Published in final edited form as:

Curr Opin Gastroenterol. 2015 January ; 31(1): 76–80. doi:10.1097/MOG.0000000000000141.

Recent Developments in Colorectal Imaging:

Current Opinions in Gastroenterology

Perry J. Pickhardt, M.D.

Department of Radiology, University of Wisconsin School of Medicine & Public Health, Madison, WI

Abstract

Purpose of review—The aim of this review is to provide an update on important recent advances in radiologic colorectal imaging, with emphasis on detection, staging, and surveillance of colorectal neoplasia.

Recent findings—Colorectal imaging advances with magnetic resonance (MR), CT colonography (CTC), and positron emission tomography (PET) over the past year or so have been substantial. Progress in MR imaging for rectal cancer was most notable in terms of assessment of response to neoadjuvant therapy. Continued maturation and clinical validation of CTC was observed for the evaluation of advanced neoplasia, among other areas. Multimodality approaches to colorectal imaging that incorporate functional PET data have also made impressive strides forward.

Summary—Recent advances in cross-sectional and functional radiologic imaging of the colorectum will positively impact the clinical capabilities for noninvasive evaluation of colorectal neoplasia

Keywords

Colorectal cancer; MR imaging; CT colonography; PET/CT; PET/MR

Introduction

Advanced medical imaging techniques play a major role in the clinical management of most organ systems, and the large intestine is no exception. In fact, the progress made in cross-sectional and functional colorectal imaging has greatly accelerated over the past decade. Over the past year or so, the contributions of magnetic resonance (MR), CT colonography (CTC), and positron emission tomography (PET) have been especially noteworthy in terms of advancing the areas of detection, staging, and surveillance of colorectal neoplasia. This review will focus upon the recent advances associated with these imaging modalities.

Recent advances in rectal MR imaging

The utility of MR for the initial staging of rectal cancer has been firmly established for some time now. Local staging of rectal cancer with MR that combines assessment of the primary tumor, regional lymph nodes, and the circumferential resection margin (CRM) allows for the identification of high-risk cohorts that will likely benefit from neoadjuvant chemoradiation therapy. More recently, there has been growing interest in the use of MR for restaging of rectal cancer after preoperative treatment, since up to 25% of patients may achieve a pathological complete response (pCR) with current regimens.¹ Going forward, the identification of complete responders versus non-responders to neoadjuvant therapy will likely continue to grow in importance as non-operative management paradigms evolve.

Restaging of rectal cancer with MR, however, is proving to be much more challenging than initial staging, due in part to post-treatment fibrosis and reaction, with mixed results to date. Two meta-analyses have recently looked at the cumulative published performance to date of MR imaging for restaging locally advanced rectal cancer after neoadjuvant treatment.^{2,3} The meta-analysis by van der Paardt et al² concluded that the diagnostic performance of MR for restaging was heterogeneous, although significantly better results were demonstrated when diffusion-weighted imaging (DWI) was incorporated, and also with more experienced observers. CRM evaluation at restaging remains an advantage of MR imaging, whereas nodal staging remains challenging. The meta-analysis by Wu et al³ found similar performance characteristics, including possible benefit related to DWI, but also improvement related to 3.0 T MR scanners. A retrospective multicenter evaluation of rectal cancer reimaging post neoadjuvant therapy (the “MERRION” study)⁴ concluded that MR was of limited value in predicting T stage, nodal involvement, and complete pathological response.

Additional rectal MR studies published within the past year have focused on the potential impact of specific techniques and parameters beyond high-resolution T2 imaging, including more functional assessment. In particular, the use of DWI in rectal cancer staging and restaging has received considerable attention.⁵⁻⁹ Ha et al⁶ showed that post-treatment changes in DWI tumor volumetry and ADC values were useful for predicting complete response. However, Sassen et al⁹ cautioned that although DWI can rule out complete response (due to high NPV), the sub-optimal PPV would preclude relying solely on MR for managing patients with a wait-and-see strategy. Unpublished data, however, suggest that the combination of endoscopy with T2-weighted and DWI MR may provide the best overall assessment for predicting pCR after neoadjuvant therapy.

