### American College of Radiology ACR Appropriateness Criteria<sup>®</sup> Staging and Disease Monitoring of Colon Cancer and Appendiceal Cancer

#### Variant 1: Adult. Staging of colon cancer.

Procedure	Appropriateness Category	<b>Relative Radiation Level</b>
CT abdomen and pelvis with IV contrast	Usually Appropriate	♥♥♥
CT chest with IV contrast	Usually Appropriate	€€€
MRI abdomen and pelvis without and with IV contrast	May Be Appropriate	0
CT chest without IV contrast	May Be Appropriate	€€€
FDG-PET/CT skull base to mid-thigh	May Be Appropriate	♦♥♥♥
MRI abdomen and pelvis with IV contrast	Usually Not Appropriate	0
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	0
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	���
CT chest without and with IV contrast	Usually Not Appropriate	♥♥♥
FDG-PET/MRI skull base to mid-thigh	Usually Not Appropriate	♥♥♥
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	€€€

#### Variant 2:

#### Adult. Colon cancer. Posttreatment evaluation.

Procedure	Appropriateness Category	Relative Radiation Level	
CT abdomen and pelvis with IV contrast	Usually Appropriate	���	
CT chest with IV contrast	Usually Appropriate	€€	
MRI abdomen and pelvis without and with IV contrast	May Be Appropriate	0	
CT chest without IV contrast	May Be Appropriate	♥♥♥	
FDG-PET/CT skull base to mid-thigh	May Be Appropriate	♦♥♥♥	
MRI abdomen and pelvis with IV contrast	Usually Not Appropriate	0	
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	0	
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	♥♥♥	
CT chest without and with IV contrast	Usually Not Appropriate	���	
FDG-PET/MRI skull base to mid-thigh	Usually Not Appropriate	���	
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	€€€	

Variant 3:

# Adult. Appendiceal cancer. Disease monitoring during treatment or posttreatment evaluation.

Procedure	Appropriateness Category	Relative Radiation Level	
CT abdomen and pelvis with IV contrast	Usually Appropriate	���	
CT chest with IV contrast	Usually Appropriate		
MRI abdomen and pelvis without and with IV contrast	May Be Appropriate	0	
CT chest without IV contrast	May Be Appropriate	���	
FDG-PET/CT skull base to mid-thigh	May Be Appropriate	<b>**</b>	
MRI abdomen and pelvis with IV contrast	Usually Not Appropriate	0	
MRI abdomen and pelvis without IV contrast	Usually Not Appropriate	0	
CT abdomen and pelvis without IV contrast	Usually Not Appropriate	���	
CT chest without and with IV contrast	Usually Not Appropriate	���	
FDG-PET/MRI skull base to mid-thigh	Usually Not Appropriate	€€€	
CT abdomen and pelvis without and with IV contrast	Usually Not Appropriate	€€€	

#### STAGING AND DISEASE MONITORING OF COLON CANCER AND APPENDICEAL CANCER

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#### **Summary of Literature Review**

#### Introduction/Background

The local treatment of colon cancer relies primarily on the resection of involved colon (partial colectomy), with removal of the associated mesentery and regional nodes. The use of selective adjuvant chemotherapy is dictated by lymph node positivity and extramural lymphovascular invasion on pathologic specimen. There is increasing use of targeted agents based on molecular subgroups, such as microsatellite-unstable, BRAF-mutant, or RAS-mutant colon cancers (identified via pathology rather than imaging), with impressive response at surgery; however, surgery remains the standard initial local treatment of colon cancer.

The role of preoperative imaging to predict T stage and N stage is an area of ongoing investigation, given that neoadjuvant therapy has not yet been shown to significantly improve overall survival over surgery (radical resection) with postoperative adjuvant treatment. The large randomized controlled Fluoropyrimidine, Oxaliplatin, and Targeted-Receptor pre-Operative Therapy (FOxTROT) trial found that preoperative (neoadjuvant) chemotherapy for operable colon cancer produces marked histopathologic downstaging, fewer incomplete resections, and better 2-year disease control than adjuvant therapy alone, and it may predict lower postoperative recurrence based on regression after neoadjuvant therapy [1].

