Clinical applications

CT colonography in early detection of colorectal cancer

Colorectal cancer is the third most common cancer worldwide and the fourth leading cause of cancer death. In the United States it occupies the second place: only lung cancer claims more lives. The prevalence of colorectal cancer amounts to about 1 million in the United States alone [1]. The American Cancer Society estimates that about 112,340 new cases of colon cancer and 41,420 new cases of rectal cancer will be diagnosed in 2007, and that 52,180 people will die of colon or rectum cancer in 2007 [2].

Most colorectal cancers arise from benign adenomatous polyps. The progression from a small - often polypoid - adenoma to a colorectal cancer has a natural history of approximately 10 years. The long time between the appearance of a polyp and the progression into cancer gives a wide window of opportunity for its detection and removal. Treatment becomes much simpler and effective if a cancer is detected in an early stage, and this is particularly true if a polyp is detected before it can even become cancer.

A variety of common and experimental screening and diagnostic methods to detect colorectal cancer are shown in Table 1. The American Cancer Society prefers an annual fecal occult blood test (FOBT) and a flexible sigmoidoscopy every 5 years, since this is the most cost-effective screening strategy today [2]. Patients have generally been reluctant to undergo colorectal screening for reasons of embarrassment and unpleasantness of the colon-cleansing process.

CT colonography

CT colonography (Figure 1) is an imaging technique that enables inspection of the inner colon wall to detect polyps or cancer. The following sections describe bowel preparation, insufflation and image acquisition.

Bowel preparation

Several methods of bowel preparation have been proposed and evaluated in CT colonography [3]. Most of the techniques were proposed in an effort to increase patient compliance by reducing the burden of bowel preparation. These techniques include extensive and limited bowel preparation, and may be performed with and without stool and/or fluid tagging. The results (sensitivity and specificity) from these techniques - sometime arguably referred to as “prepless” - have been mixed and significant technological advancements are required before these techniques are commonly adopted.

A typical and widely followed bowel preparation technique that has been tested and validated in major clinical trials is a cathartic bowel preparation with oral contrast for fluid tagging [4, 5]. It involves a 24-hour clear liquid diet prior
to the examination, with oral administration of a single dose of sodium phosphate (45 mL), 2% barium suspension (250 mL), and diatrizoate (60 mL).

Many variations to this technique are possible, depending on the condition of the patient (e.g. renal or cardiac insufficiency) and the preference of the radiologist.

Residual fluid and stool that might simulate polyps are tagged to differentiate them from real polyps. Tagged fluid that might otherwise obscure visualization of polyps during 3D evaluation can be removed using electronic cleansing software. The technique is described below in the section on Electronic Cleansing.

**Colon insufflation**
With the insertion of a small flexible rectal catheter, colon distension can be achieved through either automated CO₂ delivery or the patient-controlled insufflation of room air immediately before scanning. To increase patient comfort and image quality, spasmolytics can be administered. Lately, automated CO₂ delivery is being adopted on a larger scale because it results in slightly less post-procedure patient discomfort (mostly because the body absorbs the CO₂ more easily than room air) and better colonic distension than patient-controlled air insufflation [6].

**Acquisition**
A surview (scout view) is performed to confirm the optimal colonic distension in the patient prior to both supine and prone scans. This scanning in both positions is done to allow for proper distension of all bowel segments, and is helpful for differentiating between polyps and stool. Gravity will cause residual fluid and stool to move to the lower side, while polyps remain attached to the wall. Re-insufflation may be performed manually or automatically between the supine and prone scans to ensure optimal distention in the prone scan. This is necessary if CO₂ is absorbed by the colonic wall, or if loss of air/gas occurs due to patient movement and pressure on the patients’ colon while lying on the belly.

The advent of multidetector CT provided increased coverage and faster rotation speeds. This enabled CT colonography to become more practical with shorter breath hold times for patients, thinner slices and minimal motion artifacts due to peristalsis [7].
CT colonography is optimally performed on a multidetector CT (MDCT) scanner configuration with at least 4 slices, and a single breath-hold of around 15-20 seconds (for a 64-slice scanner this reduces to 5-10 seconds).

