoid colon or rectum (Fig. 1).

2. Fecal Tagging

Fecal and fluid tagging is the labeling of fecal residue in the colon using radiopaque contrast media. On CT, the fecal residue that is mixed with the orally administered contrast material appears hyperdense or white, making it easily distinguishable from the homogeneous soft tissue density of colonic polyps (Fig. 2). Therefore, fecal and fluid tagging have enabled the use of reduced bowel preparation regimens containing no or only limited amounts of laxatives.

Figure 1. False-positive due to dulcorax suppository. On supine 2D (A) and 3D endoluminal (B) images, a long pedunculated polyp (arrow) is seen. This lesion (arrow) seems to be submerged in the tagged fluid on prone 2D (C) and 3D endoluminal (D) images.

Figure 2. Polyp versus tagged feces. On 3D endoluminal image (A), two sessile polyloid lesions (arrow and arrowhead) are seen. On 2D axial images, one (arrowhead, B) appears white suggesting tagged feces and the other (arrow, C) shows soft tissue density suggesting a polyp.
So far, feasibility studies investigating CTC with reduced or no catharsis have shown promising results in diagnostic performance of CTC as well as patients’ acceptance. Various tagging agents such as barium, iodinated contrast, and their combination have been used. Even though, at present, there is no consensus with regard to the most effective method of fecal tagging, tagging is now advocated by an increasing number of investigators as the method of choice to prepare the colon for CTC.

CTC can theoretically be performed without bowel preparation, sometimes referred to as “prepless CTC.” A recent article regarding the performance of prepless CTC was published in which all patients were requested not to eat fiber-rich food for 3 days prior to CTC examination. They used 200 mL of iodinated contrast as a tagging regimen. In the study, prepless CTC provided an excellent 95.5% per-polyp sensitivity for polyps ≥ 8 mm and showed high patient compliance which might eventually result in the increase of CTC screening participation.

3. Use of Spasmolytic Agent

The use of spasmolytics during CTC has been controversial. It is known that smooth muscle relaxants such as hyoscine butylbromide (Buscapan®) and glucagon can improve bowel relaxation, decrease patient discomfort, and improve colonic filling during barium enema, all of which may limit colonic distention and significantly reduce CTC sensitivity. However, glucagon also enhances the reflux of colonic air into the small intestine by relaxing the ileocecal valve with the unfortunate effect of reducing colonic distention. Therefore, many CTC experts do not support the routine use of spasmolytic agents for CTC as of yet, but it can be used if patients experience pain, discomfort, or spasms.

4. Colon Distention

A well-distended colon is mandatory for proper evaluation by CTC. Determination of adequate insufflation can be assessed by volume, pressure, or patients’ tolerance. For colonic distention, either room air or CO₂ can be used. There is no consensus regarding the use of CO₂ versus room air. However, automated CO₂ delivery is not only safe but also results in improved colonic distention compared to manual techniques and also results in less post-procedural discomfort due to rapid absorption of the gas through the colonic wall. After distention is completed, a CT scout view of the abdomen is obtained to ensure optimal colonic distention and to add additional gas if collapsed segments are identified. Following supine image acquisition, the patient is turned to the prone position. Before prone image acquisition, another scout scan is obtained with additional gaseous insufflation if needed.

According to a recent article, the incidence of colonic perforation at CTC ranged from 0.009% to 0.05% which is much lower than in optical colonoscopy (0.1 ~ 0.2%). There is an increased risk of perforation when staff-controlled manual room air insufflation is used in symptomatic patients through a rigid and large-caliber retention balloon catheter. Therefore, CTC experts recommend the use of an automated CO₂ delivery system through a small flexible low-pressure balloon catheter.

5. Image Acquisition

For CT scanning, both supine and prone scans are required. Slice collimation affects polyp visualization in important ways. A recent meta-analysis suggests that multidetector row CT (MDCT) has improved performance over single detector CT. Therefore, most CTC experts have recommended the use of a slice collimation of ≤ 3 mm with a reconstruction interval of ≤ 1.5 mm.

The use of intravenously administered contrast material may improve reader confidence and the ability of CTC to depict medium-sized polyps in suboptimally prepared colons. However, the risks of intravenous contrast administration may warrant restricting its use to limited cases such as patients with symptoms of colorectal disease or with known colorectal cancers.