Despite the growing interest in identifying colon cancers that might benefit from neoadjuvant chemotherapy before resection, preoperative imaging of colon cancer appears to be of most benefit in identifying distant metastases, regardless of its ability to predict T stage and N stage. Given the limited role of locoregional staging, the imaging variant discussion for colon cancer will primarily focus on evaluation of distant metastases.

Appendiceal cancers have different biological behavior despite their morphological resemblance to colon cancer, and therefore the eighth edition of American Joint Committee on Cancer staging manual classified appendiceal carcinomas independently and separate from colon cancer [2-4]. In view of different management strategies for appendiceal tumors, they are considered separately from colon cancer in this narrative. Appendiceal epithelial neoplasms are rare, with a broad range of initial presentations ranging from a localized appendiceal mucocele to an aggressive malignancy with peritoneal spread [5]. Appendiceal adenocarcinoma can be either mucinous or nonmucinous. Metastatic disease is most commonly peritoneal disease within the abdomen and pelvis, with diffuse peritoneal mucinous involvement in the form of pseudomyxoma peritonei, an uncommon malignancy most frequently arising from a ruptured appendiceal mucocele/epithelial neoplasm. The primary treatment for peritoneal disease from appendiceal carcinoma is cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC). There are no formal surveillance guidelines for after appendectomy [6,7], and typically postoperative surveillance is individualized in these situations according to tumor presentation, pathology, and prior treatment [5].

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### **Discussion of Procedures by Variant**

### Variant 1: Adult. Staging of colon cancer.

In this clinical scenario, a patient has been recently diagnosed with colon cancer and presents for the evaluation of the primary lesion and metastatic disease in the chest, abdomen, and pelvis.

### **CT** Abdomen and Pelvis With IV Contrast

Abdominal/pelvic CT with IV contrast has a high negative predictive value of 90% for ruling out distant metastases [8]. The false-positive rate of CT in a prospective study by Valls et al [9] was 3.9% (10 of 257 findings: 95% confidence interval [CI], 1.9-7.1), with intraoperative ultrasound (US) and histopathology serving as the reference standard. Most studies show comparable or improved sensitivity for the detection of colorectal liver metastases with intravenous (IV) conventional extracellular gadolinium agent-enhanced MRI compared with CT [10,11]. An important determinant of CT performance is technique. The use of multidetector CT (MDCT), multiphase imaging, appropriate IV contrast bolus and timing, and optimal imaging parameters significantly narrows the differential between CT and MRI [12,13]. In studies evaluating the IV contrast-enhanced optimized CT technique, detection rates for liver metastases range from 85% to 91% [9,14]. CT may show more limited sensitivity in detecting metastases in the setting of fatty liver and following neoadjuvant therapy compared with MRI [10,11]. Particularly in this setting of serial imaging, MDCT has proven to be an effective tool in the assessment of the extent of liver disease in addition to providing a comprehensive assessment of extrahepatic disease. Recent studies have also noted CT morphologic criteria of responses in liver metastasis that have proven to be excellent predictors of overall survival and disease-free survival [15,16].

In local staging, CT demonstrates suboptimal evaluation in early (T1-2) and locally advanced (T3-4) stage tumors, with frequent errors of both T- and N-based assessment [17-24], suggesting that it remains primarily useful in the assessment of metastatic disease. There is some evidence showing that nodal assessment may be more sensitive based on pathologic mismatch repair or microsatellite instability status [25,26], and that CT may be effective at the local assessment of extramural vascular invasion/speculation [27-29]. In the evaluation of retroperitoneal (ascending or descending) colon cancer, CT demonstrated an 80% accuracy in predicting pathological circumferential margin [30].

### CT Abdomen and Pelvis Without and With IV Contrast

There is no specific evidence to support performing CT of both the abdomen and pelvis without and with IV contrast, rather than with IV contrast alone.

### **CT Abdomen and Pelvis Without IV Contrast**

There is no relevant literature to support the use of CT abdomen and pelvis without IV contrast.

