PICTORIAL ESSAY | Abdominal imaging

CT colonography; latest indications, methodology, and case examples

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ABSTRACT

Colorectal carcinoma is the 3rd commonest malignancy and 2nd cause of mortality due to cancer. It is the result of a multiyear, multistep transformation of an asymptomatic adenomatous polyp to a symptomatic invasive carcinoma. Optical colonoscopy (OC) and laboratory testing have been traditionally used in colorectal cancer (CRC) screening, diagnosis, and follow-up. Since its introduction in 1994 computer tomography colonoscopy (CTC) has gradually been enlisted in CRC screening and diagnosis methods functioning either as an alternative or a first-choice examination. This review focuses on CTC development, current indications, methodology, and image acquisition followed by case examples from our department, data reporting, and future directions.

KEY WORDS | colonic polyps, colonic neoplasms, colonography, computed tomographic

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Introduction

Colorectal cancer represents about 1 in 10 cancer cases and deaths worldwide, ranking 3rd in incidence and 2nd in mortality [1]. Despite the significant improvement in treatment regimens over the last decades, disease outcomes and life expectancy have moderately improved in patients with advanced disease. Both the high treatment cost and the favorably slow development of CRC render this type of cancer particularly suitable for population-screening programs [2, 3]. Even in symptomatic cases, CRC is diagnosed at an advanced stage in 60-70% highlighting the usefulness of well-established screening programs [4].

Optical colonoscopy and fecal occult blood testing (FOBT) have traditionally been used as screening tools for colorectal cancer [5, 6]. However, patients' poor compliance and endoscopy-related difficulties due to occlusive disease prevent the completion of OC in a proportion of them. Computed tomography colonography has been proposed as an alternative screening method based on data acquisition and processing by specialized imaging software. Since Vining and Gelfand first used CT to perform a 3D visual flythrough of the colon in 1994 [7], CTC has undergone various phases to eventually be characterized as the "radiological examination of choice for the diagnosis of colorectal neoplasia" (ESGE/ESGAR guidelines, 2020) [8].

In essence, CT colonography combines features of an abdominal CT scan and an optical colonoscopy offering a non-invasive, detailed, two-dimensional view of the colon and its surrounding extracolonic structures along with a three-dimensional intraluminal detection capacity of polyps and other pathology.

CTC in first clinical trials

Early clinical trials of relatively small cohorts highlighted the ability of CTC to detect polyps ≥6mm in diameter with good sensitivity (70-100%) and high specificity (>90%) [9, 10]. The early detection of polyps is crucial to hindering colon cancer development. It is well-established that most CRCs result from a multiyear, multistep transformation of an adenomatous polyp to carcinoma [11]. Incomplete optical colonoscopy gradually became the first indication for diagnostic CTC in the clinical context [12]. However, the utility of CTC in low-prevalence populations was still to be assessed, i.e. a potential role for the method in asymptomatic screening. The DoD multicenter screening trial of 1.233 asymptomatic, average-risk adults in 2003 led to the first FDA approval of software for CTC screening [13]. Large adenomas were detected through CTC screening with a 94% sensitivity and a 96% specificity. Sensitivity at the 6-mm threshold was 89% and specificity due to technical limitations of the time dropped to 80%. The DoD trial was the first to rely on CTC software for primary 3D instead of 2D polyp detection and the use of oral contrast tagging. The ACRIN trial, a multi-center trial of 2.531 asymptomatic adults, further validated the efficacy of CTC in detecting adenomas or cancers ≥10mm with a 90% sensitivity [14].

The SIGGAR randomized controlled trial, published in 2015, included 5.384 high-risk patients and compared CTC with OC and barium enema (BE) [15]. CTC proved superior to BE for the detection of cancer and large polyps in symptomatic patients. CTC and OC performed similarly in terms of cancer detection.

Indications to CT colonography

In 2020 the European Society of Gastrointestinal Endoscopy (ESGE) and the European Society of Gastrointestinal and Abdominal Radiology (ESGAR) updated their guidelines on CTC for patients screening for or suspected of CRC [8]. According to them, CTC is the recommended radiological examination for diagnosing CRC and large polyps, being similarly accurate to OC in both symptomatic and asymptomatic subjects. CTC can be performed the same or the next day in case of incomplete OC due to occlusive cancer. However, same-day CTC is contra-indicated in the clinical setting of perforation or at least moderate diverticulitis or colitis. CTC is also recommended when OC is not feasible or indicated in patients with symptoms highly suggestive of CRC or even without any alarm symptoms. In terms of CRC screening, ESGE/ESGAR strongly endorse CTC in the absence of a well-established fecal immunochemical test (FIT)-screening program. In case of a positive FOBT or FIT in patients who cannot undergo or do not complete OC, CTC is then recommended even within screening programs. Insufficient data regarding CTC cost-effec-

Table 1. C-RADS categorization and management recommendations for colonic findings. Zalis M.E. et al. Radiology 2005Vol 236:1

C0	Inadequate Study/Awaiting Prior Comparisons • inadequate prep: cannot exclude lesions ≥ 10mm owing to presence of fluid/feces • inadequate insufflation: one or more colonic segments collapsed on both views • awaiting prior colon studies for comparison
C1	Normal Colon or Benign Lesion; Continue Routine Screening*1 • no visible abnormalities of the colon • no polyp ≥ 6mm • lipoma or inverted diverticulum • nonneoplastic findings – e.g., colonic diverticula
C2	Intermediate Polyp or Indeterminate Finding: Surveillance or Colonoscopy Recommended*2 • intermediate polyp 6-9 mm, < 3 in number • indeterminate findings, cannot exclude polyp ≥ 6 mm in technically adequate exam
C3	Polyp, Possibly Advanced Adenoma: Follow-up Colonoscopy Recommended3 • polyp ≥ 10 mm • ≥ 3 polyps, each 6-9 mm
C4	Colonic Mass, Likely Malignant: Surgical Consultation Recommended*3 • lesion compromises bowel lumen, demonstrates extracolonic invasion

Prep = Preparation
**1: Every 5-10 years.*
**2: Evidence suggests surveillance can be delayed at least 3 years, subject to individual patient circumstance.*
**3: Communicate to referring physician as per accepted guidelines for communication, such as ACR Practice Guideline for Communication: Diagnostic Radiology. Subject to local practice, endoscopic biopsy may be indicated.*

tiveness compared with flexible sigmoidoscopy and FIT restrict for the time being the method's screening range.

Any patient with at least one polyp ≥6mm found at CTC should be referred for polypectomy. Close collaboration with a gastroenterologist is suggested particularly in patients with co-morbidities or patients who choose not to submit themselves to polypectomy.

