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REVIEW

CT Colonography for Population Screening: Ready for Prime Time?

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Introduction

Since its introduction 20 years ago, CT colonography (CTC), also referred to as virtual colonoscopy, has evolved from an experimental research tool with relatively limited clinical applications to a validated colorectal examination [1–3]. For certain diagnostic indications, such as following an incomplete optical colonoscopy (OC), CTC is now well established throughout most of the developed world [4–8]. CTC for the purpose of asymptomatic screening, however, is currently performed in only a handful of experienced centers. The need for additional effective screening options for colorectal cancer (CRC) is clear since this preventable condition remains the second leading cause of cancer death in the USA [9]. Although CTC is now poised for broader implementation as a frontline screening tool, a number of hurdles persist—none of which is likely insurmountable or even related to its clinical performance profile [10, 11]. This update will review the relative advantages and disadvantages of CTC for population screening compared with optical colonoscopy and emerging colorectal screening tests. Remaining barriers to widespread implementation of CTC as primary screening tool will be discussed. In general, the main focus herein will be on US-based population screening.

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Potential Advantages and Disadvantages Related to Primary Screening with CTC

There are a number of key criteria to consider when comparing colorectal screening tests, including diagnostic performance, procedural risks, patient acceptability, and cost-effectiveness [12, 13]. To be accepted, a new screening test need not outperform existing strategies in all or even any of these categories, so long as the overall profile leads to effective screening that increases adherence. Rather than evaluating an emerging screening test such as CTC in a vacuum, it is useful to consider its relative advantages and disadvantages against OC and other screening options. In the end, a menu of effective and complementary screening options should result in an overall increase in adherence rates. More importantly, the increased use of preventive tests such as OC and CTC will likely have the greatest impact on CRC incidence and death rates [14].

Relative Advantages of CTC for Screening

Primary screening with CTC, reserving OC for therapy (polypectomy), provides a number of potential advantages over primary OC screening (Table 1). Some of these aspects listed in Table 1 are briefly described in more detail below.

Efficacy

The optimal target for both prevention and detection of CRC is advanced neoplasia [15–18]. Perhaps above all, an effective CRC screening test should demonstrate high sensitivity for the critical target lesions, which primarily include large adenomas and early cancers. Detection of

Table 1 Positive aspects of screening with CTC

Equivalent to OC for detection of advanced neoplasia
Less invasive than OC
No need for IV sedation, pain medication, or recovery time
Preferred by most screening individuals over OC
Increases overall screening adherence (complementary with OC)
Provides for extracolonic evaluation and screening
More cost-effective than OC screening
Intentionally ignores isolated diminutive lesions

sub-centimeter polyps and advanced cancers provides much less benefit, as the former will rarely develop into cancer and the latter is often beyond a curable stage [19, 20]. Early CTC experience with polyp-rich cohorts demonstrated proof of concept in terms of lesion detection [21, 22]. Subsequent trials evaluating low-prevalence cohorts brought the diagnostic performance of CTC into question [23–25]. However, with advances such as the introduction of robust 3D endoluminal evaluation and oral contrast tagging [26, 27], CTC was shown to rival OC in terms of detection of advanced neoplasia (Figs. 1, 2) [3]. Not only were CTC and OC found to be comparable in terms of sensitivity, but their complementary nature likely results in fewer relevant missed lesions [28]. Subsequent CTC–OC trials have provided further validation and generalizability for lesion detection [1, 29–31]. A meta-analysis and systematic review showed an overall 96 % sensitivity for CRC, which is even higher when oral contrast tagging is applied (Fig. 2) [32]. This high sensitivity for cancer detection is comparable to performance with OC screening [2]. Due to the lack of physical constraints at CTC, there may be a specific advantage over OC in terms of right-sided cancer detection, which is a known drawback of the more invasive screening test [32–34]. In routine clinical practice, polyp prevalence rates and PPV (i.e., CTC–OC concordance) can provide useful surrogate measures, as sensitivity and specificity cannot be obtained. PPV or CTC–OC concordance rates of >90 % have been reported for all CTC-detected lesions 6 mm and larger [35–38]. Overall yield for advanced neoplasia at CTC screening has been shown to be equivalent to primary OC screening, despite the fact that < 10 % of individuals undergo invasive polypectomy [2].

Safety

CTC is a much less invasive test than OC, with little or no risk of immediate or delayed complications. We have yet to encounter a significant complication related to CTC screening at our center, which dates back to 2004. The risk of colonic perforation, perhaps the most feared complication at OC, approaches zero for CTC screening when low-pressure automated CO_2 delivery is applied [39]. Other complications related to primary OC, such as bleeding, cardiovascular events, and even death, are also avoided [40–46].

