Editorial

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CT Colonography Is the Perfect Colorectal Screening Test That Unfortunately Few People Use Yet

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Take-home points

- Computed tomography colonography (CTC) is the perfect test among the colorectal cancer screening options.
- The excellent performance of CTC is on par with colonoscopy for both cancers and precancerous polyps, yet without the risks associated with perforation and sedation.
- CTC presents an opportunity to serve as an important filter and send the small numbers of high-risk lesions for immediate removal while allowing the identification of the few true precursor targets from the large majority of benign polyps.
- This selective polypectomy strategy at CTC minimizes complications and waste of resources while maintaining advanced neoplasia detection rates.
- Biased messaging in the literature and little interest among radiologists to learn how to interpret CTC have fueled the fragmented state of colorectal cancer screening today.
- By promoting and adopting CTC, we can add to the current screening efforts to save even more lives for this truly preventable cancer.

Computed tomography colonography (CTC) is the perfect test among the colorectal cancer screening options. It combines the best aspects of the various screening studies in use. Besides high sensitivity and specificity for cancer detection, CTC is able to detect the important benign precursors (i.e., adenomatous polyps and sessile serrated lesions) that may turn into cancer over time to actually prevent a future cancer [1,2]. This is a major advantage over fecal immunochemical test (FIT) and stool DNA which largely cannot as these precursor lesions typically do not bleed or shed abnormal DNA. The excellent performance for CTC is on par with colonoscopy for both cancers and precancerous polyps yet without the risks associated with perforation and sedation that are present at colonoscopy. The risk profile for CTC is minimal [3]. At its core, CTC is simply a low dose CT exam of the abdomen and pelvis without intravenous contrast. The bowel has been simply optimized with a specific protocol to allow detection of polyps protruding into a cleansed, distended colonic lumen.

Nevertheless, unfortunately few people use CTC for colorectal cancer screening yet. Why this situation exists can be traced to two frustrating reasons. One is the continuing turf wars and biases in the research literature that lead to ignoring this important exam, which can be gleaned from the reported results of a large prospective randomized screening trial (n = 14981) recently published in *The Lancet Gastroenterology and Hepatology* [4]. This study showed that CTC significantly outperformed FIT in the detection of advanced neoplasia (5.2% vs. 1.7% detection rate, respectively, $p = 0.0002$). Even after 3 rounds of FIT,

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the detection rate for single event CTC was statistically higher at 5.2% vs. 3.1% for FIT, $p < 0.0001$. Given that advanced neoplasia represents the important histologic precursor target within the main pathway of cancer development, this is important news indeed. Furthermore, this study showed a statistically significant higher positive predictive value for CTC at 53.2% (67 true positives/126 positive exams) versus FIT at 32.3% (186 true positives/575 positive exams) with a $p < 0.0001$. I would argue that that the magnitude of the p values seen throughout the study at $p = 0.0002$ and $p < 0.0001$ would make chance as a cause of these results as a bit unlikely.

How does a study like this contribute to a lack of CTC use and acceptance? Because there is little doubt that reading the abstract of this study would lead to the conclusion that CTC had done poorly despite the above-mentioned results. The central result reported from this prospective, randomized trial was that the advanced neoplasia detection rate for *CTC was significantly less than that of FIT* when examined from an intent-to-screen analysis. Although a true statement when analyzed in this fashion, it raises the question of whether including individuals invited to screen but declined participation makes sense. Why confound the results by adding in participation levels to determine the comparison of advance neoplasia detection rates between these two screening exams? It is frustrating to see the authors frame the study results in this manner. The study has prospectively randomized the invited group into two study cohorts, one screened by CTC and the other with FIT. As with any trial, there are people who will chose not to participate but the purpose of prospectively randomizing selection between the two screening modalities is to mitigate any hidden selection bias between the cohorts. The large numbers (n = 1286 for CTC and n = 6027 for FIT) should then increase confidence in the results of this clinical trial which shows that CTC detects advanced neoplasia at a significantly higher rate with a higher positive predictive value over FIT.