Colonoscopy remains the examination of choice for surveilling patients after resection of CRC or high-risk polyps. CTC is considered an alternative when OC is contra-indicated in these patients. In general, CTC must be avoided in patients with peritonitis, bowel perforation, and active mucosal inflammation due to the risk of perforation (e.g. IBD). The safety of CTC was also confirmed by a wide Japanese national survey covering possible adverse events during CTC for screening, diagnosis, and preoperative staging [16]. Out of almost 150.000 CTCs performed, perforation was recorded in 0.014% and vasovagal reaction in 0.081%.

Methodology

Bowel preparation: Insufficient bowel preparation affects the examination's diagnostic accuracy since luminal fluid or fecal residues might mimic colonic lesions (Fig. 1). Many protocols have been suggested varying in diet, colonic cleansing, and fecal tagging. According to ESGE/ESGAR guidelines, a clear liquid diet is suggested for at least 24 hours before the examination combined with a split regimen of a laxative "wet prep" solution the day before and on the day of the examination (2 or 4 lt) [8]. Air fluid levels could hinder small polyps imaging, so excess fluid consumption should be avoided. Laxative preparation can be either a "wet prep" (polyethylene glycol, PEG) or a "dry prep" (sodium picosulphate or sodium phosphosoda).

Oral tagging: Despite efforts to thoroughly cleanse

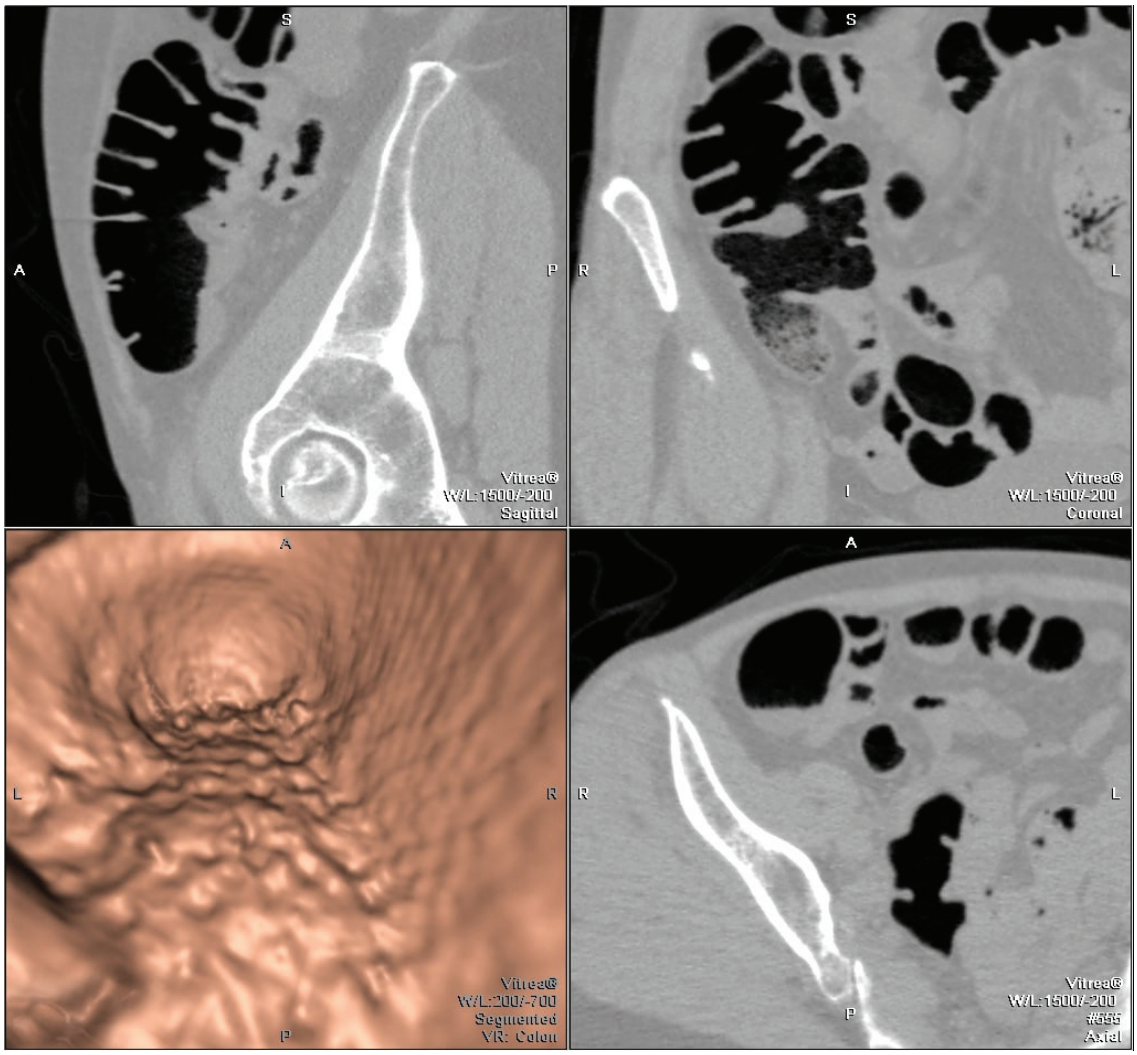

Fig. 1. *Insufficient bowel preparation as depicted in sagittal (upper left), coronal (upper right), axial (lower right), and virtual colon images (lower left). A significant part of the cecum inner wall and lumen cannot be visualized due to residual stool and fluid. (Software; Vitrea by Canon Medical Informatics. CT scanner; Toshiba Aquilion 64)*

the bowel, even minimal fluid or fecal residues may impede the distinguishment between them and polyps. Oral tagging with positive contrast media increases the density of the residuals, while the colonic structures maintain the soft-tissue density. Barium and iodinated agents have been used as tagging solutions. Barium may inhibit the same-day colonoscopy, cause colonic constipation, and result in heterogenous tagging due to its low water solubility. Therefore, sodium amidotrizoate and meglumine amidotrizoate (Gastrografin, Bayer Schering, Germany) are usually preferred in the tagging protocols. Patient compliance has always been a challenge in the multistep process of CTC examination. Neri et al. showed similar polyp detection rates between patients who underwent CTC with rectal tagging (enema of gastrografin) and patients who received oral tagging [17]. Patient acceptance was higher with rectal iodine tagging and overall examination time was lower, as well.

