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Imaging of Colorectal Carcinoma

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1 Introduction and Epidemiology

Colorectal cancer is the second most common cause of cancer-related death in the United States, where the annual incidence is estimated at 150,000 cases [1, 2]. American adults have a 5 percent chance of developing a colorectal carcinoma and approximately a 2 percent chance of dying from the disease [3]. Colorectal cancer is also an important cause of cancer-related mortality in many other Western countries, although distribution of the disease varies widely throughout the world. Mortality from colorectal cancer is similar for males and females. Importantly, as is the case for many malignancies, mortality is directly related to the stage at the time of diagnosis, with five-year survival decreasing from over 80 percent for early-stage disease, to less than 10 percent for patients with distant metastases [2]. Unfortunately, less than 40 percent of colorectal carcinomas are diagnosed before the disease has spread beyond the wall of the colon or rectum.

Factors that increase the risk for developing colorectal cancer include genetic predisposition, such as familial adenomatous polyposis syndrome (FAP), hereditary non-polyposis colorectal cancer (HNPCC), family history of colorectal cancer in a first-degree relative (especially if younger than 60 years) and personal history of colon cancer. Individuals with a first-degree relative with colorectal cancer have a lifetime risk of 12 percent to 15 percent [4]. Risk increases with age (more than 90 percent of colorectal carcinomas occur in patients older than 50 years) and with underlying conditions such as chronic inflammatory bowel disease (especially ulcerative colitis), diabetes, smoking and alcohol consumption. It is also widely believed that diets low in fiber and high in fat content and animal protein are also associated with a higher risk of developing colorectal cancer.

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2 Pathophysiology

It is well accepted that the vast majority of carcinomas arising from the mucosa of the colon and rectum originate from a precursor, namely the adenomatous polyp [5-9]. The theory that adenomas progress to carcinomas ("adenoma - carcinoma sequence") is supported by the fact that the relative frequency with which both adenomas and carcinomas are found in the rectum and the various segments of the colon is very similar, although the mean age of appearance of adenomas occurs several years before that of carcinomas. Approximately one-half of the cancers are in the rectum and sigmoid colon, whereas the remainder are scattered throughout the proximal segments of the colon [10]. Patients with large (> 1 cm) colonic adenomas develop carcinomas with a frequency that surpasses that of adults without adenomas or family history of adenomas or carcinomas ("average-risk" adults) [10-12].

Histologically, adenomas are classified as tubular, tubulovillous and villous. Most colonic adenomas begin as tubular adenomas. As they grow, however, mutations can lead adenomas to develop foci of displasia or villous changes and, when the villous component predominates, they are referred to as villous adenomas. The risk of carcinoma is directly related to the presence of villous changes. When transformation of adenomas to carcinomas does occur, this process takes place over a long period of time estimated between seven and 10 years, depending upon the size of the adenoma. Thus, the risk of harboring foci of high-grade dysplasia or carcinoma is directly proportional to the size of the adenoma. This risk is estimated at less than 1 percent for polyps less than 1 cm in size, 10 percent for polyps between 1 and 2 cm in size, and greater than 25 percent for polyps larger than 2 cm in size [3, 8]. Malignant polyps grow faster than benign polyps. Removing intermediate size and large polyps decreases the frequency of colorectal cancer. Thus, much of the effort spent in screening for colorectal cancer hinges upon the identification of advanced adenomas, the vast majority of which are 1 cm or greater in diameter.

3 Screening

Colorectal cancer is especially well suited for successfully decreasing the disease-specific mortality with the implementation of broad screening strategies. The main reason is that screening methods are directed towards detection and removal of precancerous lesions (adenomas) or early stage carcinomas. This differs from strategies used for detecting other tumors, such as breast or prostate cancer, where the lesion sought is the cancer itself. It should be noted that the terms "polyp" and "adenoma" are not interchangeable, as a "polyp" refers to any focal protrusion arising from the wall into the colonic lumen, whereas an "adenoma" refers to a neoplastic epithelial lesion. Other non-neoplastic, histological types of polyps include inflammatory or hyperplastic.

For individuals with an average risk of developing colorectal cancer, it is recommended that screening start at the age of 50 years. Various tests and methods have

been extensively studied as a means for detecting colorectal neoplasia [13]. These include fecal occult blood test (FOBT), endoscopic techniques such as sigmoidoscopy and optical colonoscopy and imaging tests such as double contrast barium enema and, more recently, CT colonography. Data have proved that screening with any method is better than no screening at all, and that the incidence of and mortality from colorectal cancer can both be decreased with adequate screening. The American Cancer Society recommends one of the following as acceptable strategies for screening: yearly FOBT, flexible sigmoidoscopy every five years, DCBE every five years or optical colonoscopy every 10 years. Unfortunately, public compliance with these strategies for colorectal cancer screening strategies is suboptimal and continues to be a main focus of attention of multiple agencies, especially the American Cancer Society. From the imaging point of view, enthusiasm about screening with double contrast barium enema has diminished considerably in recent years [14]. Many factors are responsible for this, but the most important one is the growing doubt about the performance of the test for detecting intermediate size and large polyps [14, 15]. There is, however, growing evidence that the performance of CT colonography exceeds that of double contrast barium enema and, in fact, may rival that of optical colonoscopy [16-20]. In the near future it is expected that CT colonography will be added to the list of acceptable options by the ACS. The expectation is that this will result in an increase in the fraction of eligible adults that are screened, by attracting individuals who have refused other methods.

4 Clinical Presentation

Colorectal cancer is a slow-growing tumor. Presenting symptoms vary with the specific location, size and stage of the tumor. Bleeding is a common presenting sign, and this may occur overtly as bright red blood per rectum or insidiously as iron deficiency anemia. Other presenting symptoms include abdominal pain secondary to developing bowel obstruction, changes in bowel habits or less specific symptoms such as weight loss, fever and malaise.

5 Imaging Detection of Colorectal Neoplasia

Traditionally, imaging methods have played a critical role in the detection, staging and surveillance of patients with colorectal neoplasia. The two imaging techniques commonly used today for the detection of polyps and tumors are the double contrast barium enema (DCBE) and, more recently, CT colonography. Contrast-enhanced CT and MRI techniques or PET/CT are preferred for local staging, and for evaluating regional and distant spread of cancers. Finally, high resolution MRI methods or intracavitary ultrasonography are used when accurate determination of the depth of

wall invasion is important for therapeutic decisions. Although a thorough description of the technical details that are necessary to ensure good quality imaging examinations is beyond the scope of this book, it is important to emphasize that good technique is critical for accurate detection of colorectal neoplasms.