Convenience

The lack of IV sedation and pain medication make CTC a needle-free endeavor that is not only safer, but also avoids the need for recovery time. Individuals undergoing CTC screening can also drive themselves home (or elsewhere) immediately after the examination, avoiding the need for a second driver. In fact, given the short duration of the CTC examination and absence of recovery time, there is no need to miss a day of work, unless therapeutic OC for polypectomy is needed (<10 % of cases). For cases where only left-sided polyps are detected at CTC screening, polypectomy could be more safely performed with sigmoidoscopy over full colonoscopy—with cost savings as well [47].

Acceptability

All of the aforementioned reasons of test performance, safety, and convenience likely contribute to the fact that CTC has been preferred by "patients" (i.e., asymptomatic adults over 50) over OC in virtually all head-to-head comparison between the two screening tests [48, 49]. Among individuals who had experienced both CTC and colonoscopy, Moawad et al. [48] found that 95 % preferred CTC. A larger multicenter study by Pooler et al. [49] surveying 1,400 adults who underwent CTC screening found a very high satisfaction rate, with over 90 % scoring their experience as "excellent" or "good." Over 90 % also indicated that they would choose CTC again for their next screening. Among individuals who had experienced both CTC and colonoscopy, CTC was favored by a nearly 6:1 ratio. This clear preference is even more impressive when considering the fact that most individuals are heavily sedated for colonoscopy and may not recall the procedure itself. Beyond the lack of needles, medications, and invasiveness, some folks value the ability to maintain control with CTC, even if that means feeling the transient cramping associated with colonic distention. The common use of CO_2 for distention over room air at CTC likely contributes to an improved experience, as its rapid resorption greatly minimizes post-procedural discomfort compared with room air [50]. In general, the low-volume bowel preparations commonly employed for CTC are much better tolerated than the large-volume PEG lavage still commonly in use by our gastroenterologists for OC [51, 52]. Furthermore, by working closely with our GI endoscopists, we can offer same-day polypectomy for