Bowel distension before the colonography is another central quality factor (Fig. 2). Automated distension with CO_2 through a rectal tube is the method of choice nowadays, combining minimal patient discomfort and adequate inflation [18]. Usually, 3-10 liters of gas are sufficient to enable proper visualization of the luminal surface of the colon. Ideally, the

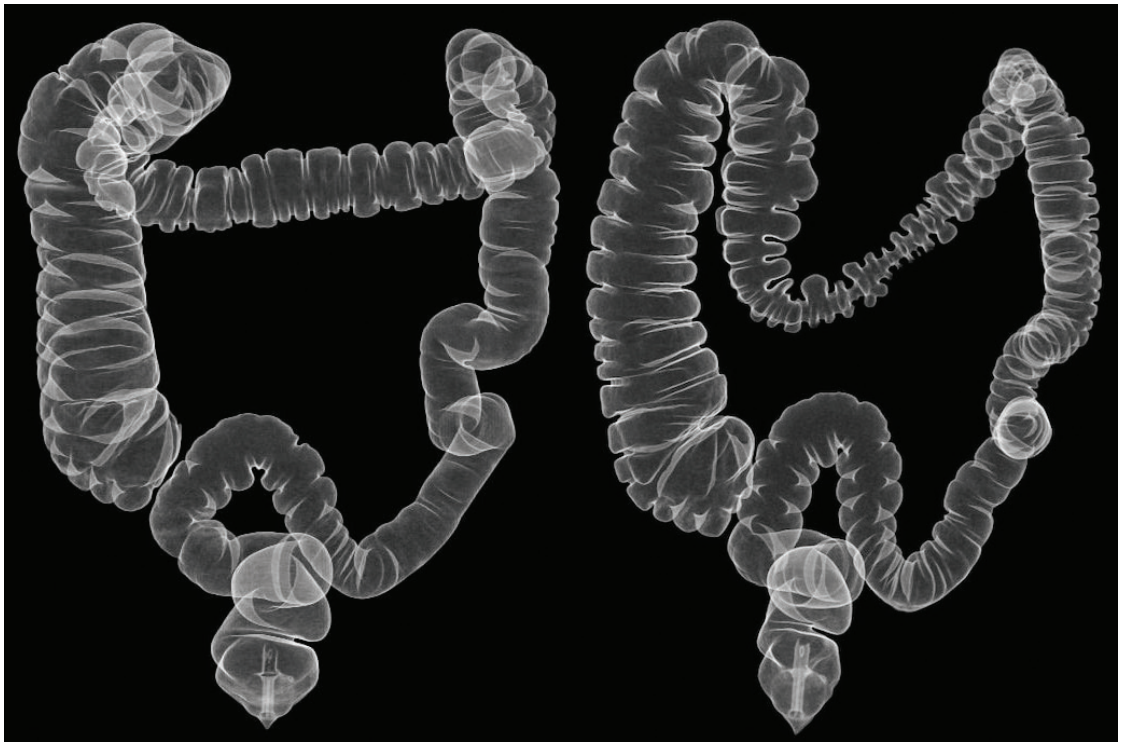

Fig. 2. Adequate distension of the colon enables proper visualization and analysis (left). Inadequate distension of the transverse colon does not allow proper lumen assessment and data collection from the area (right).

colon should be entirely visualized in both decubitus positions before full CT data acquisition. Colonic insufflation should be performed by a trained specialist and perforation should be ruled out before the patient leaves the site.

Spasmolytics: The routine use of spasmolytics for CTC is not widely supported. The decision to administer them should be based on the patient's history. Hyoscine-N-butylbromide (Buscopan) is the drug of choice and should be administered before bowel distension begins [18]. In patients with sigmoid diverticular disease intravenous Buscopan can improve the distension of proximal colonic segments [19].

Contrast-enhanced CT colonography: Routine intravenous administration of contrast medium is not required for screening purposes or evaluation of the colon's lumen. However, contrast-enhanced CTC is necessary for CRC staging and postoperative surveillance of CRC patients. Local recurrence, metachronous disease, and distant metastases can be detected with high accuracy since the display of the anastomosis, the colonic wall, and the extracolonic tissue is enabled [20].

Radiation exposure: The lifetime risk of developing colorectal cancer (5%) emphatically outweighs the risk of developing cancer due to radiation exposure after a CTC examination (0.04% in 50-year-old patients, 0.02% in 70-year-old patients) [21, 22]. According to the latest ACR practice parameter, CTC for screening adults should be performed with a low-dose, non-enhanced technique on a multidetector CT (MDCT) scanner [23]. The recommended average radiation volume CTDI (CT dose index) for screening CTC should be ≤5mGy per position. Using a 120 kVp tube potential the mean effective mAs value is around 50. Dose reduction techniques, which maintain or improve image quality, are strongly encouraged. These include altering exposure parameters, such as reduction in tube current (mA), exposure time, tube current-time product (mAs), or tube potential (kV). Automated tube current modulation (ATCM) adjusts tube current according to the size and attenuation of the examined body area. Besides scanning parameters, software options such as the sinogram-affirmed