6 Colonic Polyp Detection

On double contrast barium enema the appearance of a polyp depends upon its morphologic characteristics, the location within the colonic wall relative to the X-ray beam and the variable contact with barium and/or air of the polyp surface. Sessile polyps have a broad base of attachment to the colonic mucosa and are seen on enema examinations as filling defects (Fig. 10.1), rings or contour deformities. Sessile polyps, by definition, are fixed to the colonic wall and can be separated from fecal residue that is freely movable and almost always lies against the dependent wall. Conversely,

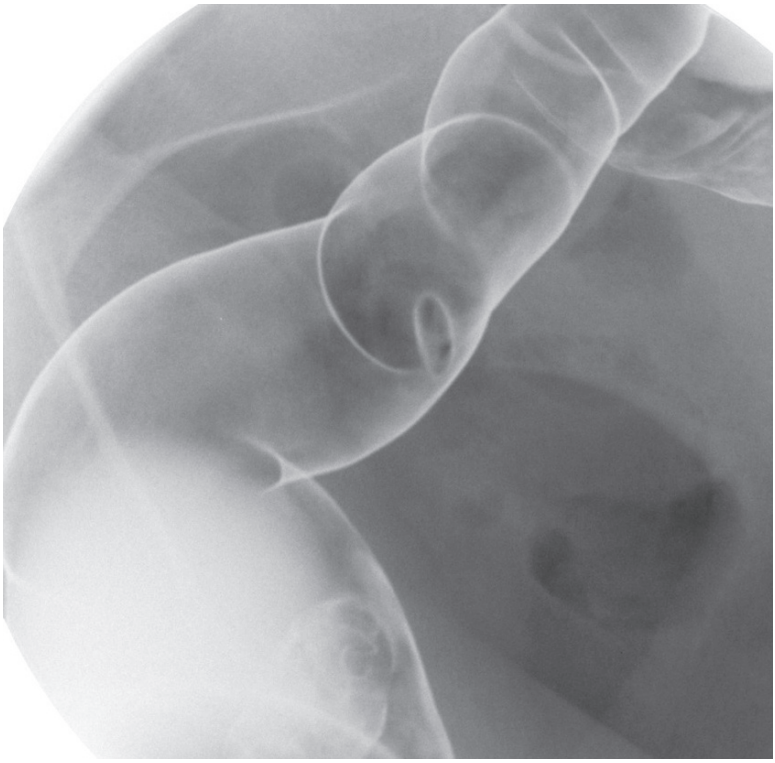


Fig. 10.1 Sessile polyp in the sigmoid colon demonstrated on a double contrast barium enema. The polyp has a broad base of attachment to the colonic mucosa and is sharply outlined by barium

pedunculated polyps are attached to the wall by a stalk (Fig. 10.2) that allows the free end of the polyp (head) to move easily within the lumen. Polyps with villous elements typically exhibit a more irregular surface with a frond-like appearance.

On CT colonography, sessile polyps are seen as focal protrusions of colonic mucosa-based lesions into the lumen of the bowel. Characteristically, sessile polyps have a smooth, cap-like surface and are seen on both the supine and prone image sets in the same location and do not move with changes in patient position (Fig. 10.3), unless the colon itself moves or rotates. CT colonography images demonstrate pedunculated polyps as focal lesions arising from the wall of the colon as well, but the free portion of the lesion changes in location when the patient moves from a supine to a prone position (Fig. 10.4). Villous adenomas are typically larger than tubular adenomas and on CT colonography also tend to have a more irregular surface (Fig. 10.5). The internal composition of colonic polyps is homogeneous and of soft tissue attenuation. On the contrary, stool residues have an irregular surface and a more heterogeneous internal attenuation with fatty and gas components. Furthermore, typical residual stool changes in position between supine and prone images, and tend to be located on the most dependent aspect of the colon. The best method to avoid misdiagnosing stool residue as polyps is to ensure adequate and complete cleansing of the colon with a full cathartic preparation. More recently, methods for stool and

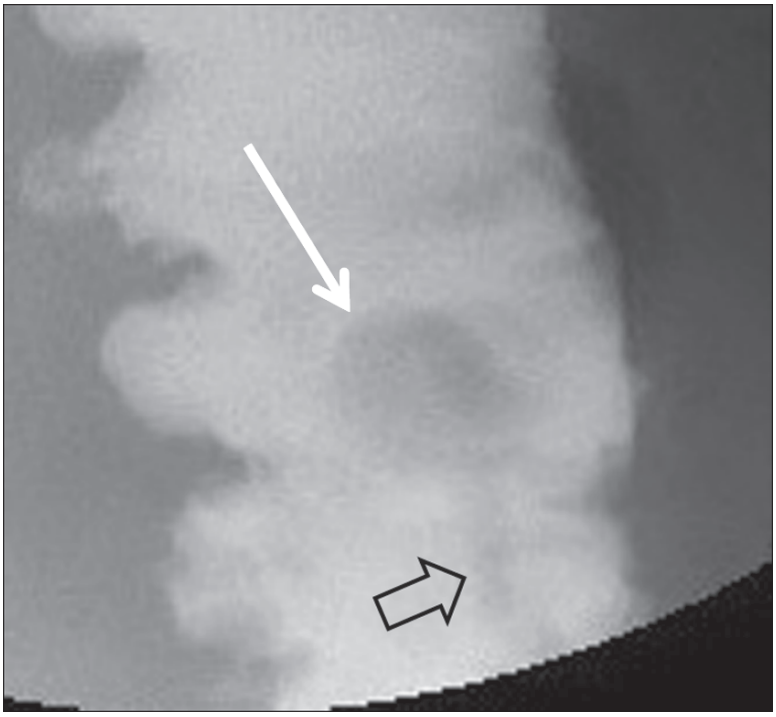


Fig. 10.2 A spot image of a single contrast barium enema shows a polypoid lesion in the descending colon (arrow). The polyp is attached to the wall of the colon by a stalk (open arrow)

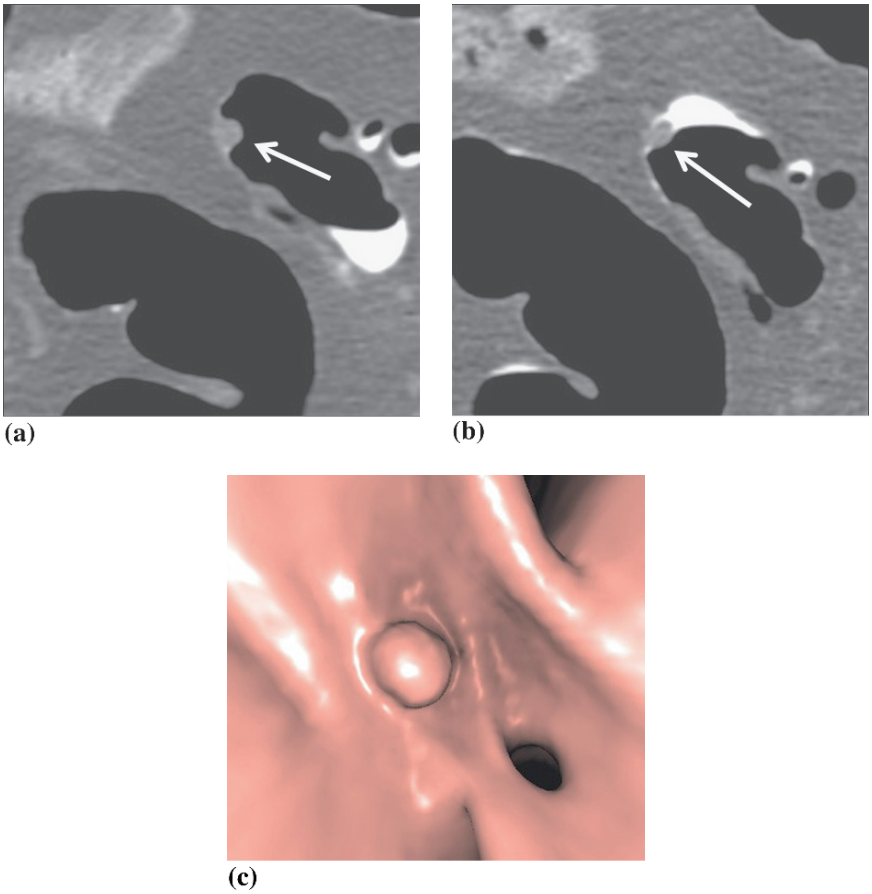


Fig. 10.3 8 mm sessile polyp seen on CT colonography. The broad-based polypoid lesion does not modify its location between the supine (**a**, arrow) and prone (**b**, arrow) positions. Note gravitational change in position of high density, iodine-tagged fluid. The endoluminal 3-D volume rendered image (**c**) confirms the sessile morphology of the polyp

fluid tagging have been added to the preparation regime for CT colonography, thus reducing the likelihood of false positive interpretations from this source (Fig. 10.3). Extensive work by several groups aims at testing the feasibility of performing CT colonography without a cathartic preparation ("prep-less" technique) [21-23].