High radiation dose delivered to the patients can be one of the problematic issues for CTC as a screening test despite of its potential advantages. However, the high contrast between the colonic wall and air can be exploited to reduce the radiation dose of CTC. Since 2002, several authors have insisted that low dose CTC may be feasible in the detection of polyps. According to a recent article, radiation dose could be decreased without sacrificing diagnostic accuracy to as low as 10 mAs (ultra low-dose) with a total effective dose of 1.8 mSv in men and 2.4 mSv in women, which is less than half the radiation dose of barium enema. However, such “ultra low-dose” protocols may not be feasible for the evaluation of extracolic structures because of the increa-
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Interpretation

After acquiring supine and prone scans, various software packages display images in both 2D and 3D endoluminal views. CTC datasets can be evaluated by a primary 2D or a primary 3D approach. In either case, the alternative viewing technique must be available for rapid correlation and characterization of any suspicious findings. The combined use of both 2D and 3D visualization techniques has been shown to be superior to the evaluation of 2D or 3D views alone, with regard to sensitivity and specificity. 27,28

1. Primary 2D versus 3D Interpretation

Primary 2D evaluation is based on “lumen tracking,” that is, interactively tracing through the 2D dataset, focusing on only the air-distended colonic lumen from one end to the other, with special focus on the cross-section of one colonic segment at a time. 26 Primary 2D evaluation provides information regarding the attenuation of findings during the search process and is more time-efficient. 27,29 Additional 3D views are often used for problem solving. Primary 3D evaluation is based on 3D virtual endoscopy in an antegrade and retrograde fashion. Primary 3D evaluation was shown to be sensitive for polyp detection because both, the conspicuity, especially of small and medium-sized polyps, and the interpretation time are increased. 30 Additional 2D views are necessary for characterization of findings. However, the primary 3D evaluation is time-consuming because it must be performed in an antegrade and retrograde fashion for the perception of lesions behind colonic folds. Collapsed segments must be evaluated alternatively, by 2D planar images. Primary 2D versus 3D evaluation is currently controversial and its use has been dependent primarily on the radiologist’s preferences and the capabilities of the workstation. However, most CTC experts agree that 2D and 3D evaluations are complementary. At present, the most commonly used platform for data interpretation of CTC is primary 2D interpretation, with 3D evaluations used for problem-solving, while primary 3D interpretation is preferred by an increasing number of experts.

2. Alternative 3D Display Methods

The 3D approach which virtually imitates colonoscopy, inevitably has the similar limitation in that it does not allow inspection of blind-spots including the parts of the mucosa that are hidden by colon folds. This is true even if both antegrade and retrograde fly-through passes of the colon are performed with markedly extended interpretation time, unless the 3D workstation supports a special function displaying the blind areas to the reviewer after 3D navigation is performed. To overcome the current limitations of 3D endo-

Figure 3. Advanced 3D display modes. (A) Filet view (Philips Medical System) is one of the virtual dissection modes. Two polyps (arrows) are well visualized on the dissection view. (B) Panoramic view (Siemens Medical System). Two pedunculated polyps (arrows) located at opposite sides of one fold are well seen on panoramic view.
luminal imaging, various modified 3D display techniques have been developed as an effective way to inspect the inner colonic surface.\textsuperscript{31,32} They include virtual dissection, or panoramic, as well as unfolded, cube projections and translucency rendering.

With “virtual dissection,” the colon is fully dissected longitudinally and unfolded, similar to pathological preparation (Fig. 3A).\textsuperscript{31} The panoramic view is a variation of the unfolded cubic view, which renders five faces of a cubic view in the plane in a continuous fashion. To minimize distortions, the front view is mapped into a square while the other four faces are mapped around it into a disk (Fig. 3B).\textsuperscript{32}

Initial results for several algorithms that have been tested showed reduced reading time without a significant difference in sensitivity.\textsuperscript{31} However, increasing surface visibility, by flattening a 3D structure into a 2D image or by changing viewing angles, is likely to suffer from the fact that luminal anatomy is distorted, especially in areas of flexures or in suboptimal distended segments.