Visualization

After the acquisition, the volumetric dataset can be visualized and inspected. Traditionally the most commonly used display is the primary two dimensional (2D) mode in which large axial images are displayed to detect abnormal polypoid shapes on the colon wall.

Three dimensional (3D) visualizations are added for problem solving and to better discriminate polyps from (complex) folds. An overview image of the colon can serve as a navigation aid. An example of primary 2D viewing is shown in Figure 2. A small polyp in the sigmoid colon is quite obvious in the 3D visualization (supine scan).

Primary 3D reading is used as valuable alternative reading technique. In such a primary 3D reading, endoluminal images are primarily used to detect polypoid shapes, while the original CT slices are used for problem solving. These endoluminal or “virtual endoscopy” images mimic the images seen on a conventional endoscope by providing internal perspective views of the colon wall.

Recent studies indicate a possible advantage of primary 3D viewing [8, 9]. It is important to note that 2D and 3D visualizations are complementary and should always be combined, whatever the primary reading method may be.

A limitation of CT Colonography is the reading and post-processing time necessary for both supine and prone positions [10]. It takes approximately 20 to 25 minutes to perform a complete analysis, which includes pre-processing, segmentation, and reading the study in two-dimensional (axial) and endoluminal views. In order to reduce the read times and expose more colonic surface, new visualization techniques have been developed. We describe two visualization methods that overcome these problems: Unfolded view and Perspective-Filet view.

Unfolded view

In the Unfolded view proposed by Vos et al. [11] the endoluminal viewing is not limited to ante- and retrograde viewing directions, but also contains up, down, left and right views, providing a complete 360° view of the colon wall. With the viewpoint at the center, images of the surroundings are projected on the faces of a cube. The six images are then unfolded into one image so that the six faces can be examined simultaneously. The principle is shown in Figure 3.

The Unfolded view allows the user to immediately see polyps on and behind haustral folds. Moreover, it provides an intuitive view, which leads to significantly less inspection time (19-20 minutes) compared with using bi-directional fly-through (approx. 36 minutes) [11]. The colon surface visibility is also improved [12] as compared with ante- and retrograde endoluminal displays. Finally, this visualization method has the advantage that the distortions are limited.

Figure 4 shows the primary 3D display mode with an Unfolded view. The same small polyp is visible, demonstrating the power of the Unfolded view to look behind the haustral folds.

Perspective-Filet view

A different visualization technique is the virtual dissection view, as proposed by Hoppe [13] and Rottgen [14], in which the entire colonic lumen is laid out like an anatomical specimen.
The virtual dissection view presents the lumen unrolled along the centerline, with all resampling performed using projection rays perpendicular to the centerline.

The Perspective-Filet view is a variation on the virtual dissection view, designed to overcome the “blind spots” sometimes created when all of the resampling is performed perpendicular to the centerline.

Figure 4. Primary 3D viewing mode with the Unfolded view, showing the full view of the colon wall as an unfolded cube. The image at top left is a zoomed axial view of the polyp (indicated by an arrow), while the view on the right shows a multiplanar reformat view through the same polyp but perpendicular to the colon centerline.

Figure 5. In the Philips Perspective-Filet view, oblique projection rays allow visualization of the antegrade and retrograde side of folds in a single fly-through. In the conventional virtual dissection view, only projection rays perpendicular to the centerline are used, with the possibility of distortion and blind spots.

Figure 6. A clinical example showing the advantage of the dynamic nature of Philips Perspective-Filet View. It makes the polyp (circled in yellow) very conspicuous compared with a conventional virtual dissection view. The latter distorts the morphology of the same polyp to make it appear like a fold, which might result in a significant oversight.