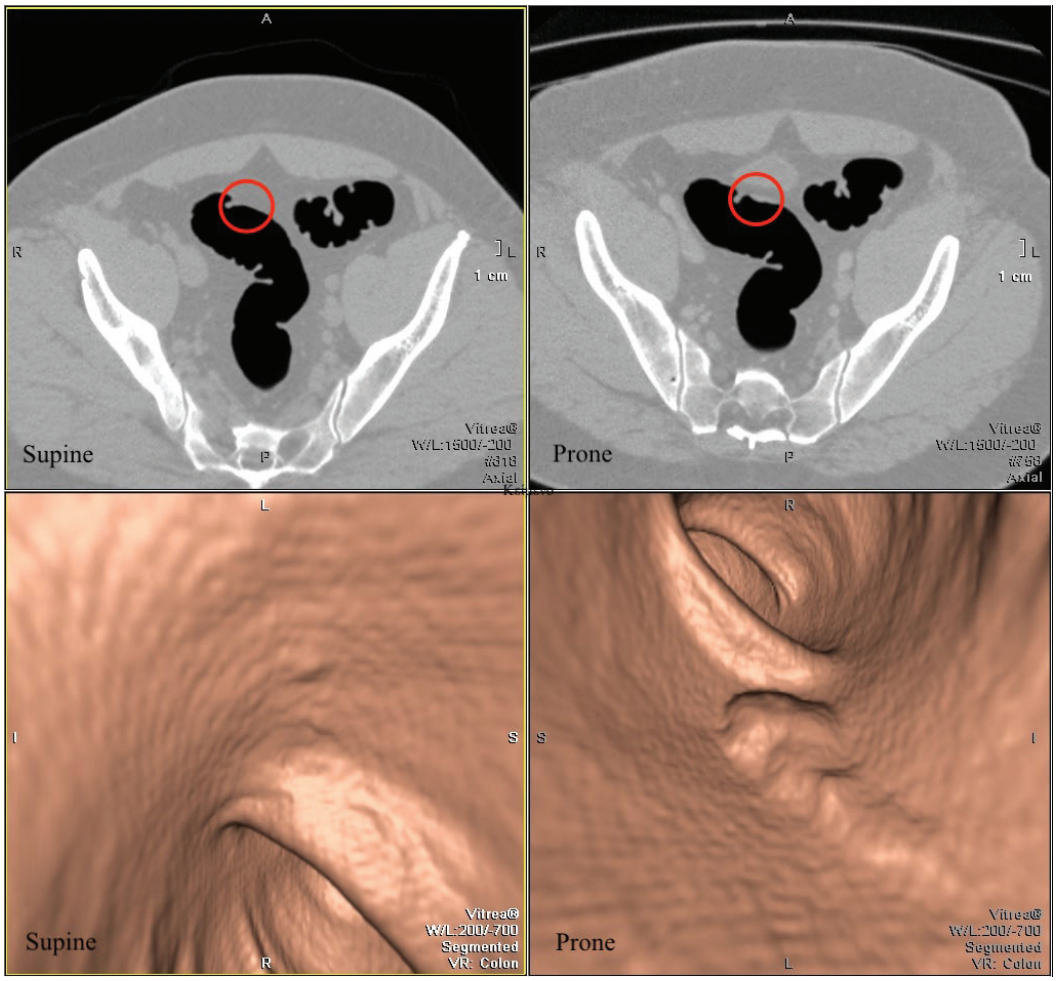

Fig. 3. *Fecal residue (circle) in the rectum can easily be differentiated from a colonic mass by changing the patient's position from prone (right upper and lower) to supine (left upper and lower).*

iterative reconstruction (SAFIRE) reduce image noise by keeping the tube current as low as possible. In a study of 82 patients, an ultra-low-dose (ULD) CTC protocol based on ATCM and SAFIRE was compared with the low-dose protocol (LD) in terms of radiation dose, image quality, image noise, and polyp detection [24]. ULD achieved a dose reduction of 63.2%, whereas image quality and noise and polyp detection rate were comparable between the two techniques. Overall, dose reduction techniques can lower radiation exposure even below the average annual background level of radiation (<3mSv).

Electronic cleansing: Fecal tagging, as described earlier, enables the electronic cleansing (EC) of colonic residue, which is a prerequisite for a low rate of false positives and false negatives. The process is performed by specialized software that distinguishes between bowel wall and residual attenuation and digitally subtracts tagged residue from the lumen. Tagged residual stool and fluid appear hyperdense compared to soft tissue structures and lesions. All voxels with a CT density higher than the appointed threshold value (often 100HU) will be identified by the EC algorithm as tagged residue [25]. Adequate bowel preparation is imperative to successful electronic cleansing. Inappropriate timing of administration of tagging agents or a reduced amount of them can lead to insufficient tagging. Furthermore, inhomogeneous tagging results in areas of mixed densities and consequently in confusion during data analysis. Due to the artifacts it produces, electronic cleansing is not always chosen in practice [27]. Aiming to diminish tagging errors,

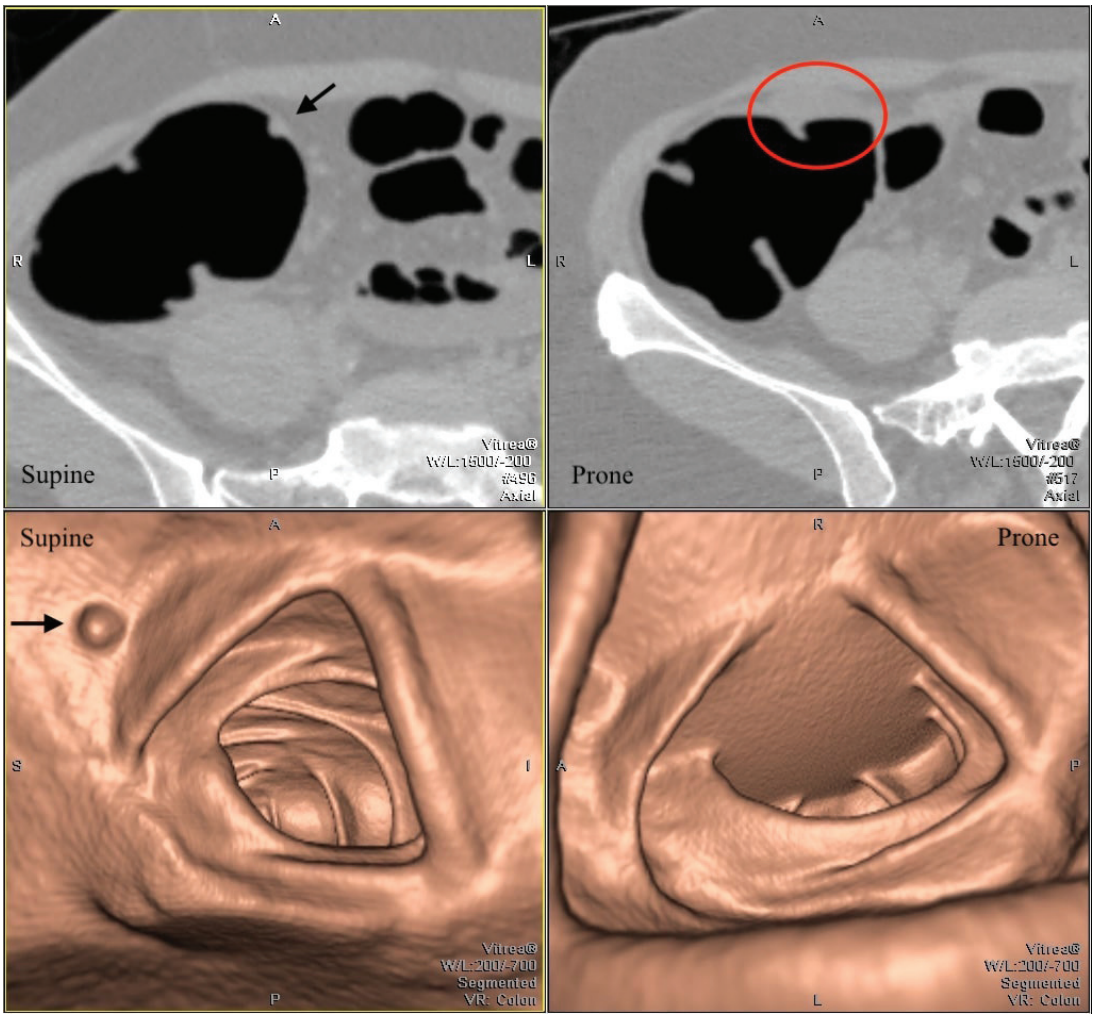

Fig. 4. *Revelation of a small polyp (arrows) in the right colon after moving the patient from prone (right upper and lower) to the supine position (left upper and lower). Residual fluid (circle) covers and hides the polyp in the prone position.*

a dual-energy CTC phantom with insufficient fecal tagging showed improved polyp detection compared with conventional imaging (120-kVp) [26].