# **CT Chest With IV Contrast**

The National Comprehensive Cancer Network (NCCN) recommends that patients with newly diagnosed colorectal cancer undergo staging chest CT because staging chest CT has been shown to detect more lung metastases than chest radiography [31]. In a series of 74 patients with newly diagnosed rectal cancer who underwent both chest CT and chest radiography, 37% of patients with a normal chest radiograph had a lesion visible only on the chest CT, and 17% of these patients were found to have at least 1 pulmonary metastasis [31]. Among patients with potentially resectable liver metastases and a negative initial chest PET, additional imaging with a chest CT revealed pulmonary metastases in 5% of patients [32]. A potential pitfall of chest CT is the detection of small indeterminate pulmonary nodules that are not metastases [33]. In pooled studies, approximately 15% patients had incidental pulmonary nodules on initial staging CT [34]; one-fourth to one-fifth of the indeterminate lesions on preoperative CT ultimately developed into metastases and 1 in 10 into other lung malignancies [35]. Because of limited sensitivity of MRI for lung nodules, a chest CT can be used in addition to abdominal MRI for complete staging.

Chest CT examinations performed to evaluate for pulmonary metastases were typically performed with IV contrast material [33,36,37], given its role in simultaneous detection evaluation of abdominopelvic lesions. Lung nodules can be identified with or without IV contrast.

# CT Chest Without and With IV Contrast

There is no specific evidence for performing CT both without and with IV contrast, instead of with IV contrast alone.

### **CT Chest Without IV Contrast**

The NCCN recommends that patients with newly diagnosed colorectal cancer undergo staging chest CT because staging chest CT has been shown to detect more lung metastases than chest radiography [31]. In a series of 74 patients with newly diagnosed rectal cancer who underwent both chest CT and chest radiography, 37% of patients with a normal chest radiograph had a lesion visible only on the chest CT, and 17% of these patients were found to have at least 1 pulmonary metastasis [31]. Among patients with potentially resectable liver metastases and a negative initial chest PET, additional imaging with a chest CT revealed pulmonary metastases in 5% of patients [32]. A potential pitfall of chest CT is the detection of small indeterminate pulmonary nodules that are not metastases [33]. In pooled studies, approximately 15% of patients had pulmonary nodules on initial staging CT [34]; one-fourth to one-fifth of the indeterminate lesions on preoperative CT ultimately developed into metastases and 1 in 10 developed into other lung malignancies [35]. Because of the limited sensitivity of MRI for lung nodules, a chest CT can be used in addition to abdominal MRI for complete staging.

Chest CT examinations performed to evaluate for pulmonary metastases were typically performed with IV contrast material [33,36,37], given its role in the detection evaluation of abdominopelvic lesions. Lung nodules can; however, be identified with or without IV contrast, and noncontrast CT chest may be indicated when performed separately from abdominopelvic CT.

# FDG-PET/CT Skull Base to Mid-Thigh

PET/CT is useful for determining overall stage and identifying patients with metastatic disease (sensitivity of 89% and specificity of 64%); however, the accuracy on a lesion-by-lesion basis is relatively low compared with IV contrast-enhanced CT and MRI for liver metastases (55% versus 89% in a study comparing PET/CT with MDCT) [38,39]. PET/CT may help to exclude other sites of disease beyond the liver [40] or, in complex cases, to improve staging accuracy. PET/CT, in addition to traditional CT or MRI staging, has been shown to result in a change in management in up to 8% to 11% of patients [38,41-43]; however, randomized controlled and nonrandomized trials, or meta-analysis, did not demonstrate any difference in recurrence rates or long-term survival based on these changes in management [44-46]. Caution should be exercised, because the findings of PET/CT may be nonspecific and could result in a negative impact on patient care in up to 9% of patients [38]. Per the American Society of Colorectal Surgeons, PET/CT is generally not recommended for routine colon cancer staging but may be useful in surgical decision making in patients with stage IV disease [47].

PET/CT may add influence in the positive predictive value of avid lymph nodes because it has a higher specificity than other modalities. The sensitivity of detecting nodal metastases is variable, ranging from 43% to 88%, with a specificity of 60% to 80%, and again size is not a helpful characteristic [48].

Limitations of PET include decreased sensitivity in detecting small colonic lesions  $\leq 10$  mm in diameter and decreased fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG) uptake by mucinous tumors [39].