Figure 6a. Philips Perspective-Filet view.
Figure 6b. Conventional virtual dissection view.
By tilting the projection rays as a function of the distance from the centerline, the Perspective-Filet view adds perspective to the previously flat view (Figure 5). This allows the user to move through the colon and see inside traditional blind spots. It also helps to evaluate the entire colon in a single fly-through, thereby significantly reducing the interpretation time [15, 16]. In a recent study by Kim et al. [17], a median interpretation time of 9.4 minutes was reported when the Perspective-Filet view was used for the primary read, compared with a median interpretation time of 14.1 minutes for a conventional 2D read. This was a statistically significant reduction in interpretation time with no compromises in sensitivity or specificity.

Another limitation of the conventional virtual dissection view - mainly because of its static nature - is the distortion caused to the colonic mucosa, folds, and most importantly, polyps. The dynamic nature of the Philips Perspective Filet view helps maintain and confirm the polyp conspicuity during its appearance (Figure 6).

### Size measurement

**Rationale**
The size of a polyp is important because it is a predicting factor for malignancy. The probability that a polyp ≥ 2 cm is malignant exceeds 50%. For polyps between 1 and 2 cm in size, this probability decreases to 9.5%. Polyps smaller than 1 cm have only a 1% probability of being malignant [18]. The probability that a polyp will develop into invasive cancer also increases with the size of the polyp.

The estimated potential for malignancy is used to decide whether a polyp should be removed to prevent the patient from developing colorectal cancer. If a polyp is small it may take several years before it develops into a cancer [19]. Thus, it is safe to leave it in situ and to let the patient return in a few years for another colon screening examination.

**C-RADS**
During procedures where a polyp cannot be removed immediately, as in CT colonography, it is important to measure the polyp size correctly. The consensus proposal for CT Colonography reporting and data (C-RADS) [20] advises on how to measure and report sizes for colonic polyps found in CT data and recommends follow-up actions for the patient, see Table 2.

**Manual measurements**
Polyp size can be measured either in 2D multi-planar reconstruction views or 3D endoluminal views. There is a possible underestimation when measuring lesions in 2D views because the view may not be aligned along the largest axis of the polyp [21]. Moreover, the size measurement in 2D also depends on the window level being used. In 3D views, polyps tend to be overestimated in

<table>
<thead>
<tr>
<th>Category</th>
<th>Definition</th>
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<tbody>
<tr>
<td>C0</td>
<td>Inadequate Study/Awaiting Prior Comparisons</td>
</tr>
<tr>
<td></td>
<td>• Inadequate prep: cannot exclude lesions ≥ 10 mm owing to presence of fluid/feces</td>
</tr>
<tr>
<td></td>
<td>• Inadequate insufflation: one or more colonic segments collapsed on both views</td>
</tr>
<tr>
<td></td>
<td>• Awaiting prior colon studies for comparison</td>
</tr>
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<td>C1</td>
<td>Normal Colon or Benign Lesion; Continue Routine Screening *</td>
</tr>
<tr>
<td></td>
<td>• No visible abnormalities of the colon</td>
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<tr>
<td></td>
<td>• No polyp ≥ 6 mm</td>
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<tr>
<td></td>
<td>• Nonneoplastic findings - e.g., colonic diverticula</td>
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<td>C2</td>
<td>Intermediate Polyp or Indeterminate Finding; Surveillance or Colonoscopy Recommended**</td>
</tr>
<tr>
<td></td>
<td>• Intermediate polyp 6-9 mm, &lt;3 in number</td>
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<tr>
<td></td>
<td>• Intermediate findings, cannot exclude polyp ≥ 6 mm in technically adequate exam</td>
</tr>
<tr>
<td>C3</td>
<td>Polyp, Possibly Advanced Adenoma; Follow-up Colonoscopy Recommended</td>
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<tr>
<td></td>
<td>• Polyp ≥ 10 mm</td>
</tr>
<tr>
<td></td>
<td>• ≥ 3 polyps, each 6-9 mm</td>
</tr>
<tr>
<td>C4</td>
<td>Colonic Mass, Likely Malignant; Surgical Consolation Recommended***</td>
</tr>
<tr>
<td></td>
<td>• Lesion compromises bowel lumen, demonstrates extraluminal invasion.</td>
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</tbody>
</table>