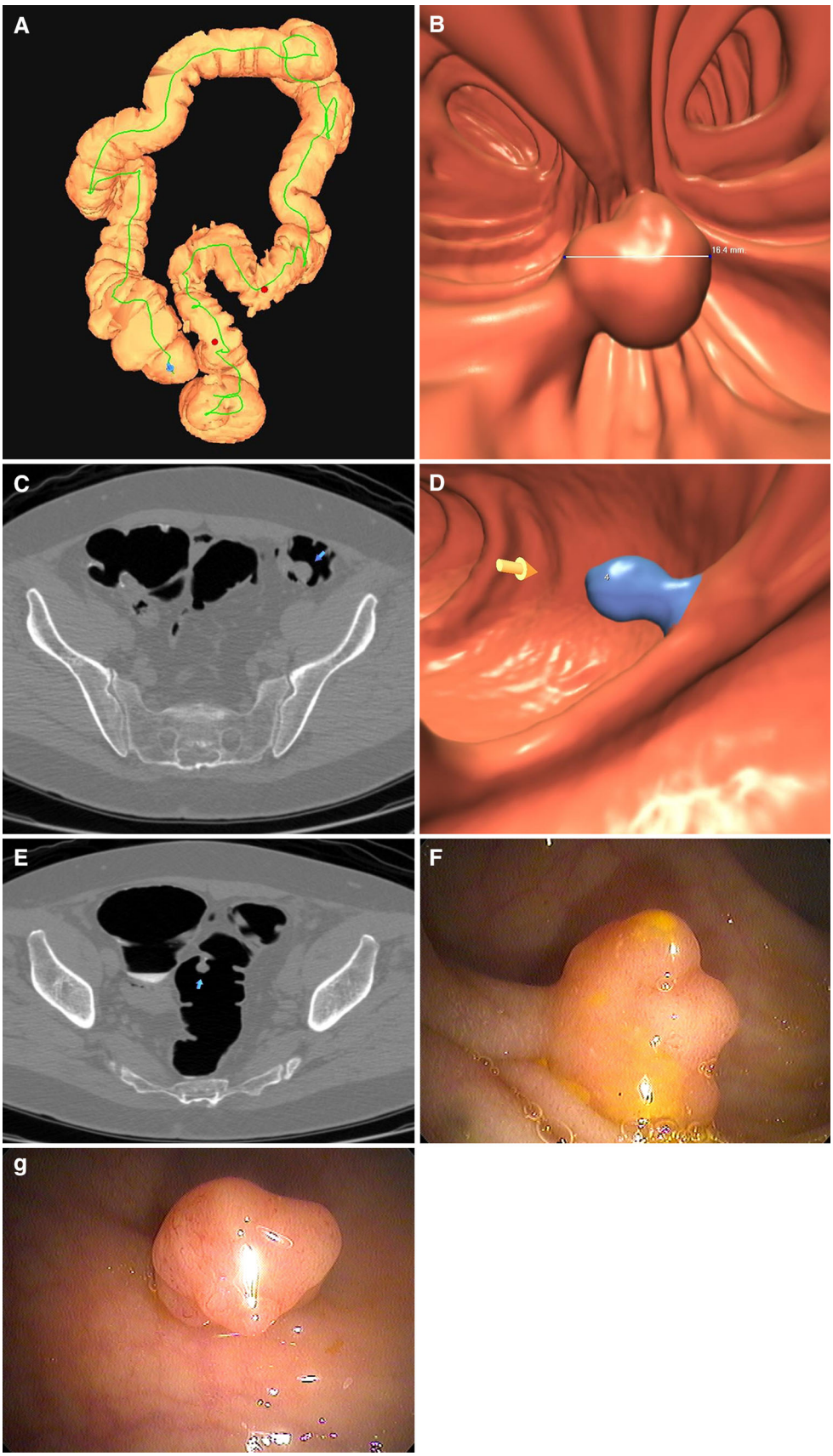

Fig. 1 Detection of advanced neoplasia at CTC screening with same-day polypectomy in asymptomatic 67-year-old man. 3D colon map from CTC (**a**) shows two *red dots* that pinpoint the location of two sigmoid polyps. Note associated diverticular disease. 3D endoluminal (**b**) and confirmatory 2D transverse (**c**) CTC images show a large 1.6-cm pedunculated polyp (*arrow*), corresponding to the more proximal lesion. Additional 3D (**d**) and 2D (**e**) CTC images show a 9-mm pedunculated polyp in the distal sigmoid. The blue color on the polyp is the result of computer-aided detection (CAD). Both lesions were removed at same-day colonoscopy, avoiding the need for a second bowel prep. The larger polyp proved to be a tubulovillous adenoma (advanced lesion), whereas the smaller polyp was a tubular adenoma

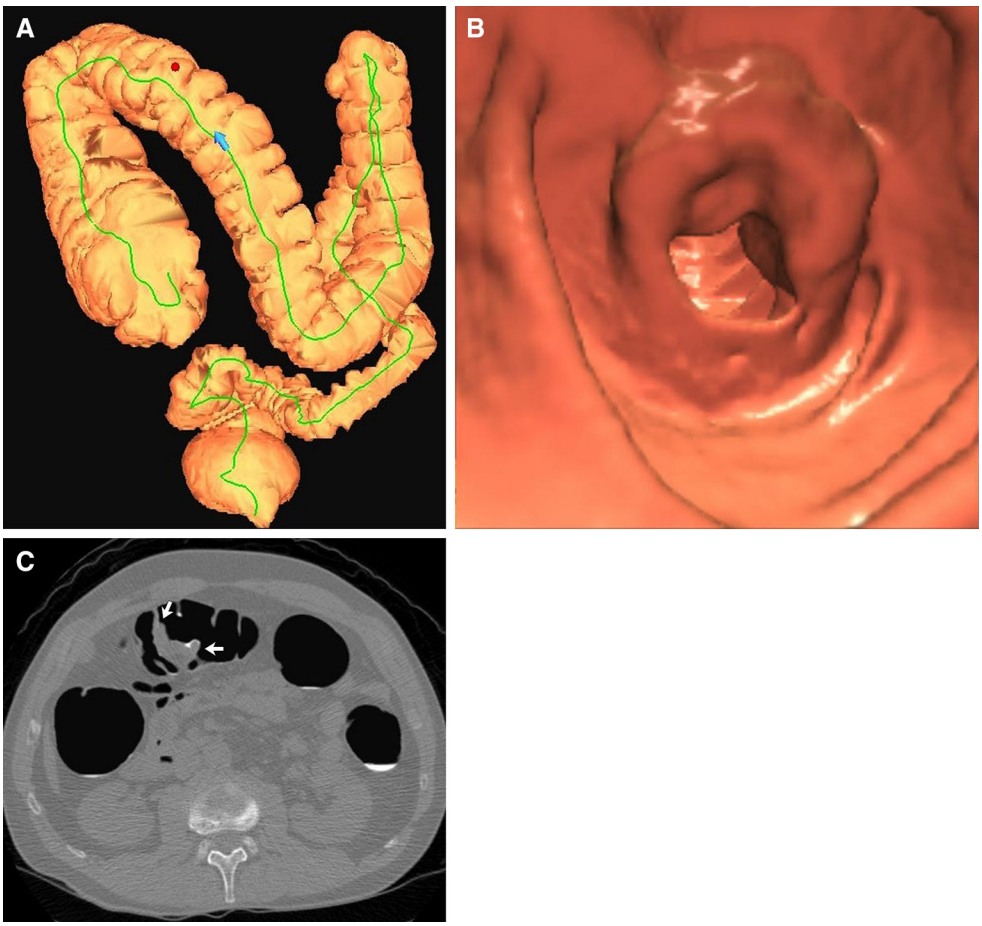

Fig. 2 Asymptomatic colon cancer found at routine CTC screening. Colon map (**a**) shows the location of the mass seen at 3D (**b**) and 2D (**c**) CTC evaluation (*arrows*). The semi-annular morphology is compatible with an asymptomatic cancer, which was proven by biopsy at same-day colonoscopy (not shown)

relevant CTC-detected lesions, ensuring that only a single low-volume bowel preparation is required [51–53]. This "one-stop shop" approach of same-day polypectomy following positive CTC is very patient friendly but requires collaboration between radiology and gastroenterology. However, we have demonstrated over the past decade that this model is readily achievable [2, 49, 52–54].