# FDG-PET/MRI Skull Base to Mid-Thigh

Multiple small studies have demonstrated high diagnostic performance of FDG-PET/MRI in the detection of primary lesions and metastases in staging and restaging of patients with colorectal cancer, including a meta-analysis of 1,534 patients with a pooled sensitivity of 94% and specificity of 89% for the detection of tumor, lymph nodes, and metastases, with the highest sensitivity for M staging at 97% [49]. PET/MRI demonstrated a pooled sensitivity of 81% and specificity of 89% for the detection of lymph node metastases [50]. However, at this time there is little indication for this examination as the primary initial staging modality, and it is not commonly performed outside of specific clinical problem-solving scenarios. Regarding pulmonary metastases, both MRI and PET are considered to have a limited role in detecting small pulmonary nodules, and in a trimodality PET/CT and MRI protocol there was limited detection of nodules <1 cm by MRI compared with CT [51,52].

# MRI Abdomen and Pelvis With IV Contrast

There are no recent publications addressing MRI abdomen and pelvis with IV contrast (ie, excluding the precontrast images). In practice, MRI is rarely if ever done solely postcontrast, particularly given the numerous range of sequences that do not involve contrast-enhancement.

# MRI Abdomen and Pelvis Without and With IV Contrast

This variant includes MRI for the assessment of hepatic metastatic disease, as well as MRI of the abdomen and pelvis for local staging and extrahepatic metastatic disease.

Most studies show comparable or improved sensitivity for the detection of colorectal liver metastases with IV conventional extracellular gadolinium agent-enhanced MRI compared with CT [10,11]. MRI is more accurate than CT in detecting liver metastases in the setting of fatty liver and following neoadjuvant therapy [10,11,53]. Many recent studies focus on the benefit of hepatobiliary contrast agent-enhanced MRI and diffusion-weighted imaging (DWI) [54-61]. In a retrospective study of 242 patients undergoing surgical resection for colorectal liver metastases (n = 92) with prechemotherapy and presurgical MRI with a hepatobiliary IV contrast agent and n = 150 without both prechemotherapy and presurgical hepatobiliary IV contrast agent-enhanced MRI), patients who underwent hepatobiliary MRI both prechemotherapy and presurgically had significantly lower rates of intrahepatic recurrence (48% versus 65%; P = .04) and fewer repeat hepatectomies (13% versus 25%; P = .03) [56]. On the basis of the results of this study, the authors suggested that a hepatobiliary IV contrast agent-enhanced MRI may improve outcomes in the era of highly active neoadjuvant chemotherapy and disappearing lesions. In a study of 28 patients with pathologically proven metastatic cancer who underwent gadolinium-ethoxybenzyl (Gd-EOB) MRI and MDCT imaging, per-lesion sensitivity in the detection of liver metastases was higher with Gd-EOB MRI (90%-96%) compared to MDCT (72%-75%) [62]. DWI-MRI is also more accurate than MDCT for the detection of liver metastases, with 100% sensitivity and specificity for DWI-MRI and 87.5% sensitivity and 95.5% specificity for MDCT [63].

MRI with DWI has become an increasingly accepted modality for the evaluation of peritoneal disease in patients who may benefit from cytoreductive surgery/HIPEC [64-69], predicting overall survival and disease-free survival, with increased detection of extraperitoneal findings over CT [70]. In a population based study, whole-body MRI was compared with standard staging with CT (followed by PET or liver MRI as needed) and revealed that whole-body MRI demonstrated a 4% improvement in sensitivity and 2% improvement in specificity for metastatic disease over conventional staging, with improved staging efficiency [71,72].

Because of limited sensitivity of MRI for lung nodules, a chest CT can be used in addition to abdominal MRI for complete staging.

Given the limitations of local staging by CT, MRI may present a more sensitive and specific option for preoperative T and N stage assessment. Multiple recent studies demonstrate improved nodal and local tumor evaluation based on enhancement and DWI/ADC findings; however, this remains investigational [48,73-77].

# MRI Abdomen and Pelvis Without IV Contrast

There is no relevant literature to support the use of MRI abdomen and pelvis without IV contrast in the initial staging of colon cancer.

# Variant 2: Adult. Colon cancer. Posttreatment evaluation.

In this clinical scenario, a patient with colon cancer has been treated either surgically or nonsurgically (chemotherapy, radiation, liver-directed therapy including ablation, chemo- or radioembolization) and presents for the evaluation of metastatic disease in the chest, abdomen, and pelvis. Because the metastatic pattern of colon cancer is similar in the initial staging and follow-up evaluations, the recommendations are similar to the initial staging.