Image acquisition: Proper bowel preparation is essential for the acquisition of quality images and their accurate interpretation. A preliminary scan to check for the extent of bowel distension should be performed first. Both supine and prone positions should be included in the regular scan so that lesions can be distinguished from residues (Fig. 3 and 4). Moreover, scanning of the same area in both positions averts the interpretation of motion artifacts as intraluminal lesions (Fig. 5). If scanning in the prone position is not feasible, at least one lateral scan decubitus is necessary (Fig. 8). During the review by a radiologist, the goal is first to recognize a target lesion and second to characterize it [27]. There are two ways to examine the lumen. The two-dimension (2D) review is based on familiar, transverse CT images, whereas the three-dimension (3D) review comprises navigation through the lumen. 2D images allow the assessment of colon wall thickness and extracolonic structures. However, small polyps may appear momentarily and be neglected. Additionally, lesions on the haustral folds can be misinterpreted as fold extensions. The 3D endoscopic-like review is more time-consuming and may create blind areas. This is overcome by both anterograde and retrograde fly-throughs, as well as by software tools. Various 3D reading methods are utilized according to the reader's experience, such

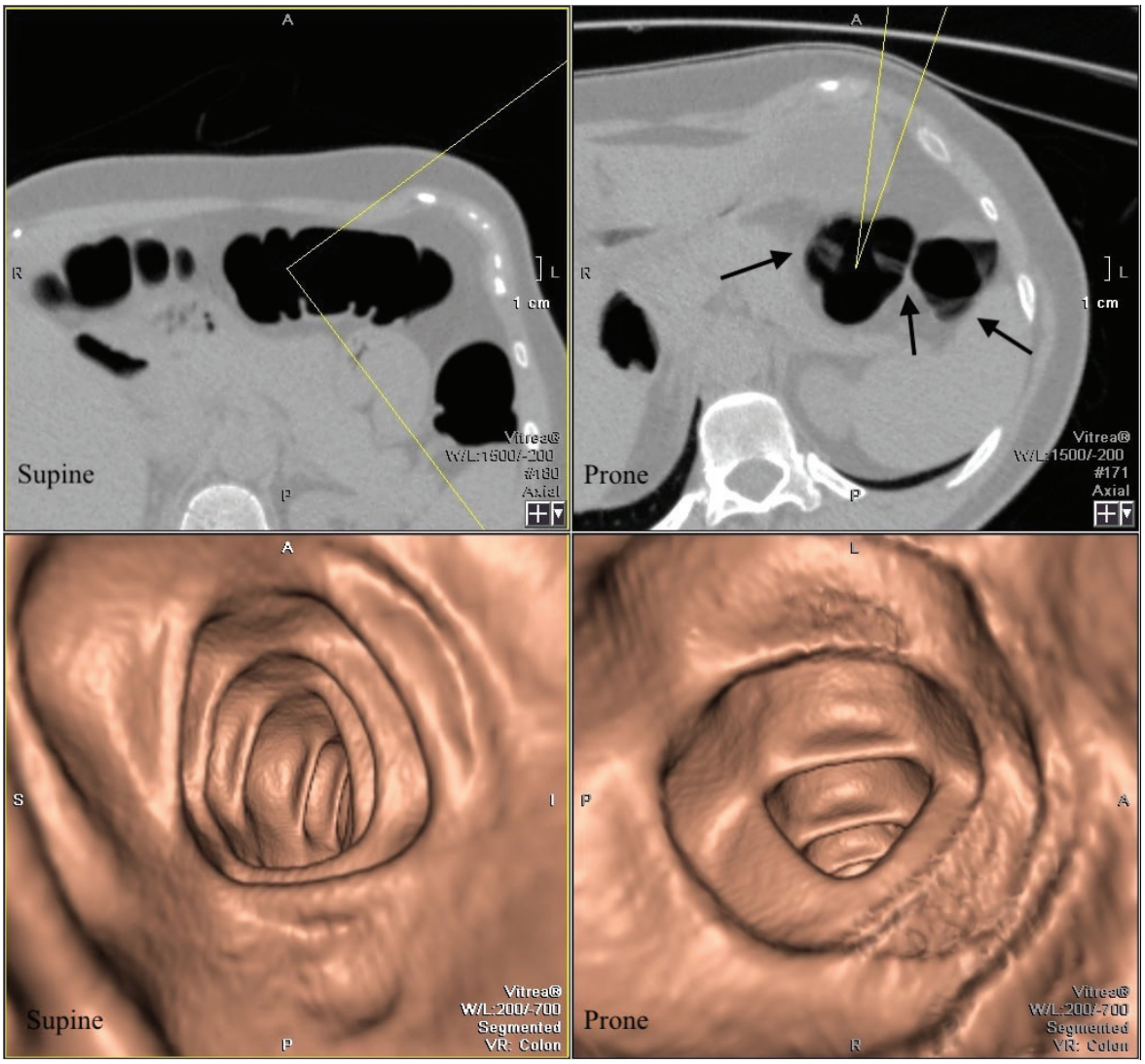

Fig. 5. *Motion artifacts in the prone position (arrows) are not repeated in the supine position (left upper and lower) excluding their misinterpretation as colon lesions.*

as panoramic view, filet view (Fig. 6), virtual dissection, and unfolded cube projection [28]. Both 3D and 2D reviews must be integrated to confirm or discard findings. The primary reading method (2D or 3D) is determined by the reader's personal preference.

Computer-aided detection (CAD) algorithms increase sensitivity for polyp detection and improve radiologists' diagnostic performance, but often result in false positives. In a study involving both experienced and inexperienced readers, a significant net benefit of 11.2% with CAD was achieved by the latter and only 3.2% by the former [29]. The authors conclude that CAD cannot compensate for the lack of training and experience.