Assessment of lymph node status remains a weakness of rectal MR, even with DWI. Heijnen et al⁷ showed that DWI can facilitate the detection of lymph nodes, but is not reliable for differentiating benign and malignant status. Application of novel MR contrast agents, particularly gadofosveset and ferumoxytol, provides hope for improved nodal assessment. Gadofosveset-trisodium acts as a blood pool MR contrast agent by binding to serum albumin. Heijnen et al¹⁰ have confirmed earlier results showing that gadofosveset improves the diagnostic performance of MR for staging and restaging of lymph nodes in rectal cancer,¹⁰ but has less impact on restaging the primary tumor.¹¹ Ferumoxytol is an

approved agent for iron replacement in anemia that has both T1 and T2* shortening properties that can be exploited at MR (off-label use) for both dynamic and delayed imaging.¹² This ultrasmall superparamagnetic iron oxide (USPIO) particle is taken up by the reticuloendothelial system, allowing for differentiation of normal versus abnormal lymph nodes. Initial results in terms of nodal staging with MR are expected within the next year or so.

Recent advances in CTC

Within the past year, a number of important papers have been published that further validate the use of CTC as both a diagnostic and screening tool. Most vital perhaps were the dual publications of the SIGGAR trial results in the Lancet.^{13, 14} This UK multicenter study actually consisted of two parallel randomized controlled trials focused on the investigation of symptoms suggestive of colorectal cancer. One study compared CTC with optical colonoscopy,¹³ while the other compared CTC with barium enema,¹⁴ both randomized in a ratio of 1 CTC to 2 of the other test. In the CTC (n=533) versus colonoscopy (n=1047) arm, detection rates for colorectal cancer and large polyps (≥ 10 mm) were equivalent at 11%. In the CTC (n=1277) versus barium enema (n=2527) arm, CTC was significantly more sensitive for detecting large polyps and cancer. Together, these studies validate the use of diagnostic CTC for suspected colorectal cancer as the preferred radiological test, providing a less invasive alternative to colonoscopy.

In the realm of screening, appropriate management of small (6–9 mm) colorectal polyps detected by CTC has long been an area of controversy, largely due to the perceived dearth of natural history data. We recently reported the results of an 8-year prospective longitudinal trial investigating the in-vivo volumetric growth rates of 6–9 mm polyps detected and followed by CTC.¹⁵ A total of 306 small polyps were followed with a mean surveillance interval of 2.3 years. A 20% change in polyp volume per year was used to categorize lesions according to progression, stability, and regression. Progression was seen in 22% (68 of 306), 50% were stable (153 of 306), and 28% regressed (85 of 306), including complete resolution in 10% (32 of 306). Of histologically-proven advanced adenomas, 91% progressed (21 of 23), compared with 37% of non-advanced adenomas and 8% of all other polyps (p<0.0001). Mean polyp volume increased 77% per year for advanced adenomas, compared with a 16% increase for non-advanced adenomas, and a 13% decrease for non-neoplastic or unresected polyps (p<0.0001). We concluded that volumetric growth assessment of small colorectal polyps was a useful biomarker for determination of clinical importance, which could allow for less invasive surveillance strategies and reserve polypectomy for lesions that show substantial growth.

Flat (nonpolypoid) lesions continue to be an area of active interest within colorectal cancer screening. For a given size, flat lesions are much less conspicuous than their polypoid and pedunculated counterparts at both CTC and colonoscopy, leading to potential missed lesions. In addition, elucidation of the serrated polyp pathway to cancer has also heightened awareness for flat right-sided lesions. Although a number of prior publications have demonstrated the ability of CTC to detect nonpolypoid lesions, Kim et al¹⁶ recently described the utility of contrast coating along the lesional surface as a marker for detection.

This etching of contrast was seen in nearly 80% of 160 flat lesions (mean size, 9.4 mm) at CTC. Large size, proximal colonic location, and serrated histology were all associated with a higher frequency of contrast coating, which serves as a beacon for detection at CTC. A separate recent CTC paper described the clinical, imaging and pathologic features of carpet lesions, which are laterally-spreading flat masses measuring 3 cm or larger across.¹⁷ Of the 18 proven carpet lesions, all demonstrated surface coating of contrast and all but two were located in the distal rectosigmoid or proximal right colon. Despite the large size (mean, 4.7 cm), most were histologically advanced adenomas but still benign. Together, these two papers provide further evidence of CTC's ability to detect clinically relevant flat colorectal lesions.