7 Colorectal Carcinoma Detection

The search for colonic carcinomas on double contrast barium enema or CT colonography entails an exercise that is similar to that of the search for polyps. Early cancers have the appearance of large polyps, more commonly sessile and

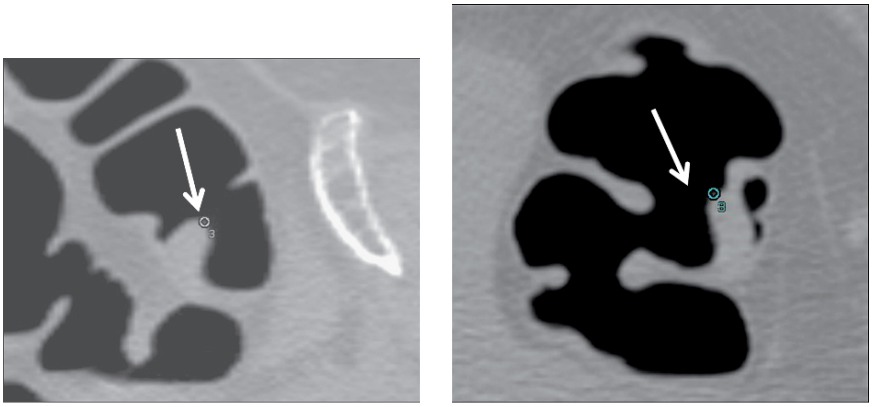


Fig. 10.4 10 mm pedunculated polyp seen on CT colonography. The polypoid lesion appears to slightly modify its location between the supine (**a**, arrow) and prone (**b**, arrow) positions. The short stalk is also seen on b (open arrow)

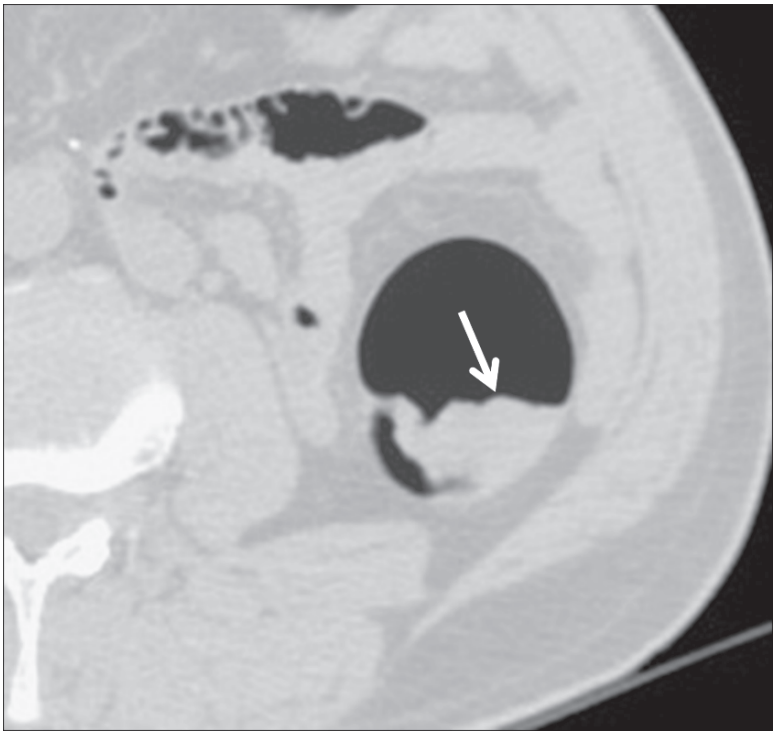


Fig. 10.5 Supine image of a CT colongraphy examination demonstrates a polypoid lesion with an irregular, frond-like surface in the descending colon (arrow). This lesion was histologically proven to be a villous adenoma

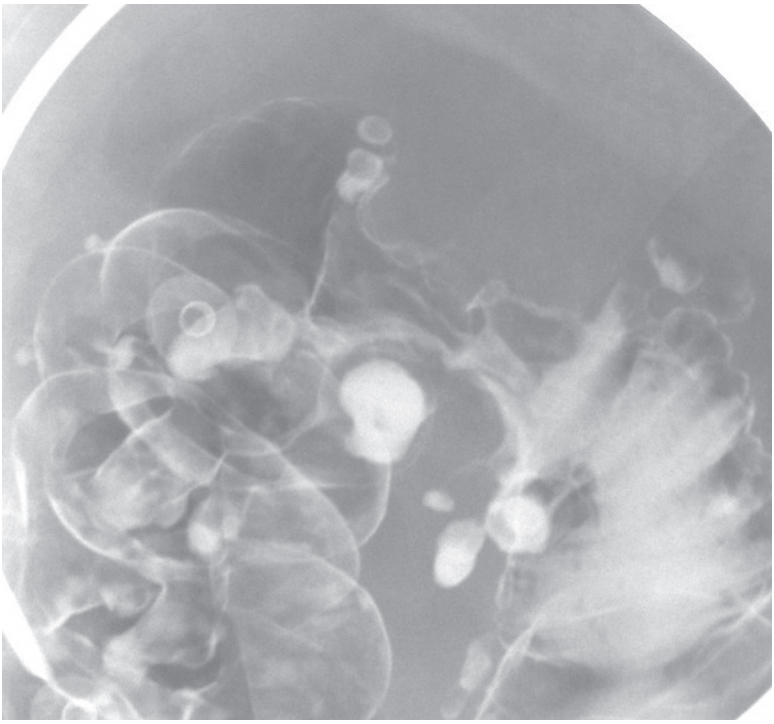


Fig. 10.6 Double contrast barium enema demonstrates circumferential narrowing of the splenic flexure caused by a mass with irregular, ulcerated, surfaces and overhanging edges. This is the typical "apple core" appearance of annular carcinomas

with a flat or irregular surface. Unfortunately, the majority of colonic carcinomas are diagnosed when they are in an advanced stage. These tumors are often polypoid or mass lesions that displace the column of barium or cause large, irregular contour defects in the colonic wall. With double contrast, the irregular surface, presence of ulcerations and broad base of attachment are better demonstrated. On CT colonography carcinomas manifest as fixed, irregular areas of wall thickening with an ulcerated surface, and cause a variable degree of lumen narrowing. As they grow, carcinomas commonly involve the wall in a circumferential fashion, leading to annular tumors which produce the typical "apple core" lesions on barium enema examinations (Fig. 10.6). Importantly, approximately 5 percent of patients with colon cancer harbor additional (synchronous) foci of carcinoma and an even larger percentage have adenomatous polyps.