# CT Abdomen and Pelvis With IV Contrast

Abdominal/pelvic CT with IV contrast has a high negative predictive value of 90% for ruling out distant metastases [8].

The false-positive rate of CT in a prospective study by Valls et al [9] was 3.9% (10 of 257 findings: 95% CI, 1.9-7.1), with intraoperative US and histopathology serving as the reference standard. Most studies show comparable or improved sensitivity for the detection of colorectal liver metastases with IV conventional extracellular gadolinium agent-enhanced MRI compared with CT [10,11]. Although CT may have diminished sensitivity compared with MRI in the detection of liver lesions, an important determinant of its accuracy is the CT technique. The use of MDCT, multiphase imaging, appropriate IV contrast bolus and timing, and optimal imaging parameters significantly narrows the differential between CT and MRI [12,13]. In studies evaluating the IV contrast-enhanced optimized CT technique, detection rates for liver metastases range from 85% to 91% [9,14]. CT may show more limited sensitivity in detecting metastases in the setting of fatty liver and following neoadjuvant therapy compared with MRI [10,11]. Particularly in this setting of serial imaging, MDCT has proven to be an effective tool in the assessment of the extent of liver disease in addition to providing a comprehensive assessment of extrahepatic disease. Recent studies have also noted CT morphologic criteria of responses in liver metastasis that have proven to be excellent predictors of overall survival and disease-free survival [15,16]. Given the performance of CT of the chest, abdomen, and pelvis with IV contrast in the detection of liver and lung metastases, this remains the standard modality for follow-up of patients after curative or palliative/neoadjuvant treatment of colon cancer [78].

### CT Abdomen and Pelvis Without and With IV Contrast

There is no specific evidence to support performing CT of both the abdomen and pelvis without and with IV contrast, rather than with IV contrast alone.

### CT Abdomen and Pelvis Without IV Contrast

There is no relevant literature to support the use of CT abdomen and pelvis without IV contrast in the initial staging of colon cancer.

#### **CT** Chest With IV Contrast

Lung metastases occur in approximately 25% of patients with resected colon cancer [79] and because of the frequency of follow-up abdominopelvic CT, chest CT is included as part of routine contrast-enhanced CT chest, abdomen, and pelvis.

#### CT Chest Without and With IV Contrast

There is no specific evidence for performing CT both without and with IV contrast, instead of with IV contrast alone.

### **CT Chest Without IV Contrast**

The NCCN recommends that patients with treated colorectal cancer undergo chest CT because staging chest CT has been shown to detect more lung metastases than chest radiography [31]. Among patients with potentially resectable liver metastases and a negative initial chest PET, additional imaging with a chest CT revealed pulmonary metastases in 5% of patients [32]. A potential pitfall of chest CT is the detection of small indeterminate pulmonary nodules that are not metastases [33]. In pooled studies, approximately 15% of patients had pulmonary nodules on initial staging CT [34]; one-fourth to one-fifth of the indeterminate lesions on preoperative CT ultimately developed into metastases, and 1 in 10 developed into other lung malignancies [35]. Because of a limited sensitivity of MRI for lung nodules, a chest CT can be used in addition to an abdominal MRI for complete staging.

Chest CT examinations performed to evaluate for pulmonary metastases were typically performed with IV contrast material [33,36,37], given its role in the detection evaluation of abdominopelvic lesions. Lung nodules can; however, be identified with or without IV contrast, and noncontrast CT chest may be useful when performed separately from abdominopelvic CT.