* : Every 5-10 years  
** : Evidence suggests surveillance can be delayed at least 3 years, subject to individual patient circumstance  
*** : Communicate to referring physician as per accepted guidelines for communication, such as ACT Practice Guideline for Communication: Diagnostic Radiology. Subject to local practice, endoscopic biopsy may be indicated.
comparison to a linear probe measurement during colonography [21,22]. Manual size measurements are also quite dependent on the operator. Examples of 2D and 3D measurements are shown in Figures 7 and 8.

**Automatic size measurement**

Automatic polyp size measurement may overcome the limitations of manual measurements in CT colonography, such as human error and reader variability. The automatic measurement algorithm computes the size of a polyp by segmenting the part of the colon wall that is actually polyp-like and measures its longest linear dimension (excluding the polyp stalk). Automatic volume measurement will play an important role in the future for better prediction of the potential for malignancy of a polyp, but requires further investigation of the techniques.

**Measurement study**

To assess the importance of automated measurement we compared the following measurement methods on CT [23]:

- manual 2D measurements using a lung and abdominal window setting
- manual 3D measurements
- automated measurements
- automated measurements after correction by the user.

To limit the influence of measurement outliers, the median of these measurements was used as the gold standard.

It appeared that the user left the automatic measurement unchanged in 40% of the cases, and corrections of more than 1 mm were only made in 30% of the cases. The automated measurement (followed by manual correction where needed) was the most precise method of the five methods considered, with the smallest limits of agreement (ranging from -1.68 to +1.61 mm). Finally, the number of polyps classified into the wrong size category as a result of the measurement error was found to be lowest for the automated measurement with manual correction (5%), while the other methods misclassified between 18% and 25% of the polyps.

**Electronic cleansing**

A prerequisite for using primary 3D visualization methods – endoluminal viewing, Unfolded view or Perspective-Filet view – is a nearly empty colon. Remains of stool and fluid may be falsely interpreted as polyps or vice versa. However, cathartic cleansing is considered burdensome by patients because it causes diarrhea, flatulence and abdominal pain. In some preparations drinking large amounts of a laxative adds to the patient burden. Bowel preparation schemes [24,25] have been introduced that opacify intracolonic remains; this is referred to as “fecal tagging”. Computed cleansing then assists in removing these remains from the colon in the 3D visualization [26]. Computed cleansing potentially also permits less strict colon preparation [27].

**Technique**

The electronic cleansing method assumes that the measured CT value arises due to a combination of three materials: air, tagged intraluminal remains and soft tissue. The contributions of these three materials are mixed during scanning. Electronic cleansing separates them by determining the fraction of materials at each voxel. Subsequently, the fraction of tagged remains is replaced by air and a new electronically cleansed CT value is determined. This allows primary 3D visualization methods to be used in a reduced prep population to study the colon as if it were clean.

An example of a dataset before and after electronic cleansing is shown in Figure 9. It clearly shows a medium sized pedunculated polyp that is hidden in the unfolded rendering of the original data, but becomes very conspicuous after electronic cleansing.

**Performance studies**

A quantitative validation was performed on a...
subset of 20 patients from a publicly available database [28]. Despite the fact that patients had undergone an extensive bowel preparation, on average 20% of the colon’s volume contained tagged material and 40% of the polyps were partly or completely covered with tagged remains. The performance of 3D reading followed by 2D reading was compared between original (uncleansed) data and cleansed data. Electronic cleansing using a primary 3D display significantly reduced evaluation time and reader assessment effort, and increased confidence in the reading.