On barium enema examinations, it may be difficult or impossible to differentiate between strictures caused by carcinomas and complicated diverticular disease. Thus, if there is any doubt about the nature of a wall abnormality, sigmoidoscopy or colonoscopy are recommended. The reported sensitivity of double contrast barium enema for detecting colorectal cancer vary in the literature from 60 percent to

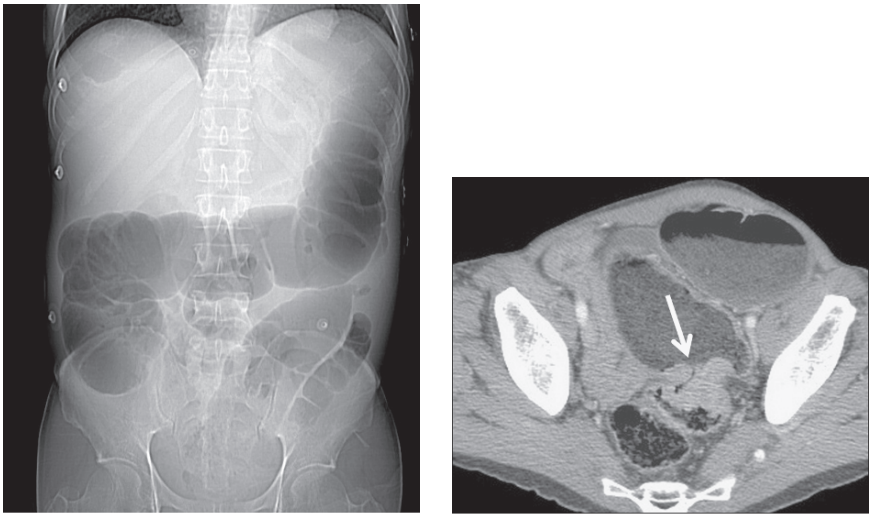


Fig. 10.7 Large bowel obstruction caused by colon cancer. The scout topogram (**a**) shows marked dilatation of the colon, with little or no gas in the rectum. Axial CT image of the pelvis demonstrates the annular obstructing sigmoid mass (arrow), as well as marked dilatation and retention of gas and fluid in the segments proximal to the mass

70 percent, to higher than 90 percent. However, as mentioned in preceding sections, the sensitivity of double contrast barium enema for detection of polyps is much lower [24-26]). Better performance results are typically obtained by radiologists who have a special interest in gastrointestinal imaging.

Complications of colorectal cancer include obstruction, perforation, fistula formation and bleeding. Colon cancer is a common cause of large bowel obstruction, especially when localized in the sigmoid or descending segments (Fig. 10.7). Perforation more commonly manifests as a pericolonic abscess, or may be the origin of a fistula communicating the lumen of the colon with nearby organs such as the urinary bladder, duodenum, stomach, gallbladder or vagina. The imaging findings of these complications will vary, depending upon the specific imaging technique used.

8 Staging of Colorectal Carcinoma

As is the case with other hollow viscera, staging of colorectal cancer takes into account the depth of invasion of the colonic wall, spread into pericolonic tissues and nearby organs, regional spread to draining lymph nodes and involvement of distant organs via hematogenous or peritoneal invasion. Even for patients who

undergo resection and are, thus, staged surgically, pathology can only identify metastases within the resection specimens and has no capability for detecting remote disease. As a result of this, many patients undergo futile operations for disease that could never have been cured by surgery alone. Several classifications of tumor stage have been described, but the TNM classification (Table 10.1) is currently the most used clinical standard to guide therapy.

Prognosis and choice of type of therapy are determined by the stage of the tumor at the time of diagnosis. Accurate preoperative staging of colorectal cancer determines the surgical approach, which differs between colon and rectal cancer. Additionally, patient eligibility for clinical trials often hinges on accurate staging. In colon cancer, generous resections are generally performed; this achieves wide tumor-free margins and includes resection of multiple regional lymph node chains, including the mesenteric root. In rectal cancer, wide tumor-free margins are more difficult to achieve. Rectal tumors with only superficial involvement of the rectal wall may be susceptible to transanal resection. Deeper or transmural involvement generally require a total mesorectal excision, in which all the mesorectal tissues enveloped by the intact visceral layer of the pelvic fascia are resected. More advanced rectal tumors, with direct invasion of perirectal tissues, may be susceptible to neoadjuvant chemotherapy or radiation therapy (or both) prior to resection [27, 28]. Preoperative radiation therapy has also been proposed prior to mesorectal excisions [29].

From the preceding discussion, it is apparent that imaging plays a critical role in TNM staging and, therefore, in determining the type of therapy offered to colorectal cancer patients. CT and MRI have been used extensively for the preoperative staging

Table 10.1 TNM Classification of Colorectal Carcinoma

Stage	Finding
Tumor	
T1	Tumor invades submucosa
T2	Tumor invades muscularis propria
T3	Tumor invades muscularis propria into subserosa or nonperitonealized pericolic or perirectal tissue
T4	Tumor directly invades other organs or structures and/or perforates visceral peritoneum
Regional nodal metastasis	
NX	Regional lymph nodes cannot be assessed
N0	No nodal metastasis
N1	Metastasis in one to three pericolic or perirectal nodes
N2	Metastasis in four or more pericolic or perirectal nodes
N3	Metastasis in any node along course of a named vascular trunk and/or metatasis to apical node(s)
Distant metastasis	
MX	Presence of distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

of colorectal carcinoma, with variable results. Findings associated with transmural spread of tumor include an irregular, serrated or spiculated outer contour of the mass (Fig. 10.8), loss of fat planes between the large bowel and surrounding muscles, a mass directly invading a nearby organ, poor definition of fascial planes or strands of soft tissue extending to the perirectal or pericolonic fat tissues. The tumor can directly invade the seminal vesicles, prostate, bladder, uterus, small bowel, bones or other organs. However, fat planes between the mass and surrounding tissues or organs can be obliterated by inflammation or fibrous reaction to the tumor without actual invasion. CT and MRI have benefited from technological advances in hardware and software, such as multi-detector technology (CT) and high resolution surface coils and parallel imaging (MRI). Unfortunately, correlation with operative findings and histopathological findings is imperfect, as definite invasion demonstrated by imaging findings is usually obvious upon macroscopic dissection, whereas microscopic invasion eludes preoperative diagnosis. Early studies showed sensitivity performance of CT between 55 percent and 60 percent for determining local

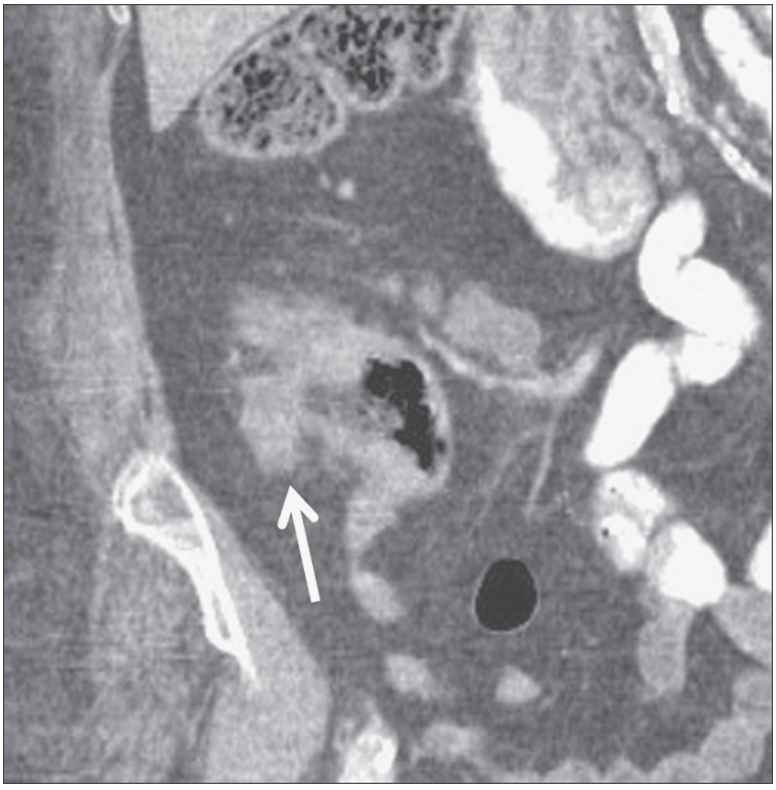


Fig. 10.8 Coronal CT reformation of axial CT data demonstrates a soft tissue mass in the wall of the cecum (arrow). Note the irregular, serrated outer contours of the mass with strands of soft tissue, indicating transmural spread of tumor, which was confirmed at laparotomy

invasion, as compared to the TNM classification [30, 31]. Multi-detector technology, with higher spatial resolution, may allow a more accurate estimation of the depth of mural invasion[32]. In general, CT is more accurate in detecting T4 and T3 lesions than T2 and T1 lesions. High resolution multi-planar MRI with surface coils compares favorably with CT for accurate staging of local extension of disease.