Adherence

For a new or additional CRC screening test to have a truly positive impact on CRC mortality, it must not only be safe and clinically effective, but also increase overall adherence to screening. All positive attributes of any given screening test are lost if individuals are unwilling to submit to it. There is now evidence that the general preference for CTC described above could translate into increased adherence by pulling OC-reluctant individuals off of the screening "sidelines." Moawad et al. [48] found that over one-third of individuals undergoing CTC screening said they would have foregone colorectal cancer screening if CTC had not been an available option. Similarly, Pooler et al. [49] reported that at least 30 % of CTC screeners likely would not have undergone screening if CTC were not an option. Cash et al. [55] showed that CTC screening at US military treatment facilities could significantly improve HEDIS measures, with an overall increase in CRC screening rates by over 15 % by adding CTC to the screening options. Over the past decade, CTC has accounted for approximately 10 % of overall CRC screening at our center [56, 57]. Finally, a well-designed randomized controlled trial by Stoop et al. [58, 59] showed that offering CTC for screening increased participation 55 % over invitation for OC screening. Such an increase in screening adherence could have enormous implications in terms of reducing CRC mortality.

Extracolonic Screening

Unlike OC, which is a luminal test that only visualizes the colonic mucosa, CTC is a cross-sectional imaging study that can evaluate the entire abdomen and pelvis. As such, CTC can provide for screening opportunities beyond the large

intestine, even though the study is performed with low-dose, unenhanced technique [60, 61]. When handled appropriately, this additional extracolonic data can greatly enhance the value of CTC screening. In fact, when grouped together, more unsuspected extracolonic cancers are detected at CTC screening than at CRC (Fig. 3) [62]. Simultaneous screening for abdominal aortic aneurysms (AAA) precludes the need for an additional ultrasound examination, increasing both efficiency and cost-effectiveness [63], especially in older individuals [64]. Opportunistic osteoporosis screening is another benefit of CTC screening that is gaining momentum [65, 66]. Regardless of indication, abdominal CT can provide robust evaluation of bone mineral density at no cost or additional radiation [67, 68]. Other screening opportunities include assessment for hepatic steatosis, visceral fat, metabolic syndrome, and urolithiasis [69–72]. The CT colonography reporting and data system (C-RADS) allows for systematic categorization and follow-up of relevant extracolonic findings [73, 74]. In brief, E1 is normal/no extracolonic findings, E2 implies an insignificant finding, E3 implies an indeterminate finding that is likely unimportant but may require an additional test, and E4 implies a clinically significant finding [73, 74]. Another benefit of the global abdominal assessment at CTC is that the lack of ominous findings seen in the vast majority of screening individuals can be very reassuring to a healthy adult. Potential drawbacks related to extracolonic evaluation at CTC are discussed later on.

Cost-Effectiveness

Cost-effectiveness analysis (CEA) studies are important to consider when discussing potential CRC screening options. These CEA studies, however, involve simulation models that are often complex and require careful review of the specific model inputs to ensure valid results. From a practical standpoint, it stands to reason that primary CTC with selective polypectomy should be more cost-effective than primary colonoscopy, as long as certain basic assumptions are met. One key assumption that was missing from the early CEA papers is that polypectomy should be avoided for isolated diminutive lesions seen at CTC [75–79]. The diagnostic performance of CTC should also reflect current practice, and the input cost for CTC should be considerably less costly than colonoscopy, especially given the increasing use of advanced sedation methods at OC. Ideally, extracolonic assessment should be factored in as well [63]. In general, it is quite easy to demonstrate that CTC is cost-effective compared with no screening [80], but with realistic input assumptions, it can also be shown to be more cost-effective than the more invasive endoscopic strategies [63, 64, 76]. Most CEA studies comparing CTC and OC assume equal adherence rates. However, given the aforementioned evidence that CTC could substantially increase participation in screening, nearly all CEA models would likely favor CTC if this input were adjusted [12]. Beyond the typical Markov modeling, other decision analyses have been applied to certain key aspects of CTC screening, such as the management of small (6–9 mm) polyps [81, 82].

Potential Drawbacks with CTC Screening

There are a number of perceived disadvantages to CTC screening that merit discussion (Table 2). Upon closer inspection, many of these potential drawbacks prove to be more areas of misunderstanding, or related to outdated information.