Machine learning and deep learning methods were used to differentiate between benign and premalignant colorectal polyps with CTC [30, 31]. A random forest classification algorithm that predicted the polyp character was created based on histopathologic reference standards. Differentiation of polyps was achieved with an AUC of 0.91, 85% specificity, and 82% sensitivity. Particularly notably, the size of the polyp was ranked only fourth in decision-making, whereas distribution and texture of gray levels were the critical features [30]. Deep learning compared to machine learning does not require polyp segmentation, but

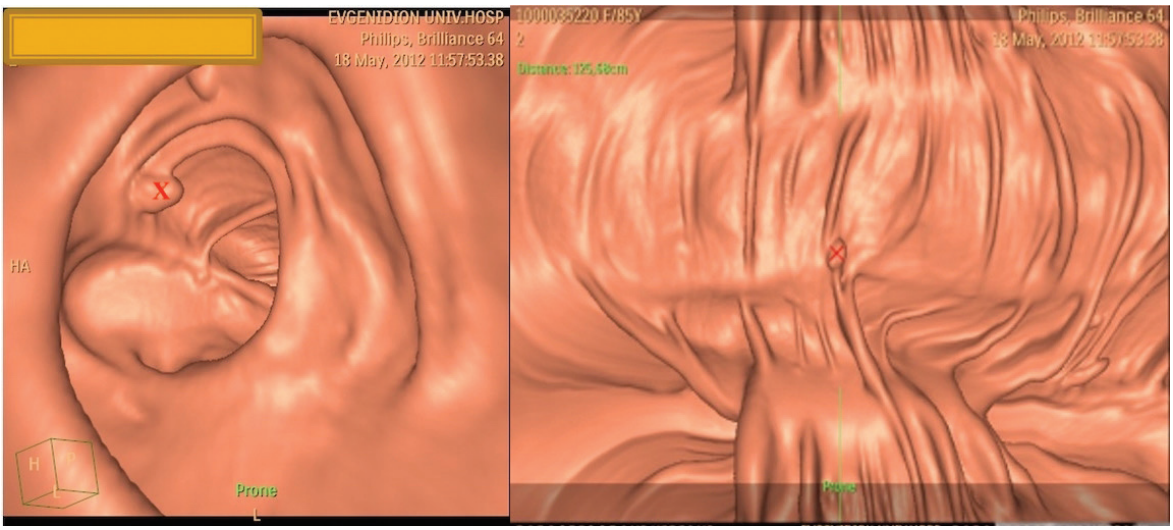

Fig. 6. *A small colon polyp (noted X) as depicted by virtual colon imaging (left) and by filet view (right). The filet view allows simultaneous analysis of supine and prone acquisitions. The colon is virtually bisected and spread flat along the longitudinal axis. (Software; Brilliance CT 64 2.6.2. Workstation; Extended Brilliance Workspace)*

merely its localization, offering the advantage of potentially identifying high-risk polyps as an automated second reader [31].

Data reporting: Reporting is pivotal in achieving the appropriate patient management by the referring physician. The ideal report should be clear, accurate, and brief but not deficient [28]. According to ESGAR, the radiologist's report should provide all the clinical information and basic technical data such as low or normal dose protocol, use of intravenous contrast, use of spasmolytics, and insufflation procedure [32]. Whether the examination is performed for screening or other clinical reasons must be highlighted. The description of polyps or other lesions should include shape, texture, location, density, maximum diameter, and measurements in 2D and 3D images (Fig. 7a and b). All polyps regardless of size should be reported in both asymptomatic and symptomatic patients. Findings from extracolonic organs such as infiltration of pericolic fat, metastases, and enlarged lymph nodes should be also featured.

The ACR colonography reporting and data system (C-RADS) is a standardized reporting and management algorithm [33]. Classification of lesions ranges from C0 to C4 and depends on size and number (Table 1). C1 lesions include normal or benign lesions, such as colonic diverticula, and guidance on routine screening should be provided (Fig. 8). C4 lesions compromise the bowel lumen and require surgical consultation (Fig. 9, 10, 11). Recommendations for surveillance periods according to CTC findings are also provided.

Broadening the use of Computed Tomography Colonography

The capability of CTC to provide information about extra-colonic structures besides its endoscopic modality has already been exploited in various clinical settings. In a retrospective study, a biomechanical CT analysis at the hip and spine for 136 women who underwent both CTC and DXA was performed [34]. BMD and osteoporosis calcifications were in excellent agreement between DXA and the biomechanical CT analysis. The same examination protocol could hence conduct a simultaneous, thorough analysis of the colon for lesions and the hips and spine for osteoporosis and fracture risk. The role of CTC in the pre-operative workup for non-metastatic colon cancer has also been evaluated [35]. Imaging of the mesenteric and colonic vessels can reveal any possible anatomical variations that could modify the surgical plan. Moreover, the inclusion of neo-adjuvant chemotherapy can be decided by the degree of parietal tumor extension. Most recently, the role of CTC in the early detection of peri-

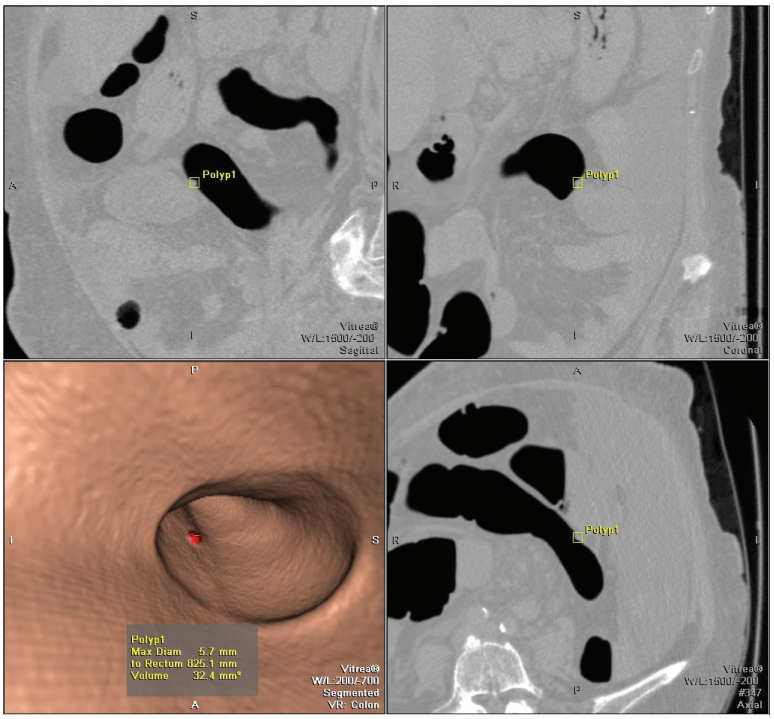

Fig. 7a. *Detection of a small, sessile polyp in the left colon (square in sagittal, coronal, and axial images, noted red in the virtual colon image). Maximal diameter (5.7mm), volume (32.4 mm3), and distance from the rectum (825.1mm) are automatically measured.*