9 Rectal Cancer Staging

Rectal cancer is associated with a poor prognosis because of the risk both for metastases and for local recurrence after surgery. Incomplete removal of the lateral spread of the tumor is the cause of the majority of these recurrences. Results of several histopathologic studies have revealed the importance of extramural tumor spread and the influence of this spreading on prognosis [33-36]. In one of the largest series published, T3 tumors with extramural spread of more than 5 mm were associated with a five-year cancer-specific patient survival rate of only 54 percent, but T3 tumors with 5 mm or less of extramural spread—regardless of whether lymph node involvement was present—were associated with a five-year cancer-specific survival rate of greater than 85 percent [33]. With the increasing availability of newer preoperative (neoadjuvant) therapy options, an accurate and reproducible staging technique is, therefore, essential to enabling colorectal specialist multidisciplinary teams to consider potentially complex treatment options. The challenge for preoperative imaging in rectal cancer is to accurately determine the depth of mural involvement by the tumor (T stage), and the distance from the tumor to the circumferential mesorectal resection plane. Endorectal US, MRI and CT (Fig. 10.9) have been used for this purpose [37].

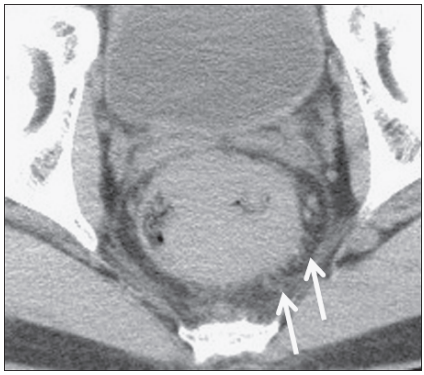


Fig. 10.9 Axial CT scan of rectal cancer. The mass involves nearly the entire circumference of the rectal wall. Note the strands of soft tissue extending to the peri-rectal fat (arrows), suggesting transmural extension of tumor. At surgery, this was, in fact, proven to represent tumor extending beyond the rectal wall (T3 disease)

Endorectal US is now an established modality for evaluation of the integrity of the rectal wall layers. With accuracies for T staging varying between 65 percent and 95 percent [38-40], endorectal US is very accurate for staging of superficial rectal tumors, but is not as useful for staging of advanced rectal cancer [19]. The overall staging accuracy for US in bulky tumors is less because the limited depth of acoustic penetration prevents accurate assessment of local tumor extent. Thus, although endorectal US is useful for staging of superficial rectal cancer, it is less suitable for evaluation of the mesorectal excision plane. Moreover, endoluminal US is not able to depict lymph nodes that are outside the range of the transducer, and cannot discriminate between lymph nodes inside or outside the mesorectal fascia, since the fascia is not identified at endoluminal US. This may explain the more recent widespread use of MRI, since these limitations do not apply to MRI with external coils.

CT has the advantage of evaluating the whole pelvis. Although early studies [41, 42] with CT reported high accuracy for staging locally advanced rectal cancer, more recent work, including a larger percentage of less advanced tumors, showed less encouraging results [43, 44] with accuracies varying between 52 percent and 74 percent. The low contrast and spatial resolution of CT protocols does not allow a detailed evaluation of the different layers of the rectal wall and may contribute to the low performance of CT for staging of superficial tumors. It is possible that the new-generation multi–detector row CT scanners, with improved spatial resolution and reconstructions in multiple planes, may provide better performance than conventional CT scanners [45, 46].

MRI is the most widely used technique for the local staging of rectal cancer [47-50]. The two major advantages of thin-section MRI are the ability to differentiate malignant tissue from the muscularis propria, allowing differentiation between T2 and T3 lesions (Fig. 10.10) and clear delineation of the mesorectal fascia (Fig. 10.11), which forms the circumferential resection margin at total mesorectal excision. This is a definite advantage over US, as determining the relationship of tumors with the mesorectal fascia has become increasingly important, perhaps as important as T stage determination. A standard protocol for MRI of rectal cancer consists of high-resolution T2-weighted fast spin-echo sequences, with or without the addition of contrast-enhanced sequences. Although endorectal coils have been used [51-53], most institutions prefer surface phased-array coil [54-56]. Staging failures, however, have been known to occur with MRI in the differentiation of T2 tumors (e.g., those confined to the rectal wall) and borderline T3 tumors (e.g., those that infiltrate the mesorectum). There is also a tendency for overstaging that is mainly attributed to desmoplastic reaction, which can cause spiculations in the perirectal fat that may or may not contain viable tumor cells. In a recent large multi-center study that compared high resolution MRI with mesorectal excision specimens, the depth of tumor spread depicted on the thin-section MR images was within 5 mm of the histopathologic measurement in the majority of patients [57]. Early work with 3 Tesla MRI suggests that improvement in accuracy for rectal cancer staging is only marginal [58].

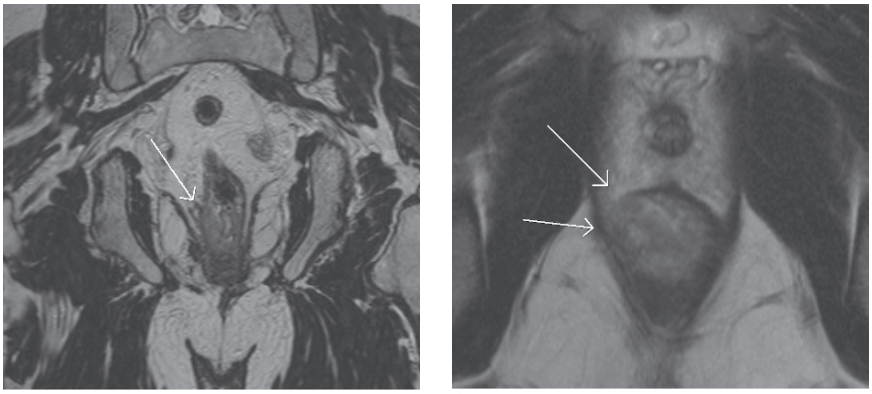


Fig. 10.10 These two cases illustrate the ability of MRI to differentiate between T2 and T3 rectal tumors. A coronal T2-weighted image **(a)** demonstrates neoplastic thickening of the right rectal wall (arrow), without transmural extension. On a different patient **(b)**, an axial T2-weighted image shows a tumor infiltrating beyond the outline of the rectal wall (arrow). Both cases courtesy of Michael A. Blake, MD

10 Lymph Node Detection

One of the major roles of preoperative imaging in colorectal cancer is the identification of a tumor that has spread beyond the wall of the colon. At any phase in the evaluation of patients with colorectal cancer, demonstration of systemic metastasis has profound therapeutic and prognostic implications. In the absence of systemic metastases nodal status become important, and when unresectable nodal metastases have been excluded, T-stage becomes important. However, identification of nodal disease is still a diagnostic problem for the radiologist.