### FDG-PET/CT Skull Base to Mid-Thigh

PET/CT is useful for determining overall stage and identifying patients with metastatic disease (sensitivity of 89% and specificity of 64%); however, the accuracy on a lesion-by-lesion basis is relatively low compared with IV contrast-enhanced CT and MRI for liver metastases (55% versus 89% in a study comparing PET/CT with MDCT) [38,39]. PET/CT may help to exclude other sites of disease beyond the liver or, in complex cases, to improve staging accuracy, in which it has been shown to result in a change in management in up to 8% to 11% of patients [38,41-43]. Caution should be exercised; however, as the findings of PET/CT may be nonspecific and could result in a negative impact on patient care in up to 9% of patients [38]. Additionally, PET/CT has further reduced sensitivity for lesions in the setting of neoadjuvant therapy and should be used in conjunction with IV contrast CT or MRI for presurgical planning of liver metastases [80]. PET/CT may add influence in the positive predictive value of avid lymph nodes because it has a higher specificity than other modalities. The sensitivity of detecting nodal metastases is only 43%, with a specificity of 80%, and again size is not a helpful characteristic.

PET/CT in the postoperative setting of patients with pathological stage III colon cancer resulted in the modified management of 13% of patients, with 11% demonstrating metastatic disease not identified on preoperative staging, and 38% of those upstaged patients undergoing curative treatment based on the PET/CT [81]. There is also a potential role for PET/CT in restaging colorectal cancer after chemoradiation therapy by measuring the pretreatment and posttreatment standardized uptake value and assessing response by decreasing standardized uptake value [82]. Limitations of PET include decreased sensitivity in detecting small colonic lesions  $\leq 10$  mm in diameter and decreased FDG uptake by mucinous tumors [39,83].

### FDG-PET/MRI Skull Base to Mid-Thigh

In a small trial of PET/MRI versus standard of care imaging in treated patients with colorectal cancer, PET/MRI changed clinical management in 36% of patients, with upstaging in 21% and downstaging in 14%, and outperformed

conventional posttreatment evaluation in oncologic restaging [84], prompting further evaluation in this area. However, at this time there is little indication for this examination as the primary restaging or surveillance modality, and it is not commonly performed outside of specific clinical problem-solving scenarios. PET-MRI has limited sensitivity for lung nodules, and a chest CT should be performed in addition to PET/MRI if used in restaging.

# MRI Abdomen and Pelvis With IV Contrast

There are no recent publications addressing MRI abdomen and pelvis with IV contrast (excluding the precontrast images). In practice, MRI is rarely, if ever, done solely postcontrast, particularly given the numerous ranges of sequences that do not involve contrast enhancement.

# MRI Abdomen and Pelvis Without and With IV Contrast

This variant includes MRI for the assessment of hepatic metastatic disease, as well as MRI of the abdomen and pelvis for extrahepatic metastatic disease.

Most studies show comparable or improved sensitivity for the detection of colorectal liver metastases with IV conventional extracellular gadolinium agent-enhanced MRI compared with CT [10,11]. MRI is more accurate than CT in detecting liver metastases in the setting of fatty liver and following neoadjuvant therapy [10,11,53]. Many recent studies focus on the benefit of hepatobiliary contrast agent-enhanced MRI and DWI [54-61]. In a retrospective study of 242 patients undergoing surgical resection for colorectal liver metastases (n = 92 with prechemotherapy and presurgical MRI with a hepatobiliary IV contrast agent and n = 150 without both prechemotherapy and presurgical hepatobiliary IV contrast agent-enhanced MRI), patients who underwent hepatobiliary MRI both prechemotherapy and presurgically had significantly lower rates of intrahepatic recurrence (48% versus 65%; P = .04) and fewer repeat hepatectomies (13% versus 25%; P = .03) [56]. On the basis of the results of this study, the authors suggested that a hepatobiliary IV contrast agent-enhanced MRI may improve outcomes in the era of highly active neoadjuvant chemotherapy and disappearing lesions. In a study of 28 patients with pathologically proven metastatic cancer who underwent Gd-EOB MRI and MDCT imaging, per-lesion sensitivity in the detection of liver metastases was higher with Gd-EOB MRI (90%-96%) compared with MDCT (72%-75%) [62]. DWI-MRI is also more accurate than MDCT for the detection of liver metastases, with 100% sensitivity and specificity for DWI-MRI and 87.5% sensitivity and 95.5% specificity for MDCT [63]. Compared with CT, gadoxetic acid-enhanced liver MRI demonstrates higher per-patient liver lesion detection, particularly in patients treated with chemotherapy, in subcapsular lesions, and in peribiliary metastases [62].