**Reporting and Management**

In 2005, a working group on virtual colonoscopy proposed a reporting scheme, C-RADS (CT Colonography Reporting and Data System), that included recommendations for the follow-up of colonic polyps.\textsuperscript{33} They discriminated between “diminutive”, “intermediate”, “multiple intermediate” and “lesions that are 1 cm in size or larger”. According to the report, “diminutive” lesions (smaller than 5 mm) should not be reported. Patients with one or two “intermediate” lesions (6−9 mm) should be recommended interval surveillance after three years depending on several factors, including patient age, sex, co-morbidities, preference, and local practice. More than three lesions of 6−9 mm or one lesion of at least 10 mm required immediate colonoscopy. Although aspects of this proposal may be discussed controversially, the proposed framework addresses the definite need to have a reference guide for interpretation of CTC results.

**Performance**

The largest clinical study to date using CTC as a screening tool for colorectal neoplasms\textsuperscript{30} included 1,233 adults who were at average-risk for colorectal cancer, and showed impressive per-patient and per-lesion sensitivities of 93.8% and 92.2%, respectively, for adenomatous polyps ≤10 mm, and 88.7% and 85.7%, respectively, for adenomatous polyps ≥6 mm.\textsuperscript{1} However, follow-up studies have shown contradicting results, i.e., 59% per-patient sensitivity for polyps ≥10 mm.\textsuperscript{34} The exact reason for this striking difference in the reported performance of CTC is yet unclear, although both papers were extensively discussed and commented on in the scientific community. Most recently, the eagerly awaited results of the American College of Radiology Imaging Network screening trial has been released.\textsuperscript{35} According to the study results, CTC is comparable to colonoscopy for intermediate to large adenomas, CTC showed 90% sensitivity and 86% specificity for adenomas 1 cm or larger. Performance characteristics remained high in smaller sized polyps, with 84% sensitivity in lesions 6mm or greater. Specificity remained high (86% to 89%) across all relevant lesion sizes. Furthermore, the ACRIN trial showed CTC gets is now ready as an alternative tool for colorectal screening.

**Imaging Findings**

1. Polyp

Polyps are the most common benign lesions of the colon.
The risk of malignant transformation increases with the size of the polyp. Most polyps are sessile although some have a stalk. On 3D CTC images, polypoid lesions present as a sessile or stalked, round, oval, or lobulated intraluminal filling defect (Fig. 4). On 2D images, polyps have homogenous soft tissue attenuation. Generally, polyps maintain their position with respect to the bowel surface, with the exception of stalked polyps or polyps in mobile colon segments (Fig. 5). CTC is not able to reliably distinguish between hyperplastic and adenomatous polyps using morphological features alone, although 50% of polyps <5 mm are hyperplastic.

2. Cancer

Most large colorectal carcinomas appear as fungating masses or areas of mucosal irregularity with shouldering and luminal narrowing at 3D endoluminal imaging (Fig. 6). When a large distal colonic lesion is present, endoscopists may be unable to advance endoscopy proximal to the lesion. However, CTC has an advantage over optical colonoscopy in the evaluation of the entire colon. In up to 5% of cases, a synchronous carcinoma is present and prospective identification of a significant synchronous lesion may alter the surgical approach to colorectal resection.

3. Submucosal Lesion

Lipomas, the most common submucosal lesions in the colon, are present as a sessile or pedunculated intraluminal filling defect, most often with a smooth surface on 3D endoluminal images (Fig. 7). CTC allows the confident diagnosis of lipomas based on their characteristic fatty attenuation. Because lipomas are soft lesions, their shape may change when moving from the prone to the supine position. In general, small lipomas need no further treatment; only large lipomas require endoscopic resection as they can lead to intussusception.
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Pitfalls

CTC has numerous potential pitfalls that often can be avoided by careful analysis of the morphology of every potential lesion on multiple views and with several methods. Technical errors can be reduced or avoided by adequate bowel cleansing, adequate colonic distention, and adherence to the CT scanning protocol. Residual feces in a poorly-prepared colon can obscure or mimic a colonic lesion. Several maneuvers can differentiate residual fecal material from true colonic polyps. With colonic under-distention, a narrowed colonic segment can mimic an annular lesion, and a collapsed colonic segment can prevent visualization of a true colonic lesion (Fig. 8). Each colonic segment therefore must be adequately distended on at least one of the two position scans. Perception errors (failure to detect a lesion) may be caused by technical factors (e.g., bowel preparation, bowel distention), the primary reading technique (2D versus 3D), or reader skill and experience. Misinterpretation of findings is a major source of error.