To determine the nodal stage of colorectal carcinoma, a radiologist must be aware of the predictable patterns of lymph node drainage from the affected portion of the colon [40, 59, 60]. The distribution of regional lymph node metastases in carcinoma of the left side of the colon, rectum and anus can be well shown with CT or MRI. Recognizing the location of nodes in the mesocolic, left colic and inferior mesenteric artery nodal groups is helpful for developing a systematic approach for detecting nodal metastases [60]. Carcinomas of the cecum, right colon and proximal transverse colon can metastasize to local mesenteric nodes (Fig. 10.12), and then to peripancreatic lymph nodes, simulating primary pancreatic cancer [61]. Tumors arising from the upper portion of the rectum drain to the inferior mesenteric nodal chain, whereas those arising from the lower rectum drain laterally and into the internal iliac node groups (Fig. 10-11).

Imaging is capable only of depicting enlarged lymph nodes, recognizing that enlargement can also be secondary to reactive or hyperplastic nodes from associated inflammation. Lymph nodes should be measured in short axis, and the upper limit of normal varies with the specific location but, in general, is accepted to be 10 mm for retroperitoneal, mesenteric, external iliac and inguinal nodes, 8 mm for internal iliac, obturator and lateral sacral nodes and 5 mm for perirectal nodes. The

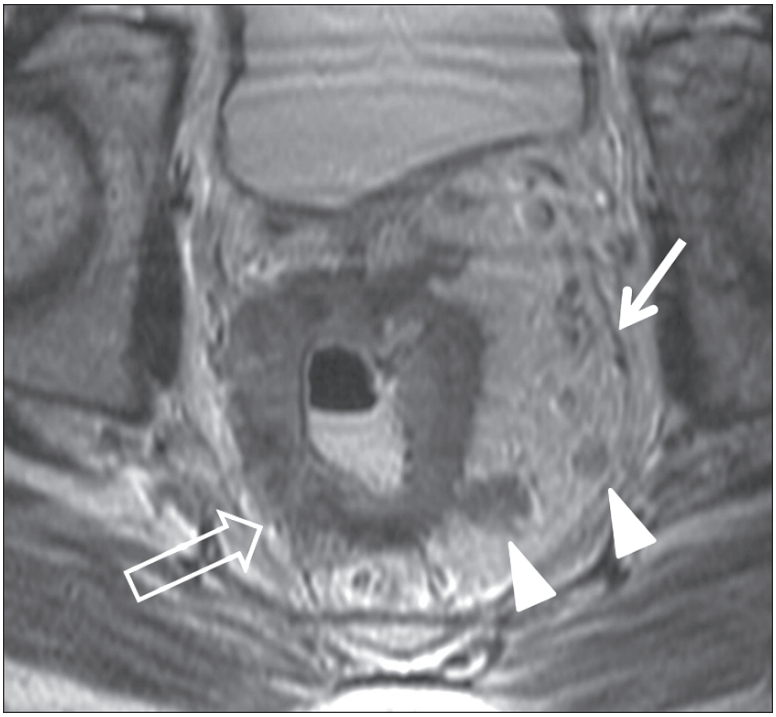


Fig. 10.11 Axial T2-weighted MRI image demonstrates a tumor mass involving the complete circumference of the rectum. The mesorectal fascia is preserved on the left side (arrow), but appears to be involved on the right side (open arrow). In addition, note multiple enlarged perirectal nodes (arrowheads). Other images (not shown) demonstrated clear evidence of invasion of the prostate gland (T4 stage). Case courtesy of Michael A. Blake, MD

addition of [18F] Fluorodeoxyglucose (FDG) positron emission tomography (PET) aids in increasing the specificity of CT by adding a functional element to the purely anatomical and morphological information provided by CT [62]. Sensitivity for detecting of tumors in normal-size lymph nodes can also be improved by MRI after administration of ultra-small particles of iron oxide [63]. Early experience with this agent indicates that high resolution T2-weighted images can detect foci of rectal cancer in mesorectal lymph nodes 3 to 4 mm in size [63].

11 Search for Liver Metastases: US, CT, MRI

Hematogenous spread of colorectal cancer tumor cells to the liver is a common problem in clinical practice and is likely the result of the dual blood supply of the liver through the hepatic artery and portal vein. The liver serves as the first end-capillary bed and can easily trap the tumor cells or emboli. Liver metastases ultimately develop in approximately 40 percent of patients who undergo curative resection of colorectal

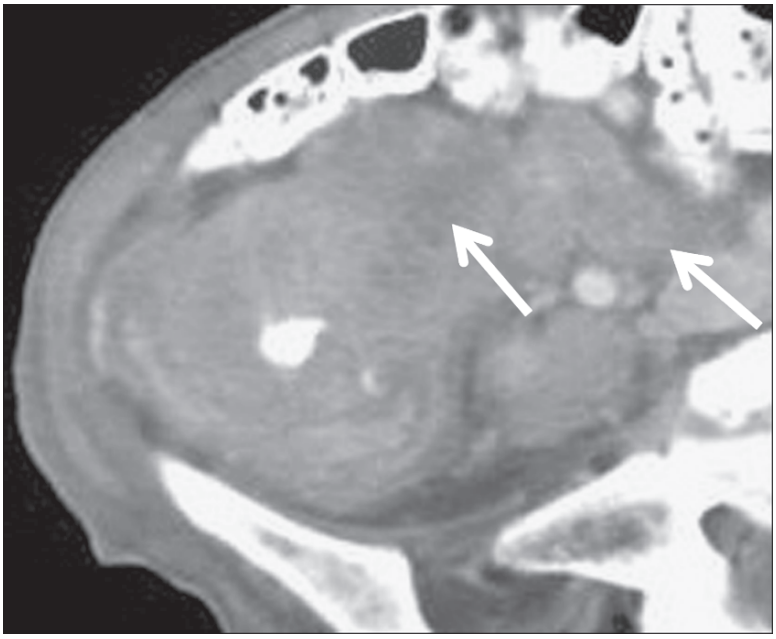


Fig. 10.12 Axial contrast-enhanced CT scan demonstrates a bulky mass arising from the cecum, with enlarged lymph nodes in the regional mesentery (arrows)

cancer. The development of liver metastases is a poor prognostic sign. For other cancers this usually indicates that disease is no longer curable. However, aggressive resection of a limited number of colorectal cancer liver metastases may be associated with long term survival [64-66]. Therefore, detection and accurate determination of the precise number and size of liver metastases is particularly important. Survival rates of up to 20 percent to 40 percent have been reported after wide resections of liver metastases from colorectal cancer. As image- guided therapy of liver tumors increases in popularity, the need for accurate staging will also increase. Thus, in a patient with newly diagnosed colorectal cancer, a thorough evaluation of the liver to rule out metastases is mandatory prior to bowel resection with curative intent.