A number of other CTC papers have advanced our knowledge in terms of interpretation and clinical implementation. Pooler et al¹⁸ showed that variation in the detection of adenomas and advanced neoplasia amongst radiologists in one CTC screening program was considerably less than that previously reported for colonoscopy. Pooler et al¹⁹ also provided benchmark screening values for the detection of relevant colorectal and extracolonic findings according to the established CT colonography reporting and data system (C-RADS), which can be used for comparison by other screening programs. Lung et al²⁰ reported their 5-year experience with CTC in a high-risk population, demonstrating a high PPV for polyps (92%) and high NPV for cancer (99.9%). Of note, PPV for small polyps significantly improved after the introduction of fecal contrast tagging. Pickhardt et al reviewed interpretive pitfalls²¹ and missed lesions²² at CTC, drawing from their experience with population screening. Flor et al²³ proposed a diverticular disease severity score based on findings at CTC, which represents an ideal tool for non-invasive evaluation of this common abnormality. In two separate papers, Flor et al also assessed the utility of CTC for preoperative surgical planning in patients with occlusive colorectal cancer²⁴ and for preoperative distinction between T1-T2 and T3-T4 cancers.²⁵ The information obtained from CTC changed that surgical approach in a number of cases. These combined works by Flor et al²³⁻²⁵ may ultimately lead to increased utilization of preoperative CTC for both benign and malignant surgical conditions.

Recent advances in PET

PET imaging provides functional information that is complementary to anatomic cross-sectional imaging. As such, multi-modality imaging that incorporates PET is gaining significant traction, especially for oncologic investigation. ¹⁸F-fluorodeoxyglucose (FDG) PET/CT is well established as a diagnostic tool in the evaluation of patients with rising CEA and suspected recurrence of colorectal cancer, as shown in a recent review by Lu et al.²⁶ Its use in initial staging and restaging, however, remains unclear, due in part to the mixed results to date. Guillem et al²⁷ showed in a prospective trial that neither PET nor CT has adequate predictive value in distinguishing pCR from an incomplete response to neoadjuvant chemoradiation. However, a systematic review by Memon et al²⁸ concluded that FDG PET measures are useful in this regard.

It has been recognized for many years that incidental colorectal adenomas and cancers may be FDG avid on PET studies, leading some to wonder about its potential screening role.

However, two recent publication by Gollub et al²⁹ and by Minamimoto et al³⁰ emphasize the fact that although incidental PET detection of colorectal neoplasia may lead to early detection in many cases, significant tumors will still be missed if used for screen detection. Cost implications would also preclude the use of PET/CT for asymptomatic screening.

The combination of PET and MR offers the prospect of functional imaging with improved anatomic soft tissue contrast resolution. Despite the substantial technical and economic hurdles encountered with the introduction of PET/MR, the early clinical results are encouraging.^{31–33} Combining state-of-the-art rectal MR, as described above, with FDG PET offers the potential for improved staging, restaging, and surveillance of rectal cancer. Data are expected to surface in the near future.

Although FDG remains the workhorse PET agent for oncologic imaging, it has issues of both decreased specificity (eg, inflammatory lesions) and sensitivity (eg, mucinous tumors). Newer PET agents that are more cancer specific may one day replace FDG for oncologic imaging, including colorectal cancer. For example, Weichert et al³⁴ recently reported a novel PET tracer (¹²⁴I-CLR1404) that is highly selective for cancer, demonstrating prolonged uptake in a broad spectrum of human malignancies, while not being retained within benign or inflammatory lesions. Furthermore, this agent can serve as a therapeutic by replacing the ¹²⁴I label with ¹³¹I. Preliminary investigations underway in humans appear to confirm the earlier animal studies.

Conclusion

In summary, recent advances in cross-sectional and functional radiologic imaging hold enormous potential for transforming the clinical evaluation and management of colorectal neoplasia.

Acknowledgments

Conflicts of interest and funding sources: Dr. Pickhardt has consulted for Braintree Laboratories, Mindways, and Viatronix; owns stock in Collectar Biosciences; and is co-founder of VirtuoCTC. Grant funding: National Institutes of Health NCI grants 1R01CA144835-01, 1R01CA155347-01, 1R01 CA169331-011, and R37 CA63677-19

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Key bullet points

1. Progress in rectal MR imaging over the past year was most notable in terms of assessment of cancer response to neoadjuvant therapy to guide management.
2. Progress in CTC over the past year has included further clinical validation for detection of advanced neoplasia, in vivo surveillance of small colorectal polyps, and overall maturation of the technique.
3. Progress in functional PET imaging for colorectal cancer over the past year has included multimodality incorporation of both CT and MR techniques, as well as novel tracers that are more cancer selective.