Radiation Exposure

The issue of exposure to ionizing radiation related to CT imaging has captured mainstream attention in the lay press,

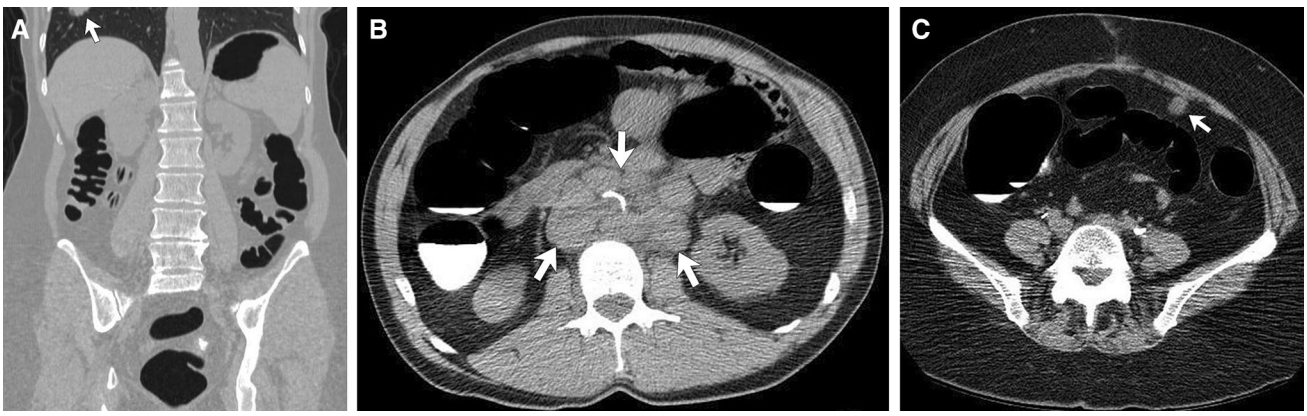

Fig. 3 Unsuspected extracolonic cancers identified at CTC screening in three different individuals. **a** Bronchogenic adenocarcinoma at the right lung base (*arrow*). **b** Non-Hodgkin's lymphoma manifesting with bulky retroperitoneal lymphadenopathy (*arrows*). **c** Peritoneal implant (*arrow*) representing unsuspected metastatic disease from a stage 1 endometrial cancer diagnosed previously

Table 2 Potential drawbacks with CTC screening

Radiation exposure
Extracolonic findings
Non-therapeutic test
Flat colorectal lesions
Diverticular disease
Handling of small and diminutive polyps
Generalizability to community-level practice
Variable availability of same-day polypectomy

as well as the medical literature [83]. Unfortunately, misinformation has largely fueled irrational fear in terms of actual risk assessment. In general, the very small theoretical risk related to low-dose radiation exposure was derived from very conservative (and likely incorrect) assumptions—namely, the "linear no threshold" model. What is often lost in discussions surrounding low-dose exposures is that below 50–100 mSv, the actual risk of a measurable health effect is either too small to be observed or nonexistent, according to expert health physicists [84]. Substantial longitudinal experience exists for adult cohorts exposed to low-level radiation, including radiation workers, airline pilots, TB patients, atomic bomb survivors, and high background radon levels. Despite this, there is no definitive evidence of deleterious effects at low levels (on the contrary, there is evidence to support a "hormesis" effect, which suggests a protective effect related to lower radiation doses). For CTC screening, the issue of radiation exposure holds even less relevance. CTC is already a relatively low-dose CT examination, on the order of 5 mSv or less [85, 86]. With the emergence of new iterative CT reconstruction algorithms such as MBIR, effective doses for CTC will likely be in the sub-mSv range [87, 88]. Because CTC is applied to older adults, the theoretical risk of future harm is much less relevant. Furthermore, the thorax is largely excluded, which carries a greater theoretical risk. In the end, the remote theoretical risk related to radiation is dwarfed by the large measurable benefit related to colorectal and extracolonic screening with CTC.

Incidental Findings

The benefits of extracolonic evaluation at CTC have been discussed, but it is also important to consider its potential negative impact. As with any CT scan, there is a chance that an unsuspected finding is uncovered, generally termed an "incidentaloma" [89]. Insignificant extracolonic findings (i.e., category E2 in C-RADS), such as hepatic steatosis, non-obstructing renal calculi benign-appearing renal cysts, are commonly identified and should not lead to further work-up [69, 70, 90]. However, inappropriate recommendations on the part of an "overcalling" radiologist or "defensive medicine" on the part of the ordering provider could generate unnecessary additional studies [60]. Some extracolonic findings are truly indeterminate (i.e., C-RADS E3 category) and, although likely of no real clinical significance, may require further imaging evaluation due to the non-diagnostic low-dose, non-contrast CTC technique. The majority of these E3 category findings will ultimately prove to be benign or insignificant, whereas most E4 findings (2 % prevalence at CTC screening) will prove to be relevant [73]. When handled responsibly, extracolonic evaluation at CTC screening should result in a net benefit, especially if one takes advantage of opportunistic screening as previously described.