As metastases grow they become progressively easier to detect with imaging modalities. Blood tests that are commonly used to follow patients with colorectal cancer, and to identify those patients that require additional evaluation, include measurements of serum carcinoembryonic antigen (CEA) and liver function tests. Unfortunately, the sensitivity of CEA measurements is low (50 percent to 60 percent) [67, 68], and its use in practice is limited. Many imaging modalities have been used for detecting liver metastases with variable success. Regardless of the technique used, the ability to detect a focal space- occupying lesion in the liver depends on the size of the tumor, the spatial and contrast resolution of the imaging method, the difference in contrast and perfusion between the tumor and background liver parenchyma, and the adequacy of the method used for displaying images after

acquired [69]. In general, a test is useful if sensitivity remains high at an acceptable specificity level. In a meta-analysis that studied the detection rate of liver metastases with multiple modalities, Kinkel, et al. [70] suggested that the minimum acceptable specificity of imaging tests for this indication should be 85 percent.

CT and MRI are the most widely used techniques for evaluating the liver in the initial staging and follow-up of colorectal cancer patients. For detecting liver metastases, carefully performed CT and MRI studies with state-of-the-art equipment and interpretation by experienced radiologists afford similar good results [44, 71, 72]. Other modalities such as ultrasonography and, more recently, PET imaging are also used in specific circumstances. The sensitivity and specificity of ultrasonography improve substantially with the addition of microbubble contrast agents, which essentially augment the doppler and harmonic ultrasound signal [73, 74]. Ultrasound contrast materials, however, are not widely used due to limited availability and a general perception that the examination becomes excessively time consuming and elaborate. Intraoperative ultrasonography has higher sensitivity than transabdominal ultrasound, CT and MRI [75, 76]. Therefore, during resection of liver metastases, intraoperative ultrasound provides valuable information that may alter the preoperative surgical plan. CT is usually preferred because it is more widely available and because it is well established for evaluating the extra-hepatic abdominal organs and other tissues.

On CT the typical colorectal cancer metastasis is hypovascular and appears hypoattenuating relative to background liver parenchyma (Fig. 10.13). Thus, for adequate detection, administration of intravenous contrast material and scanning during the peak of liver enhancement are critical. Peak enhancement typically occurs during the portal venous dominant phase, which occurs approximately 60 to 80 seconds after the initiation of contrast injection. Parenchymal attenuation should increase by at least 50 Hounsfield units with intravenous contrast for an adequate CT examination. Therefore, good CT technique requires administration of appropriate volume and concentration of iodine in the contrast material used, as well as adequate technique for contrast delivery. Studies using intraoperative palpation and ultrasound as standard of reference have reported high per-lesion sensitivity of greater than 85 percent [77, 78]. With the recent introduction of multi-detector CT scanners, it is likely that sensitivity may increase to 90 percent to 95 percent on a per-lesion basis using intraoperative findings, with ultrasonography as the standard of reference. Early data suggests that this is the case [79]. Enthusiasm about the use of CT during arterial photography, an invasive technique that requires catheterization of the superior mesenteric or splenic artery for direct injection of contrast, has decreased since the arrival of the latest generation CT scanners.

Detection of metastases with MRI requires the acquisition of multiple sequences and administration of intravenous contrast. Although the appearance of colorectal cancer metastases on MRI is variable, the T1 and T2 relaxation times of metastases are prolonged relative to normal liver parenchyma. This typically results in hipointensity on T1-weighted sequences and hyperintensity on T2-weighted images (Fig. 10-14). Metastases can also have a perilesional halo of high signal, indicating viable tumor, or demonstrate a “doughnut” or “target” appearance (Fig. 10.14). An advantage of MRI is the superior ability to characterize multiple lesions and

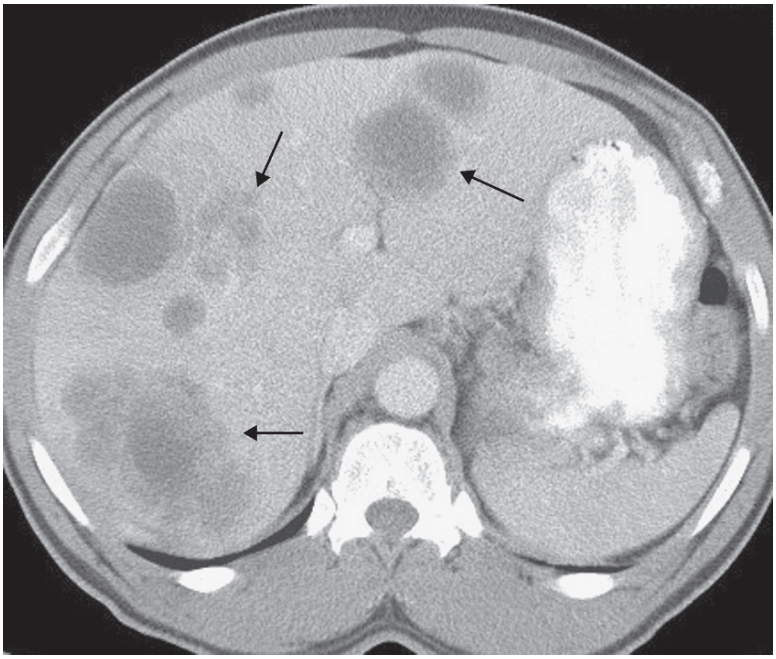


Fig. 10.13 Axial contrast-enhanced CT image demonstrates multiple low attenuation, poorly circumscribed masses in the liver. Some lesions demonstrate central areas of necrosis

differentiate solid, benign lesions such as cysts and hemangiomas from metastases. On heavily T2-weighted scans, fluid-containing lesions (cysts and hemangiomas) typically remain hyperintense, whereas metastases drop signal and demonstrate lower intensity. Similar to CT, detection of metastases with contrast-enhanced MRI is maximized during the portal venous phase (Fig. 10-14). The reported sensitivity of MRI using multiple combinations of sequences and gadolinium chelates as contrast material varies between 65 percent and 95 percent [70, 80-82], with a mean of approximately 80 percent. Administration of liver-specific contrast agents that are taken up selectively by the hepatocytes or, less often, Kupffer cells provide a modest increase in sensitivity [83-85]. Benefits of their use have not been broadly accepted, though their use in specific circumstances is likely to increase in the future.

12 PET and PET/CT

FDG-PET is a useful imaging tool in the management of patients with colorectal carcinoma. This technique is able to measure and visualize metabolic changes in tumor cells. Interestingly, avidity for FDG is not limited to carcinomatous cells, but is also seen in adenomatous polyps [86]. This feature results in the theoretical ability to distinguish viable tumors from scar tissue, and in the detection of tumor foci at an earlier stage than generally possible with CT or MRI. There are now