1. Fecal Materials

Fecal material usually does not adhere to the colonic wall and will move to the dependent colon when the patient turns from the supine to prone position. Rarely, stool adheres to the colonic wall, rendering it difficult to

Figure 8. Effect of colonic distension on the visualization of the lesion. (A, B) On 3D surface-shaded image (A), sigmoid and descending colons (arrows) are not fully distended. On corresponding endoluminal image (B), no lesion is clearly depicted. (C, D) However, when the colon is fully distended, a small sessile polyp (arrow in D) is clearly demonstrated in the descending colon. (E) Optical colonoscopy revealed a small sessile polyp (arrow).

Figure 9. Tagged feces. On 3D endoluminal image (A), a small sessile polypoid lesion (arrow) is seen. However, on 2D axial image (B), this lesion (arrow) appears white, suggesting well-tagged feces in the colon.

Figure 10. Diverticula in the ascending colon. 3D image (A) shows two diverticular orifices (arrows) projecting from the colonic lumen at the area just proximal to the ileocecal valve (*). 2D axial image (B) shows a focal out-pouching (arrow) of the colonic lumen.
Figure 11. Inverted diverticulum. On 3D endoluminal image (A), a well-demarcated sessile polypoid lesion (arrow) is seen. However, on 2D axial image (B), this lesion is found to be an inverted diverticulum which is inspissated with feces and projects into the lumen.

Figure 12. Variable appearances of normal ileocecal valve. On 3D endoluminal images, normal ileocecal valve (arrows) appears as a labial feature (A) and dome-like protrusion (B). On 2D axial image with soft tissue window setting (C), the lesion (arrow) stands in a characteristic location and possesses fatty internal attenuation, indicating an ileocecal valve.

differentiate it from a colonic polyp, 2D images are a useful adjunct to primary 3D interpretation in differentiating feces from polyps or masses. Adherent stool typically has an irregular shape, contains air, and contains foci of high attenuation (Fig. 9). 40

Figure 13. Polyp on the ileocecal valve. On 3D endoluminal (A), supine (B), and prone (C) 2D axial images, a flat elevated lesion (arrow) is seen on the ileocecal (IC) valve. This lesion was interpreted as the IC valve itself. However, this lesion (arrow) was proven to be a tubular adenoma on optical colonoscopy (D). Note the normal IC valve (arrowhead).

2. Diverticulum
One of the most common findings detected with CTC is diverticular disease. Diverticula sometimes simulate polyps on 3D CTC images. However, on careful inspection the diverticular orifice can be recognized as a complete dark ring, whereas a polyp will have an incomplete ring shadow (Fig. 10). 41 When a diverticulum is inspissated with feces and projects into the colonic lumen, it simulates a polyp on 3D endoluminal images (Fig. 11). However, hyperdense material admixed with air within the lesion and part of the impacted diverticulum projecting outside the lumen may be seen on 2D images. In this case, radiologists can easily dismiss this as an impacted diverticulum. 42

3. Ileocecal Valve
The ileocecal valve may show a variable appearance at imaging. 43 It manifests as a filling defect along the medial aspect of the cecum in most patients. On CTC, the valve may have one of three appearances: labial, in which the mouth of the valve is set between an upper and lower fold; papillary, in which the valve appears as a domelike protrusion; and mixed, with features of both types (Fig. 12). 44 Considering its typical location and appearance,
radiologists do not have any difficulty in differentiating it from true polyps. 2D imaging also helps to make a correct diagnosis by demonstrating macroscopic fat within the valve. However, it is important to remember that the valve is covered by colonic mucosa, and polyps and cancers may develop on the valve (Fig. 13). Therefore, if the appearance of the ileocecal valve is abnormal or unusual, endoscopy should be performed to exclude a neoplasm arising on the valve.