MRI with DWI has become an increasingly accepted modality for evaluation of peritoneal disease [64-69], with increased detection of extraperitoneal findings over CT [70]. In a population-based study, whole-body MRI was compared with standard staging with CT (followed by PET or liver MRI as needed) and revealed that whole-body MRI demonstrated a 4% improvement in sensitivity and 2% improvement in specificity for metastatic disease over conventional staging, with improved staging efficiency [71,72].

Because of limited sensitivity of MRI for lung nodules, a chest CT can be used in addition to abdominal MRI for complete staging.

# MRI Abdomen and Pelvis Without IV Contrast

There is no recent evidence to support MRI abdomen and pelvis without IV contrast in the posttreatment evaluation for colon cancer.

# Variant 3: Adult. Appendiceal cancer. Disease monitoring during treatment or posttreatment evaluation.

In this variant, a patient has been diagnosed with appendiceal cancer/neoplasm based on appendectomy or, less commonly, colonoscopy. Metastatic disease from appendiceal epithelial neoplasm is most commonly peritoneal disease within the abdomen and pelvis, with diffuse peritoneal mucinous involvement in the form of pseudomyxoma peritonei, an uncommon malignancy most frequently arising from a ruptured appendiceal muccele/epithelial neoplasm. The primary treatment for peritoneal disease from appendiceal carcinoma is cytoreductive surgery and HIPEC. A thorough evaluation of imaging recommendations for staging and follow-up of peritoneal disease in the more common setting of ovarian cancer is provided in the ACR Appropriateness Criteria<sup>®</sup> topic on "Staging and Follow-up of Ovarian Cancer" [85].

There are no formal surveillance guidelines for after appendectomy [6,7], and typically postoperative surveillance is individualized in these situations according to tumor presentation, pathology, and previous treatment [5].

### CT Abdomen and Pelvis With IV Contrast

Areas in the abdomen and pelvis, which are poorly evaluated by laparoscopy, may be better assessed by CT (intrahepatic or other solid organ parenchymal metastases and metastases to the porta or lesser sac). In addition, there are multiple bowel and peritoneal findings on CT, which can guide surgical approach or predict surgical outcome [86]. CT demonstrates little success in the differentiation of benign from malignant disease [87,88].

The sensitivity of CT in detecting peritoneal implants was influenced by lesion size. Sensitivity for small nodules (<0.5 cm) was 11%, which is in contrast to 94% with nodules >5 cm. Radiological (CT) peritoneal cancer index (PCI) scores significantly underestimate intraoperative PCI (P < .001) [89]. In a separate study of all peritoneal disease, CT PCI score had a sensitivity of 76%, a specificity of 69%, a positive predictive value of 85%, and a negative predictive value of 56% when compared with the surgical PCI [90]. The US HIPEC collaborative demonstrated correlation of CT-PCI of 55% to 70% with intraoperative PCI [91].

Postcytoreduction, CT or MRI of the abdomen and pelvis appears to be appropriate follow-up for low-grade pseudomyxoma peritonei [6,92,93].

### CT Abdomen and Pelvis Without and With IV Contrast

There is no specific evidence to support performing CT both without and with IV contrast, instead of with IV contrast alone.

### **CT Abdomen and Pelvis Without IV Contrast**

There is no specific evidence to support performing CT without contrast.

### **CT Chest With IV Contrast**

In higher-grade appendiceal neoplasm, or neuroendocrine appendiceal cancer, CT of the chest is useful to supplement abdominopelvic imaging [6].

### CT Chest Without and With IV Contrast

There is no specific evidence for performing CT both without and with IV contrast, instead of with IV contrast alone.

### **CT Chest Without IV Contrast**

In higher-grade appendiceal neoplasm, or neuroendocrine appendiceal cancer, CT of the chest is useful to supplement abdominopelvic imaging [6].

# FDG-PET/CT Skull Base to Mid-Thigh

Multiple studies have shown that PET/CT is insensitive for the evaluation of peritoneal disease and mucinous disease, both of which are primary characteristics of appendiceal cancer [94,95]. PET/CT coregistered with IV contrast-enhanced CT is more accurate than PET/CT alone, but it does not improve detection more than CT with IV contrast alone [96]. PET is not useful for patients with peritoneal cancer of appendiceal origin. In the rare case of neuroendocrine appendiceal cancer, PET may be used for poorly differentiated tumors [97].