In a second study [29] the influence of electronic cleansing on the polyp conspicuity was measured. Two observers rated the conspicuity of uncleansed polyps (bordering air) and cleansed polyps (bordering contrast material) using 3D views of these polyps in random order. There was no difference in conspicuity between both types of polyps, which means that polyps with a shape and size that should be obvious to the eye using a primary 3D display did not become less obvious after applying electronic cleansing. Note that the submerged polyps were not visible in 3D without electronic cleansing.

**Computer-Aided Detection**

**Role**

Computer-Aided Detection can be helpful in “needle in a haystack” tasks where large amounts of data have to be inspected for small abnormalities. In the case of screening with CT colonography, large amounts of scanned data from many patients have to be read to detect polyps down to a size of 6 mm. Small lesions are easily missed, and computer assistance will be helpful in reducing these observational oversights (known as perceptive errors).

**Reader paradigms**

Most CAD systems are used in a second-reader paradigm, in which the physicians analyze the study without the help of CAD, make a decision, and only then consult the CAD. The second-reader paradigm will probably increase the performance of an expert, but will also increase the reading time because of the extra analysis of CAD findings. Some studies indicate that the sensitivity of an expert in detecting medium and large polyps can be improved by around 10-15% when using CAD as a second reader [30,31,32].

Computer-aided detection can also play a role in narrowing the gap in sensitivity between less experienced readers and experts [33,34]. CAD shows potential for turning a less experienced reader into an expert. This will be particularly useful when screening programs emerge and the lack of trained observers will start playing a role. Note that the final diagnosis is made by the human reader, who also determines the final performance.

**Performance**

The performance of a CAD algorithm is a trade-off between true detection (sensitivity) and over-detection (false positives). Every CAD algorithm is designed to detect as many polyps as possible, but will always find other structures that are not polyps.

Most CAD algorithms attach a score to every candidate polyp. Above a certain threshold value of the score the candidate will be classified as a...
polyp. This threshold is variable and often under user control. Since it influences the performance directly, it must be taken into account when presenting performance results.

A comparison between three available CAD systems (Philips, Siemens and MedicSight) [35] on a dataset of 32 patients with a total amount of 53 polyps with sizes ranging from 3 to 40 mm is shown in Table 3. A similar comparison between Siemens and a research algorithm by the NIH on 65 datasets has been published by Fletcher et al. [36]. Other reports on CAD performance have been published by Summers et al. [37] and Halligan et al. [38].

**Conclusion**

During the past decade CT colonography has matured from research to clinical practice as a primary method for colon imaging to detect polyps and colorectal cancer. New developments in both data acquisition and image post processing have improved results and reduced costs, and will undoubtedly continue to do so.

CT scanners have become better and faster, allowing for the acquisition of high-resolution isotropic abdominal data within seconds. Advanced visualization and navigation tools, and especially the introduction of CAD, are expected to increase the detection performance of human readers, particularly less experienced experts, and will eventually reduce reading time.

In the near future, CAD systems will have to be extensively validated by multiple readers on different types of data with varying acquisition settings and patient preparations. Further research will be aimed at improving patient safety and comfort by reducing radiation dose and patient preparation. Electronic cleansing is expected to play an important role in improving patient comfort and could eventually allow for a prepless diet. All these developments help in preparing CT colonography to play an important role in population surveys for colon cancer screening.

### Table 3. Comparison of three different CAD systems for virtual colonoscopy.

<table>
<thead>
<tr>
<th>Product/manufacturer</th>
<th>Leonardo2 with PEV, Siemens</th>
<th>ViewForum, Philips</th>
<th>Medicsight, Vitrea 3.8, Vital Images</th>
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<tbody>
<tr>
<td>High sensitivity</td>
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<td>90% sensitivity</td>
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</tr>
<tr>
<td>operating point</td>
<td>5 false positives</td>
<td>12 false positives</td>
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<tr>
<td>Low sensitivity</td>
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<tr>
<td>operating point</td>
<td>3 false positives</td>
<td>1 false positives</td>
<td>6 false positives</td>
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**References**