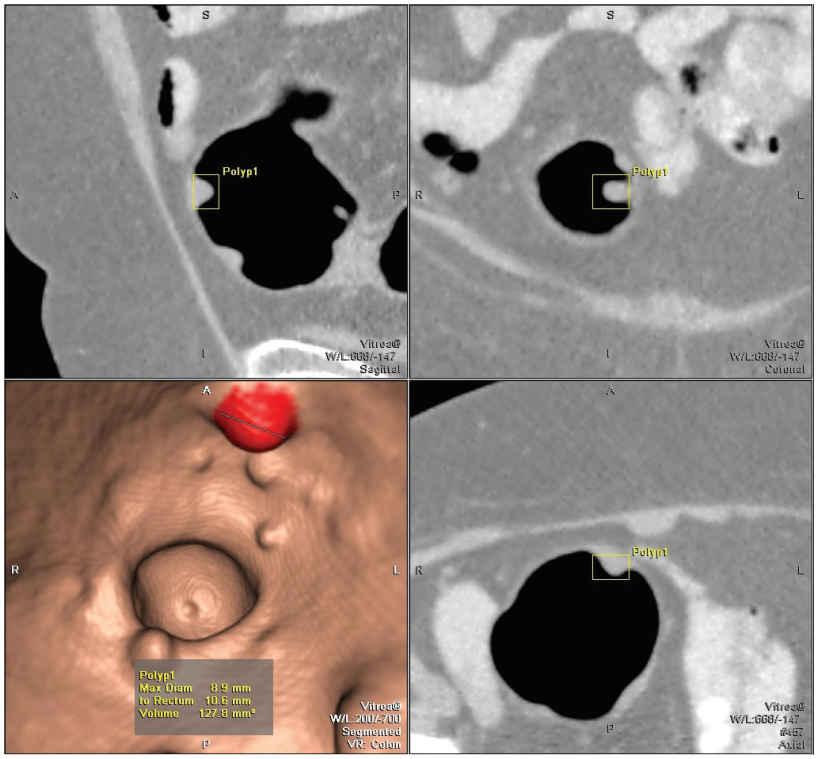

Fig. 7b. *CT colonography after incomplete optical colonoscopy. Detection of multiple polyps in the distal sigmoid colon. The largest polyp (square in sagittal, coronal, and axial images, noted red in the virtual colon image) is located on the anterior wall of the colon. Maximal diameter (8.9mm), volume (127.8 mm3), and distance from the rectum (10.6mm) are provided.*

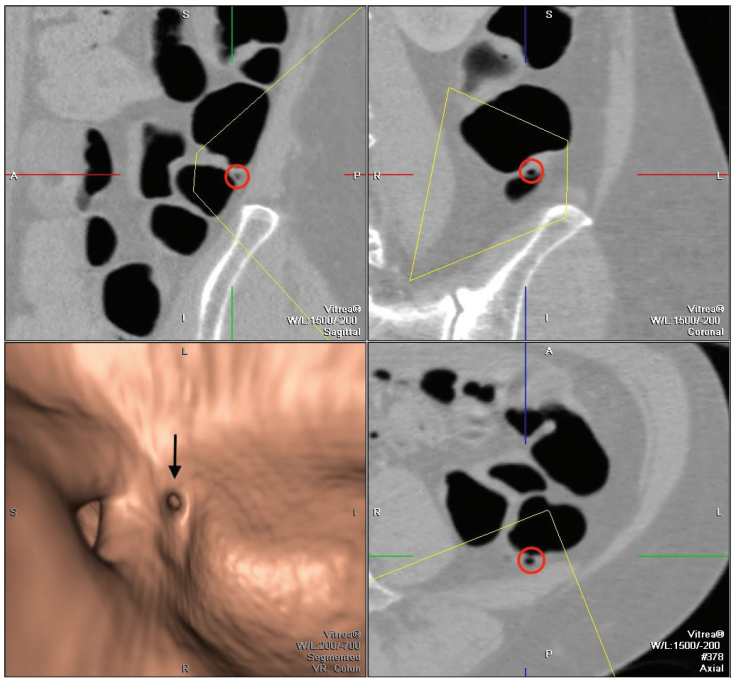

Fig. 8. *A small colonic diverticulum is found in the descending colon (circles and arrow). The lesion is classified as C1 according to the C-RADS categorization system.*

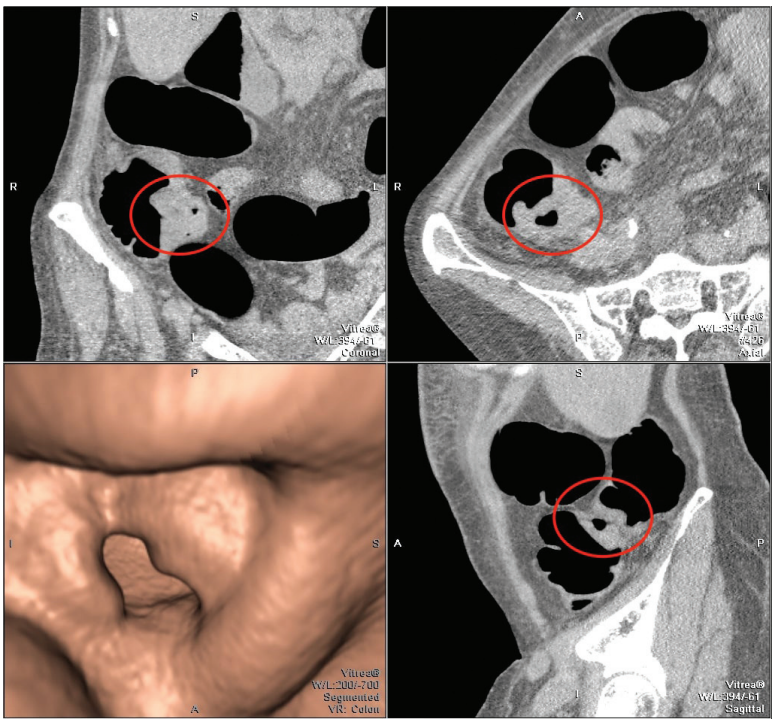

Fig. 9. *Irregular, intraluminal mass at the ileocecal junction (circle in coronal, axial, and sagittal images). The patient was unable to retain the supine position and was scanned in right and left decubitus positions. Ascites, multiple focal hypodense liver lesions, and fat stranding around the ileocecal junction were also found in the CT scan. Colon biopsy confirmed the diagnosis of colon cancer.*