4. Flat Lesions

Flat or nonpolypoid lesions can be depressed or elevated. When elevated, their height is less than twice the height of adjacent normal mucosa. Even though there has been debate, flat lesions are believed to have a higher degree of dysplasia and malignant potential for a given size than polypoid lesions.\(^4^3\)\(^-\)\(^4^5\) Flat lesions are more difficult to detect than polypoid lesions on both optical colonoscopy and CTC. On CTC, flat lesions appear as thickened haustral folds, plaque-like mucosal elevations, or nodular elevations (Fig. 14).\(^4^6\) These appearances can mimic those of adherent fecal material. Tagging of fecal material can help differentiate flat lesions from adherent stool.

5. Extrinsic Compression

Organs or structures adjacent to the colon can produce a mass effect that mimics a colonic polyp or mass on 3D endoluminal view. In these cases, 2D evaluation should demonstrate the abnormality as extrinsic (Fig. 15).

![Figure 14. Flat polyp. On 3D endoluminal image (A), a lobulating and slightly elevated lesion (arrow) is visualized. However, on 2D axial supine image (B), this lesion (arrow) is barely visible. Optical colonoscopy (C) confirmed an 8 mm flat tubular adenoma (arrow).](image1)

![Figure 15. Extrinsic compression by iliac vessels. On 3D endoluminal image (A), a smoothly elevated mass-like lesion (arrow) is visualized. However, on 2D axial image (B), we can easily guess that this lesion (arrow) is caused by extrinsic compression due to iliac vessels. Note the annulo-constricting cancer (*) on both 3D endoluminal (A) and 2D axial (B) images.](image2)

![Figure 16. Inverted appendiceal stump. On 3D endoluminal image (A), a sessile polypoid (arrow) is visualized at the tip of the cecum. On 2D axial image (B), this lesion (arrow) shows homogeneous soft tissue attenuation. Optical colonoscopy (C) confirmed this lesion (arrow) as an inverted appendiceal stump.](image3)
6. Inverted Appendiceal Stump

An inverted appendiceal stump may mimic a cecal lesion on 2D and 3D images (Fig. 16). When a suspected lesion is demonstrated in the expected region of the appendiceal orifice, an attempt should be made to identify a normal appendix. If the appendix is not identified, it is important to determine whether the patient has had prior inversion-ligation appendectomy.67

7. Bulbous Fold

Bulbous colonic folds may mimic colonic polyps on both 2D and 3D images, but sequential review of the suspected abnormality in axial, coronal, and sagittal images should clarify that the abnormality represents a fold rather than a polyp.

Computer-Aided Diagnosis

Computer aided diagnosis (CAD) for CTC is an automated process that detects configurations of the colon wall that might represent polyps (Fig. 17). It is a method that has the potential to increase the diagnostic performance of radiologists in detecting polyps and cancers at CTC and to decrease the inter- or intra-observer variability of diagnostic accuracy among readers without significantly increasing the reading time.48-50 Preliminary studies have demonstrated that CAD programs are capable of identifying some polyps missed by CTC readers, but at the expense of false-positive findings.51 Such studies indicate that CAD has the potential to reduce perceptual errors with a relatively low false-positive rate, but further improvements in technology are required. Some of the current challenges faced by CAD researchers are optimizing the trade-off between sensitivity and specificity, establishing a strategy for reading paradigm, developing programs that detect polyps in patients who have undergone stool and fluid tagging, developing other algorithms that are tuned to detect flat polyps or cancers, and insuring that the programs are robust even when ultra-low radiation dose CTC techniques are used.52

Conclusion

CTC requires high standards in technique and interpretation performance, as well as a robust reporting and training system and is currently undergoing intensive development and investigation. Even though the role of CTC in a screening population remains to be determined, CTC meets the criteria for a screening test because it is safe, relatively inexpensive, and acceptable to patients with encouraging results according to studies performed in the last two years. In addition, the development of patient-friendly bowel preparation regimens and powerful CAD algorithms has brought CTC one step closer as a screening test for colorectal polyps and cancers.

References


Figure 17. Computer-aided diagnosis. Polyp Enhanced View® (PEV®, Siemens Medical System) image shows a sessile polyp (arrow) marked as "c6a" where the prefix "c" indicates that the marker was located by the CAD system.


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