So why present the results in this fashion with 'intent to screen' which obscures the true meaning of the study results (and I would argue guides the reader to a wrong conclusion regarding advanced neoplasia detection abilities between these screening tests)? In my opinion, it reveals the reality of colorectal cancer screening research and policy making for many years now where each method of screening has been pitted against each other with specific stakeholders framing results in a light favorable to their screening approach. For this study, certainly the levels of participation for a given exam and its ultimate impact on advanced neoplasia detection levels are important from a population screening perspective. However, it should put in the correct context of the screening exam's true ability to detect this lesion which is based on the detection rates seen of people who actually underwent the exam. The bottom line is that *CTC detects a significantly higher rate of advanced neoplasia over FIT* proven by a randomized prospective trial. Unfortunately, the framing and presentation of results in this study is not unique. This sort of biased messaging is present in much of the colorectal cancer screening literature and has fueled the sad fragmented state of screening today. It is particularly frustrating because with all of the current options that are in widespread use (which I would argue does not include CTC), we are woefully short of the targeted goal of a 80% screening adherence rate set by the National Colorectal Cancer Roundtable many years ago [5].

But the onus is not just on others who obscure study results and downplay CTC, it also rests squarely on radiologists and is the second major reason leading to CTC's underutilized state. It appears that there is little enthusiasm among radiologists to learn how to interpret this exam, yet alone promote its use. Part of the reticence is related to the need to learn the nuances of this CT-based exam. There is an unquestioned learning curve where an experienced cross-sectional imager must gain CTC-specific skills and knowledge in order not to miss polyps [6]. In particular, sessile serrated lesions can present difficulties with their flat, more subtle presentation [7], However, these can be accurately identified with appropriate training. Like mammography, there is a fear of missing a lesion that turns into a future cancer and likely adds to this barrier against adoption. However, from my experience training residents and fellows in CTC for nearly two decades, this skill set can be easily acquired by a radiologist. Once the foundation is in place, the interpretation can be done quickly, efficiently, and without excessive mental intensity. Honestly, the search pattern and interpretation are enjoyable and is similar to working through an abdominal CT for me.

CTC excels at colorectal screening, particularly over colonoscopy-based screening, as it can identify a more efficient precursor target. Colonoscopy utilizes a strategy of universal polypectomy to remove all detected polyps even though the vast majority of diminutive (5 mm or less) and small polyps (6–9 mm) would never progress to a future cancer. Albeit effective, universal polypectomy

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removes much pseudodisease which holds no benefit to the patient but exposes them to the inherent risks of a polypectomy. One can argue that this approach makes sense at colonoscopy as the patient has already accepted the risks of the procedure and the scope is in a position to easily remove the polyp and eliminate a potential future risk however tiny as it cannot be known on the front end.

In contrast, such an approach makes little sense at CTC because CTC must send an individual to polypectomy. This presents an opportunity to serve as an important filter and send the small numbers of high-risk lesions for immediate removal while allowing identification of the few true precursor targets from the large majority of benign polyps. The polyps that grow over surveillance can be then removed at a future exam as they are likely on that pathway of accumulating genetic abnormalities and becoming a future cancer. This selective polypectomy strategy at CTC based on size identifies a more efficient polyp target, minimizing complications and waste of resources yet maintaining advanced neoplasia detection rates. Our past study in *The New England Journal of Medicine* confirmed this indeed occurs at CTC with over a 4-fold decrease in the number of polypectomies (561 at CTC vs. 2434 at colonoscopy, $p < 0.001$) between parallel screening CTC and colonoscopy-based screening programs [8]. Despite the marked polypectomy difference, similar numbers of advanced neoplasia were seen between the program ($p = 0.81$) [8]. Now, with the benefit of time where we have had a screening program in place since 2004 (having screened and followed over 13000 individuals over nearly 20 years), our confidence in this approach has only strengthened. Placing 6–9 mm polyps in 3-year imaging surveillance and ≤ 5 mm diminutive polyps in a five-year normal screening window (which occurs as diminutive polyps are not reported at CTC) are safe practices without unacceptably high rates of interval cancers [9,10].

As an academic radiologist involved with colorectal screening now for nearly 25 years, CTC has been a major source of joy for me as a radiologist despite the frustration mentioned earlier. It is one of few exams that I interpret that makes a true difference for an individual. CTC has led to detection of unsuspected large adenomatous polyps and sessile serrated lesions in heathy, active people and where the removal of this lesion has dramatically changed their future. Now instead of dealing with cancer and a probable cancer-related death several years distant, they will enjoy a continued healthy life and age gracefully. This is not abstract concept for me as I know several of these people personally as colleagues and friends.

Ultimately, we can make an outsized impact on the future health of our patients through CTC. I urge all radiologists to become involved and engage in the fight against colorectal cancer. By promoting and adopting CTC, we can add to the current screening efforts to save even more lives for this truly preventable cancer.

Availability of Data and Material

Data sharing does not apply to this article as no datasets were generated or analyzed during the current study.

Conflicts of Interest

The author has no potential conflicts of interest to disclose.

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