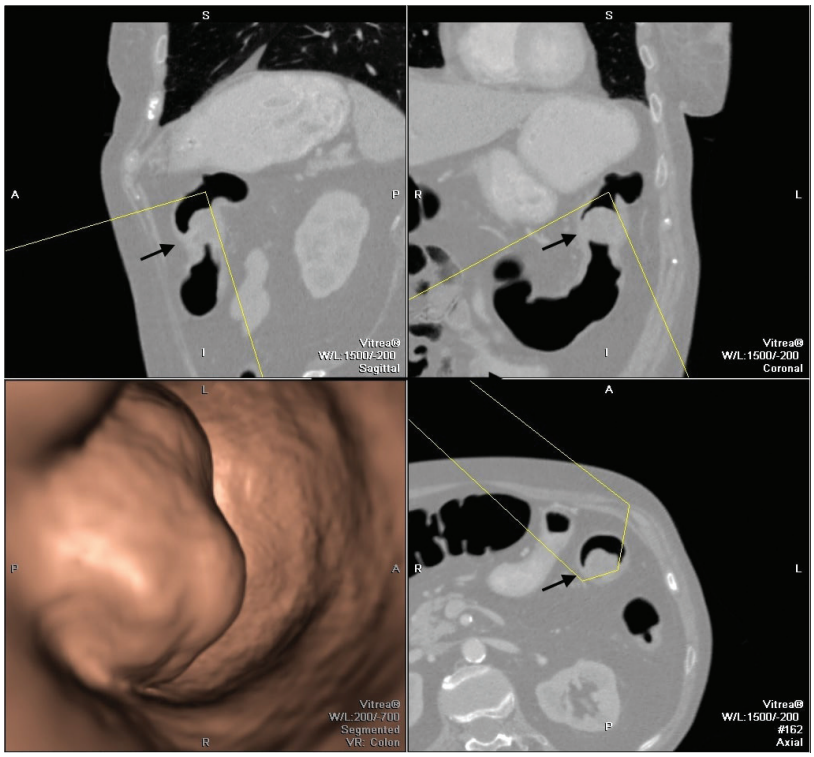

Fig. 10. *A solid, intraluminal mass of maximal diameter 2.5cm is detected in the distal sigmoid colon compromising its lumen (arrow in sagittal, coronal, and axial images). The lesion is classified as C4 according to the C-RADS categorization system and the referring physician was instantly communicated. Angle view is also provided (yellow lines).*

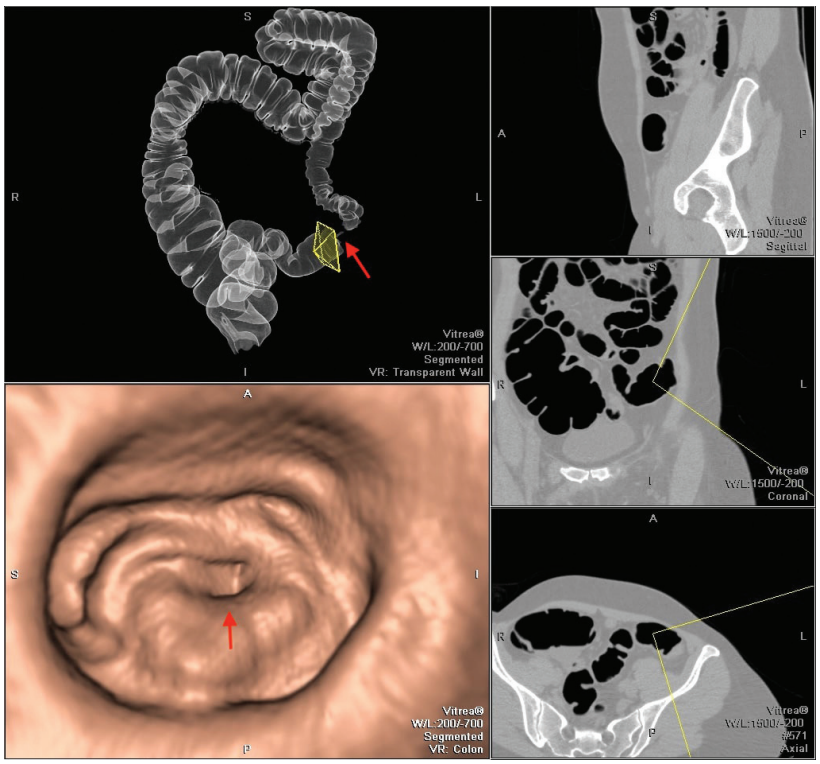

Fig. 11. *Patient, 46 years old, was referred to our department after an incomplete optical colonoscopy due to extensive narrowing of the proximal sigmoid lumen (arrows). Patient complained of "blood in stool" for two months. A C4 lesion with a maximal longitudinal diameter of 4.8cm was identified. An 8mm polyp was also found in the cecum.*

toneal metastasis of gastric cancer was also assessed [36]. Compared with CT and FDG-PET, CTC detected early, small peritoneal metastases with 83% sensitivity and 100% specificity.

Discussion

The development of CT colonography addresses the growing demands of modern medicine to apply less- or non-invasive techniques to answer clinical questions. Many of them arise from an increasingly ageing population with many co-morbidities that restrict the physician's examination panel. CTC compared with optical colonoscopy is faster, cheaper, safer, and better tolerated by patients. It can overcome the obstacle of lumen blockage in areas where the colonoscope cannot pass through. CTC offers extracolonic imaging of tumor spread, vasculature, anatomical variations, and metastases [37]. Both techniques have similar sensitivity and specificity in colorectal polyp detection. Optical colonoscopy has the advantage of being both diagnostic and curative allowing sampling and removal of lesions. Additionally, it is better at detecting flat adenomas and does not include radiation in its protocol.

The role of CTC rather as a screening tool and OC as the modality to refer to for sampling and removal of polyps can therefore easily be concluded. CTC can raise colon cancer screening rates since it is better accepted by patients. However, the overdetection of non-malignant lesions and unnecessary referrals for OC could become a future problem of the widespread use of CTC in screening for colorectal cancer. Focus on radiologists' training to reduce variation in quality of practice and misinterpretation of CTC findings, along with efficient communication between them and gastroenterologists could diminish over-referring [38]. In addition, machine learning-assisted CTC and deep learning analysis of its findings can increase CTC efficiency and specificity by differentiating between benign and premalignant colorectal polyps [30, 31]. **R**

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