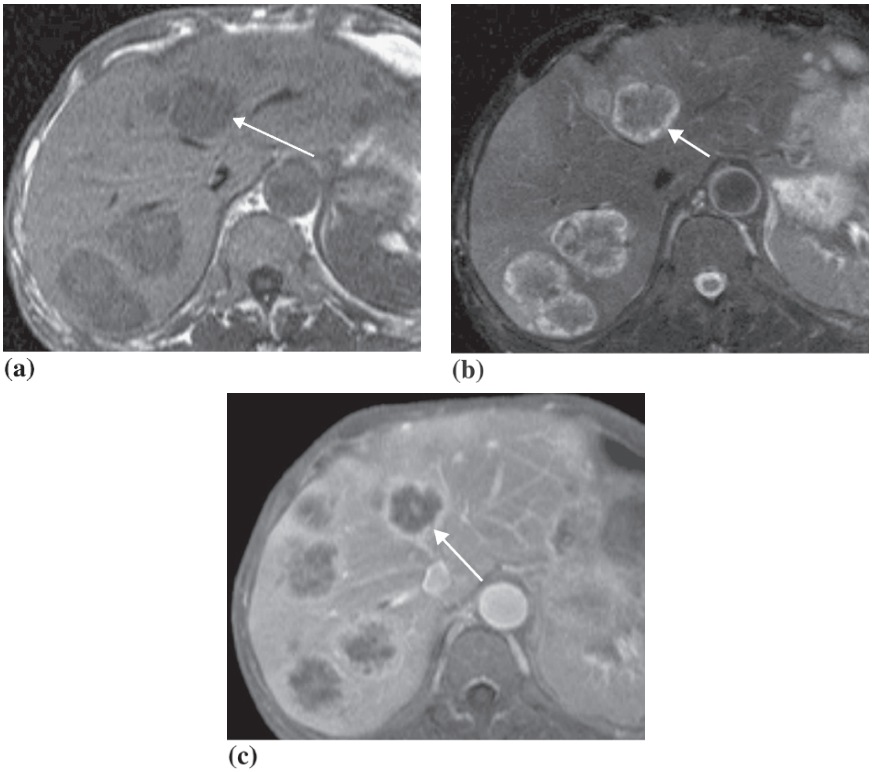
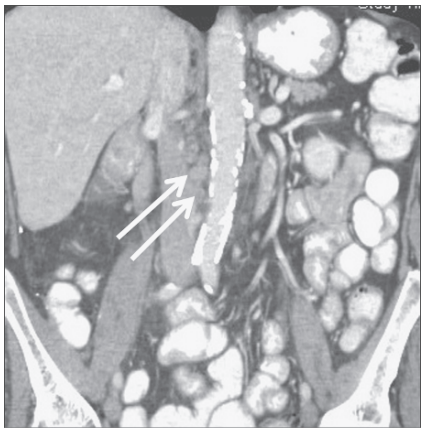
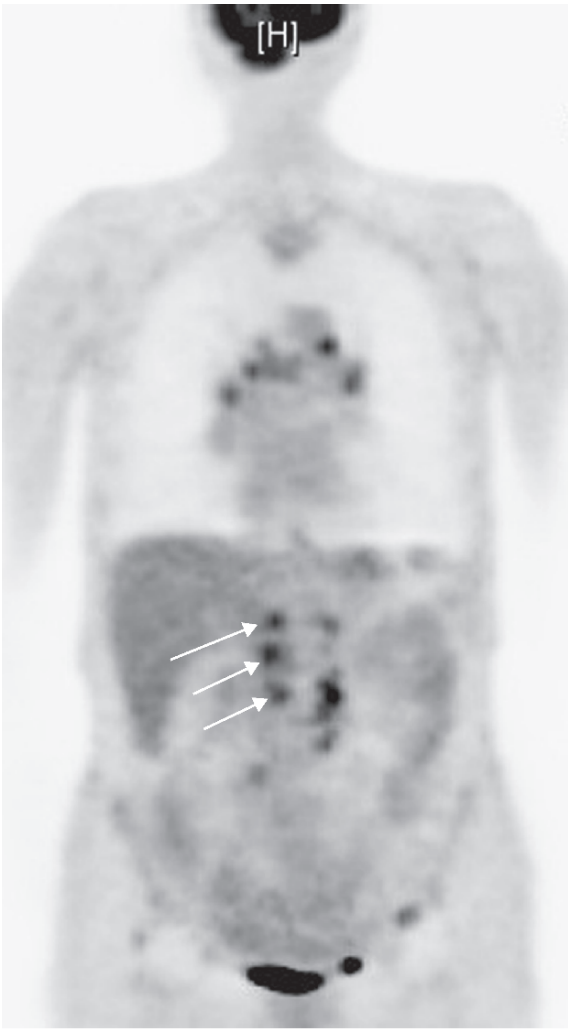


Fig. 10.14 Typical appearance of colorectal cancer metastases on MRI. The lesions demonstrate low signal intensity on T1-weighted images (**a**), intermediate signal intensity with a perilesional halo of high signal on T2-weighted images (**b**) and peripheral, annular, enhancement after intravenous administration of gadolinium chelates (**c**)

accumulating data that PET/CT could be used as the first test to assess metastatic disease and lymphadenopathy (M- and N-stage, respectively) for evaluating cancers with an intermediate to high pre-test likelihood of metastatic disease [62, 87, 88]. In this setting there is great opportunity for subsequently selecting and tailoring the performance of CT or MRI to define the structural relations of abnormalities identified by PET, when this information would be of relevance to management planning. FDG-PET plays a pivotal role in staging patients before surgical resection of recurrence and metastases, in the localization of recurrence in patients with an unexplained rise in serum carcinoembryonic antigen (Fig. 10-15) and in assessment of residual masses after treatment. In the presurgical evaluation FDG-PET is also best used in conjunction with anatomic imaging to combine the benefits of both anatomical and functional information, which leads to improvements in preoperative staging and preoperative judgment on the feasibility of resection. Another advantage of FDG-PET is the ability to evaluate the whole body with a single examination (Fig. 10-15). Although the ability of FDG-PET to detect small



(a)



(b)

(subcentimeter) liver metastases is inferior to high resolution MRI or state-of-the-art CT, it increases the specificity of cross-sectional imaging methods for detecting extra-hepatic disease in the abdomen [89]. It also appears that FDG-PET (especially when combined with CT) has great potential in monitoring the success of ablative therapies, and in the prediction and evaluation of response to radiotherapy, systemic therapy and combinations. Integration of FDG-PET into the management algorithm of colorectal cancer patients alters and improves therapeutic decisions, and may also reduce morbidity due to unnecessary surgery.

13 Post-treatment Follow-up

Imaging re-staging of colorectal carcinoma after treatment with surgery, radiation and/or chemotherapy poses additional challenges. The sequelae of prior treatment can be difficult to differentiate from residual cancer, and the likelihood of successful salvage therapy is even less than at presentation. Falsely assigning post-therapy changes to recurrent disease may potentially lead to subjecting patients to additional morbid treatments when cure has already been achieved. Thus, in post-treatment follow-up, the presence and extent of disease is equally critical to treatment selection and patient outcome as it is in primary staging. Unfortunately, in most patients receiving chemotherapy for colorectal metastases, a complete response on CT scan does not mean cure [90]. As stated in the preceding section, there is increasing evidence that FDG-PET (combined with CT or MRI for anatomical correlation of findings) may be the best modality for a comprehensive imaging monitoring of progression or regression of disease.

Key Points

- Colorectal cancer continues to be a common and deadly disease.
- Since many of the disease-specific cancer deaths are potentially preventable by timely removal of adenomatous polyps, continued efforts focus on educating the public to achieve population-wide screening of average risk adults.
- It is expected that CT colonography will play a major role in achieving this goal.
- However, once colorectal cancer develops, the most important role of imaging is accurately staging the disease.

Fig. 10.15 Utility of FDG-PET following resection of colorectal carcinoma. Coronal CT reformation (**a**) demonstrates slightly enlarged retroperitoneal lymph nodes (arrows). Whole-body FDG-PET image shows hypermetabolic foci matching the location of these lymph nodes. Additional hypermetabolic foci are seen in the mediastinum and hila. Tumor recurrence was confirmed in this patient with prior left hemicolectomy for colon cancer and rising CEA levels

- The TNM classification is currently the preferred method for staging.
- Precise delineation of depth of mural involvement, transmural extension, lymph node invasion and detection of liver metastases are specific tasks that the various imaging techniques and methods are expected to perform.
- Recent developments that have improved performance of imaging tests include MDCT, high-resolution MRI with endocavitary coils in some cases, high resolution endosonography, PET and PET/CT and organ-specific contrast agents for MRI.

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