# FDG-PET/MRI Skull Base to Mid-Thigh

Although there have been some small investigational studies on the role of PET/MRI in gastrointestinal malignancies, including colorectal cancer, there is not recent evidence supporting the role of routine PET/MRI in appendiceal cancer staging or restaging [98,99], and it is likely that further knowledge will be inferred from the assessment of other malignancies that tend to spread similarly (ovarian, peritoneal, and signet ring gastric cancers).

# MRI Abdomen and Pelvis With IV Contrast

There are no recent publications addressing MRI abdomen and pelvis with IV contrast (excluding the precontrast images). In practice, MRI is rarely, if ever, done solely postcontrast, particularly given the numerous ranges of sequences that do not involve contrast enhancement.

# MRI Abdomen and Pelvis Without and With IV Contrast

Delayed postcontrast-enhanced MRI coupled with DWI has been shown to have high sensitivity for the detection of small peritoneal implants and is potentially helpful for differentiation of acellular mucin from more cellular disease [97,100]. In evaluating peritoneal carcinomatosis index with CT and MRI, MRI is more sensitive and specific than CT [91,97] and there was improved sensitivity when both CT and MRI were used together as compared with CT or MRI alone [101]. Surveillance MRI demonstrates improved performance (91% sensitivity, 95% specificity) over serial tumor markers [102].

Postcytoreduction, CT or MRI of the abdomen and pelvis appears to be appropriate follow-up for low-grade PMP [6,92,93] given its low rate of local recurrence.

# MRI Abdomen and Pelvis Without IV Contrast

Given the demonstrated role of IV gadolinium in the evaluation of liver disease and the assessment of other potential sites of disease, MRI abdomen and pelvis without IV contrast is not generally useful.

### Summary of Highlights

This is a summary of the key recommendations from the variant tables. Refer to the complete narrative document for more information.

- Variant 1 and 2: For the initial staging and imaging of treated/resected colon cancer, CT of the chest with IV contrast and CT of the abdomen and pelvis with IV contrast are recommended, primarily to assess for distant metastatic disease. MRI of the abdomen may be useful, primarily for the detection of liver metastases, with increasing use of hepatobiliary IV contrast agents, which demonstrate improved performance for this indication compared with conventional gadolinium agents. Noncontrast chest CT may be indicated when performed separately from abdominal/pelvic CT or MRI. FDG-PET/CT is complementary and may be appropriate in combination with diagnostic CT or MRI to provide metabolic information.
- Variant 3: For the initial staging and imaging of treated/resected appendiceal cancer, CT of the abdomen and pelvis with IV contrast is recommended, primarily to assess for distant metastatic disease, most commonly peritoneal disease. CT of the chest with IV contrast is useful to supplement abdominopelvic imaging if there is concern for thoracic metastatic disease. MRI of the abdomen and pelvis may be useful, primarily for the detection of peritoneal or liver metastases. Noncontrast chest CT may be indicated when performed separately from abdominal/pelvic CT or MRI. FDG-PET/CT is complementary and may be appropriate in combination with diagnostic CT or MRI to provide metabolic information.

### **Supporting Documents**

The evidence table, literature search, and appendix for this topic are available at <u>https://acsearch.acr.org/list</u>. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, click here.

### Gender Equality and Inclusivity Clause

The ACR acknowledges the limitations in applying inclusive language when citing research studies that predates the use of the current understanding of language inclusive of diversity in sex, intersex, gender, and genderdiverse people. The data variables regarding sex and gender used in the cited literature will not be changed. However, this guideline will use the terminology and definitions as proposed by the National Institutes of Health [103].

#### **Appropriateness Category Names and Definitions**

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

### **Relative Radiation Level Information**

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria<sup>®</sup> Radiation Dose Assessment Introduction document [104].

Relative Radiation Level Designations			
<b>Relative Radiation Level*</b>	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range	
0	0 mSv	0 mSv	
۲	<0.1 mSv	<0.03 mSv	
<b>*</b>	0.1-1 mSv	0.03-0.3 mSv	
���	1-10 mSv	0.3-3 mSv	
\$\$\$\$	10-30 mSv	3-10 mSv	
****	30-100 mSv	10-30 mSv	

\*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.