Non-therapeutic

As with almost all screening tests used in medicine, CTC is non-therapeutic. OC is a rare exception to this rule, and one could question whether its degree of invasiveness and high associated costs warrant its use for primary screening. Since <5 % of a typical screening population will harbor advanced neoplasia [17, 91], it would seem more logical to reserve colonoscopy for therapy in those cases, especially since CTC is equally effective for the detection of these target lesions. However, for the stool-based screening tests, the inability to detect most advanced adenomas means that the key preventive component of CRC screening is largely lost [92]. Another issue that frequently surfaces is the availability of same-day polypectomy following detection at CTC screening to avoid a second bowel preparation. This practice pattern requires an ongoing collaboration between Radiology and GI groups, but many such relationships already exist through same-day CTC following incomplete colonoscopy. Furthermore, the actual strain on the endoscopy schedule is mitigated by the fact that fewer than 10 % of cases will require same-day polypectomy.

Detection of Flat Polyps

Flat (non-polypoid) colorectal lesions are a subset of sessile polyps that have generated considerable attention in recent years. Although some have previously used a definition of polyp height less than half its width [93], this morphologic criterion is far too inclusive. For flat lesions measuring up to 1–2 cm in width, an elevation of 3 mm or less above the surrounding normal mucosa is a better definition [94]. For larger "carpet lesions," or superficially spreading tumors that generally measure greater than 3 cm across, maximal height will usually exceed 3 mm [95]. The prevalence and clinical significance of flat colorectal lesions have been a source of ongoing debate [96–98]. The vast majority flat polyps fall into the category of

superficially elevated lesions, with a very small minority being centrally depressed or truly flat [93, 98]. In general, flat lesions are much less conspicuous than polypoid lesions of a similar size at both OC and CTC; fortunately, they are also less histologically aggressive as well [94, 97]. Nonetheless, CTC can detect flat lesions with reasonably high sensitivity (80–90 %) when standard techniques of oral contrast tagging and combined 2D/3D interpretation are applied [94, 95, 99–101]. In particular, the tendency for oral contrast to cling to the mucosal surface of flat lesions greatly exaggerates their conspicuity at CTC, allowing for detection [102, 103]. CTC accuracy for carpet lesions appears to be quite high [95]. Increased awareness of right-sided flat serrated lesions leads to higher detection rates at both OC and CTC (Fig. 4) [102, 104, 105]. Although CTC sensitivity for flat lesions is good, these lesions are more likely to result in discordance, where a CTC-detected flat lesion is not confirmed at subsequent OC [36, 106]. In our experience, these discordant cases represent a fairly even mix of CTC false positives and OC false negatives (unpublished data).

Diverticular Disease

Sigmoid diverticular disease presents a singular challenge to CTC interpretation, largely related to the luminal narrowing that results [107]. Although CTC has certain advantages in evaluating the right colon compared with colonoscopy, the physical scope may have its own advantages in the left colon. This complementary nature suggests that an alternating screening regimen of CTC and flexible sigmoidoscopy might be worth considering. Polyp detection within a diverticular segment at CTC, however, does not appear to suffer when primary 3D evaluation is included [108]. In addition, the use of continuous, low-pressure automated CO_2 further improves sigmoid assessment [50]. Although confident distinction between sigmoid carcinoma and chronic diverticular disease may prove challenging on occasion at CTC, a number of key imaging findings have been described to aid in their differentiation [107, 109]. Finally, grading the severity of diverticular disease at CTC may have some prognostic utility [110]. For presurgical planning, CTC can provide an exquisite roadmap for the surgeon.

Diminutive and Small Polyps

Important differences exist in the detection rate and handling of diminutive (≤5 mm) and small (6–9 mm) polyps at OC screening compared with the noninvasive approaches [100, 111]. Although all colorectal cancers presumably arise from smaller benign polyps, this does not imply that polypectomy is indicated for every benign sub-centimeter lesion. Because OC screening doubles as a therapeutic test, the mindset of universal polypectomy has become entrenched. However, such an aggressive management approach to small benign colorectal lesions makes no sense when applying safer non-therapeutic tests such as CTC, which provide a filter between polyp detection and invasive therapy. More recent screening data on the low prevalence rates of important histology in small and diminutive lesions further support a non-aggressive approach [112–114]. Although CTC can detect many diminutive lesions, matching with OC can be problematic and is not warranted given the limited clinical yield of polypectomy and the associated costs and complications. Therefore, isolated diminutive lesions (i.e., when no synchronous non-diminutive polyps are detected) at CTC screening are intentionally ignored, as patient management is not changed by their presence [52]. This practice has proven to be of benefit in terms of both clinical outcomes and cost-effectiveness, as there has been no evidence of interval cancer development at routine 5-year CTC screening and fewer endoscopic resources are utilized [81, 82, 100, 111, 115].

Small (6–9 mm) colorectal polyps are intermediate in both size and clinical relevance, making their management

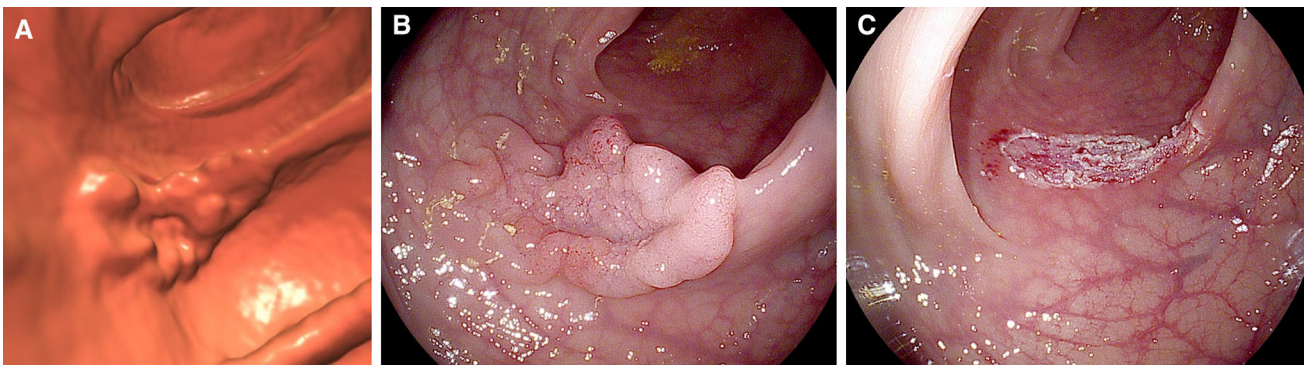

Fig. 4 Large flat serrated polyp identified at screening CTC. 3D endoluminal CTC image (**a**) shows a relatively flat, large lobulated lesion that was confirmed (**b**) and removed (**c**) at subsequent same-day colonoscopy. The lesion proved to be a serrated adenoma

at CTC screening more controversial. The vast majority of small polyps are benign [112, 114], but have nonetheless progressed beyond the diminutive stage. CTC can detect the majority of these lesions and in clinical practice is associated with a PPV of approximately 90 % (Fig. 1) [3, 36]. Although most small polyps will never develop into advanced adenomas and cancers, current clinical management generally consists of polypectomy to reduce this risk. We have found that in vivo CTC surveillance of small polyps provides a useful biomarker for selectively identifying the lesions of clinical significance through interval growth [116]. In our experience, about 20 % of small polyps demonstrate growth at surveillance CTC, whereas 50 % remain stable and 30 % regress [116].

Generalizability

One legitimate concern regarding the potential widespread use of CTC is whether the results seen at centers of excellence can be generalized to community-level practice. Of course, similar quality issues apply to optical colonoscopy as well. In fact, reported differences in polyp detection rates between gastroenterologists at screening OC (tenfold or more) vary much more than that of radiologists at screening CTC, where differences are less than twofold [117, 118]. The use of both 3D and 2D views for polyp detection at CTC can help ensure good performance over 2D detection alone [119]. With proper training, including both didactic and hands-on experience, radiologists adept at body CT interpretation can generally master CTC without great difficulty [120]. Some motivated gastroenterologists would also likely be able to adequately interpret CTC, although the training involved would be onerous and impractical [121].

Comparison with Other Emerging Screening Tests

A variety of other emerging CRC screening tests, such as fecal immunochemical tests for detection of blood, stool DNA, serum markers, and capsule endoscopy, are reviewed in other articles in the supplement. [Editors note—See articles by Young et al., Ahlquist, Bresalier and Eliakim and N Adler]. Nonetheless, these deserve brief consideration herein in terms of how they compare with CTC in terms of primary screening. Despite progressive advances, emerging evidence suggests that stool DNA and other stool-based screening strategies remain relatively insensitive for advanced adenomas [122, 123], resulting in a lack of cancer prevention that makes both optical and virtual colonoscopy much more attractive. A high sensitivity for cancer is important, but the relatively low specificity and the lack of substantial cancer prevention dampen enthusiasm for stool DNA as a primary screening test. The serum-based marker tests are considerably less mature than the stool-based tests and are not yet ready for serious consideration [124]. Wireless capsule endoscopy has had a major clinical impact on small bowel evaluation and is now being evaluated for colorectal polyp detection [125]. Beyond achieving adequate polyp detection rates, additional major challenges related to colorectal capsule endoscopy include the need for vigorous bowel preparation, the delayed nature of interpretation (necessitating an additional prep if positive), and the inconsistent transit time through the large intestine. As such, CTC continues to be the most promising of the emerging screening tools but remains grossly underutilized at the time of this writing.

Remaining Barriers to Widespread Implementation of CTC Screening

Considering that CTC appears to meet or exceed all the key criteria for an acceptable CRC screening test, including a number of distinct advantages over OC for primary screening, the absence of widespread implementation in the USA may be a bit surprising at first. However, upon more careful inspection of the current situation, there are a number of key barriers to implementation that persist (Table 3).

The single greatest impediment to CTC screening is the lack of broad coverage from third-party payers, especially from by the Centers for Medicare and Medicaid Services (CMS) for Medicare beneficiaries [126]. President Obama opted for CTC screening for his routine physical examination in 2010, despite the fact that this screening test is not covered for Medicare beneficiaries. Early reimbursement for CTC screening by the locally owned managed care organizations back in 2004 allowed for our CTC screening program to develop [53, 54]. Without a critical mass of covered patients, a new screening test such as CTC has little chance of gaining a foothold against existing tests that are covered by health insurance plans. From a national perspective, inclusion of CTC as a preferred preventive screening test in the revised 2008 guidelines from the American Cancer Society (in conjunction with the major GI societies and the American College of Radiology) offered great promise [14, 127]. However, the US Preventive Services Task Force (USPSTF) soon followed in 2008 with an "I" rating, indicating "insufficient evidence" to support CTC screening [128]. The

Table 3 Barriers to implementation of CTC screening

Lack of broad coverage from CMS and other third-party payers
Lack of overt support from the gastroenterology community
Lack of early adoption by primary care providers
Inertia within the radiology community

USPSTF report highlighted three areas of uncertainty with regard to CTC screening: extracolonic findings, radiation exposure, and performance at the community level, all of which are addressed above. In May 2009, CMS followed the lead of the USPSTF by keeping CTC screening non-covered for Medicare beneficiaries in its updated national coverage determination.

Going forward, the following sequence of events is likely necessary to establish a realistic pathway for widespread implementation of CTC screening in the USA. An "A" or "B" grade from the USPSTF from its ongoing reassessment of CTC screening would effectively result in a reversal of the previous negative coverage determination by CMS, as mandated by the Affordable Care Act of 2010. The recent endorsement of CTC screening by the FDA Medical Devices Advisory Committee that convened in September 2013 might have a positive influence on these deliberations. An alternate but unlikely pathway to Medicare coverage for CTC screening would be passage of the bills currently sitting in the US Senate and House of Representatives, which was actually the path taken by optical colonoscopy over a decade ago. Regardless of the precise route, Medicare coverage would then presumably give rise to widespread coverage of CTC screening through other third-party payers that generally follow CMS. After all, it is the younger screening cohort in the 50–64 year age range that would likely benefit most from access to preventive CTC. In reality, a number of national plans now cover CTC screening, but these decisions generally fall under the radar compared with CMS.

Barriers to implementation at the provider level are threefold and include (1) a lack of overt support from the gastroenterology community, (2) lack of early adoption by primary care providers, and (3) inertia within the radiology community itself. As long as screening colonoscopy continues to account for the major source of income for gastroenterologists, the resulting protection of "turf" may continue to be insurmountable for CTC in the near term. However, there is a growing awareness of the exorbitant cost of primary colonoscopy screening among policy makers, insurers, and the public at large [129]. Furthermore, in the midst of US healthcare reform that seeks to improve efficiency and cost-effectiveness, a test that simultaneously screens for colorectal cancer, other cancers, abdominal aortic aneurysm, and osteoporosis, among other things, should be quite appealing [62, 63, 66]. At our own medical center, the overall volume of optical colonoscopy has significantly increased since the introduction of a parallel CTC screening program, allaying any fears of a turf battle [56, 57]. Issues related to lack of early adoption by primary care providers are complex [130] and are the focus of an active NIH R01 grant at our institution. Finally, without a "champion" from within each local radiology practice, CTC will have a difficult uphill battle in getting established in practice. A general reluctance by many radiologists to get actively involved in CTC screening is due in part to the current lack of coverage, but other factors likely contribute, such as misperceptions related to interpretation. As with optical colonoscopy, capacity for CTC could also become an issue if the demand rapidly increased [131].

Summary

In conclusion, CTC matches or exceeds optical colonoscopy in terms of the key criteria for a colorectal screening test, yet it remains vastly underutilized, largely due to lack of coverage by CMS and other payers. CTC is equivalent to colonoscopy for the screen detection of advanced adenomas, whereas the noninvasive stool-based tests largely lack this preventive benefit. CTC is considerably safer than colonoscopy as a primary colorectal screening test and would result in fewer hospitalizations and urgent surgical repairs. CTC is generally preferred over colonoscopy by individuals undergoing screening, which is an important factor for adherence. CTC is likely more cost-effective than optical colonoscopy for primary colorectal cancer screening, particularly if subcentimeter polyps are not aggressively managed. The reassessment of CTC screening by the USPSTF will be critical for a subsequent favorable national coverage determination by CMS. Once CTC screening is covered for Medicare beneficiaries, other third-party payers would presumably follow suit for the key 50- to 64-year-old demographic. At that point, CTC will be "ready for prime time."

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