42. The Preoperative Staging of Rectal Cancer

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Introduction

- The effective evaluation of a newly diagnosed rectal cancer should result in a determination of the need for neoadjuvant therapy, the potential for sphincter preservation, and the expected quality of life following treatment. The currently used system proposed by American Joint Committee on Cancer (AJCC) for staging rectal cancer is listed in Table 40.1.
- The tumor-related factors of prognostic significance, which may be evaluated prior to the treatment of rectal cancer, include the depth of penetration of the tumor through the rectal wall, the presence or absence of metastases to the regional and pelvic lymph nodes, and the presence of distant metastases.
- Clinicians have a variety of diagnostic tools at their disposal that can aid in delineating these aforementioned factors.
- The most commonly used modalities for the preoperative staging of rectal tumors available today are digital rectal examination, computed tomography (CT), endorectal ultrasonography (ERUS), magnetic resonance imaging (MRI), and positron emission tomography combined with computerized tomography (PET/CT).

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Local and Regional Staging

Digital Rectal Examination (DRE)

- Careful digital exam of a rectal tumor may yield valuable information regarding the location and degree of fixation of the tumor to the rectal wall and sphincter muscles (Table 42.1).
- DRE alone is considered inadequate in the staging of rectal cancer.

Rectal Ultrasound

- Endorectal ultrasound (EUS) is an outpatient procedure requiring only enema preparation and often no sedation.
- The accuracy of ERUS is user dependent and variable (Fig. 42.1).
- The Minnesota series, one of the largest series published in 2002 by Garcia-Aguilar et al., describes 1,184 patients with rectal carcinoma or villous adenoma that underwent ERUS. Histopathologic correlation was available for the 545 patients who had no prior radiotherapy.
  - The accuracy of ERUS in assessing the level of penetration was only 69 %, with 18 % overstaged and 13 % understaged.
  - For nodal involvement, the accuracy in the 238 patients who had radical surgery was poor, 64 % with 25 % overstaged and 11 % understaged.
- Limitations to ERUS:
  - A significant learning curve associated with the interpretation of the endorectal ultrasound image.
    - Rafalesen et al. reported that the reader experience had a significant effect on the assessment of penetration of the bowel wall by tumor. When comparing more experienced with less experienced radiologists, the accuracy for bowel wall penetration was 90 % vs. 66 %, respectively.
  - Overstaging of a tumor is common because of the inability of ultrasound to differentiate perirectal inflammation from tumor infiltration in the perirectal fat.
  - ERUS is difficult to perform in near obstructing lesions and those higher up in the rectum.

Table 42.1 Tumor characteristics to assess and record on digital examination

Location
Morphology
Number of quadrants involved
Degree of fixation
Mobility
Extrarectal growths
Direct continuity with other structures (vagina)

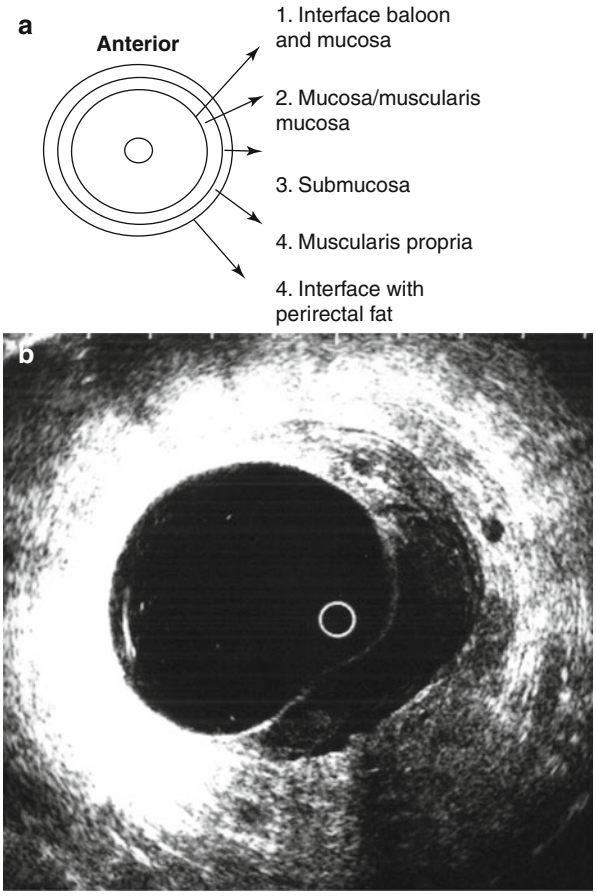

Fig. 42.1 The main concept in the use of MRI to stage rectal cancer is to obtain high-resolution images within small field-of-view thin sections with fast/turbo spin echo (FSE/TSE) T2-weighted axial and coronal views of the rectum. (**a**) EUS demonstrating the five layers of the rectum, (**b**) Standard EUS of a rectal tumor

Magnetic Resonance Imaging

- MRI use in staging rectal cancer was originally described in 1986.
- Kim et al. compared the histopathologic staging with the preoperative staging in 217 rectal cancer patients. The accuracy for the depth of invasion was 81 % and for regional lymph node metastasis was 63 %.
- MRI T staging has been defined (Table 42.2).
- MRI identification of metastatic lymph node involvement has not been standardized.
  - Criteria that are most predictable for determining lymph node metastasis are signal heterogeneity and an irregular border. Size criteria are not adequate. It is important to remember that in patients

Table 42.2 MRI T staging as proposed by Brown et al.

MRI T stage
T1: Low signal in the submucosal layer or replacement of the submucosal layer by abnormal signal not extending into circular muscle layer
T2: Intermediate signal intensity within muscularis propria. Outer muscle coat replaced by tumor of intermediate signal intensity that does not extend beyond the outer rectal muscle into perirectal fat
T3: Broad-based bulge or nodular projection (not fine speculation) of intermediate signal intensity projecting beyond outer muscle coat
T4: Extension of abnormal signal into adjacent organ, extension of tumor signal through the peritoneal reflection

with rectal cancer, approximately 15 % of lymph nodes smaller than 5 mm are positive for metastasis.
  - With the use of ultrasmall superparamagnetic iron oxide (USPIO)-enhanced MRI, recent advances have been made in the evaluation of lymph nodes. The iron oxide nanoparticle is given intravenously and is transported to the lymphatic system where it is picked by macrophages. The nanoparticle causes a decrease in signal intensity, and therefore, inflammatory lymph nodes exhibit less signal intensity.
- Initial results using this technique demonstrate up to 93 % sensitivity and 96 % specificity for perirectal lymph node metastasis. However, larger prospective trials are needed.
- In recent years, tumor involvement of the circumferential resection margin (CRM) has been identified as an important predictor of locoregional recurrence in rectal cancer patients undergoing a radical proctectomy with total mesorectal excision (TME).
- The preoperative assessment of the relationship of the tumor with the fascia propria of the rectum, the CRM in patients treated with TME, has become of upmost importance in selecting neoadjuvant therapy and planning the surgical resection.
- The fascia propria of the rectum is well visualized by phased-array coil MRI, and several studies have suggested that MRI can predict with high degree of accuracy the distance of the tumor to the fascia propria of the rectum (Fig. 42.2).

Distant Metastases

- Detection of distant metastasis is of prime importance for the accurate staging.
- The most common metastatic sites include the liver and lung.

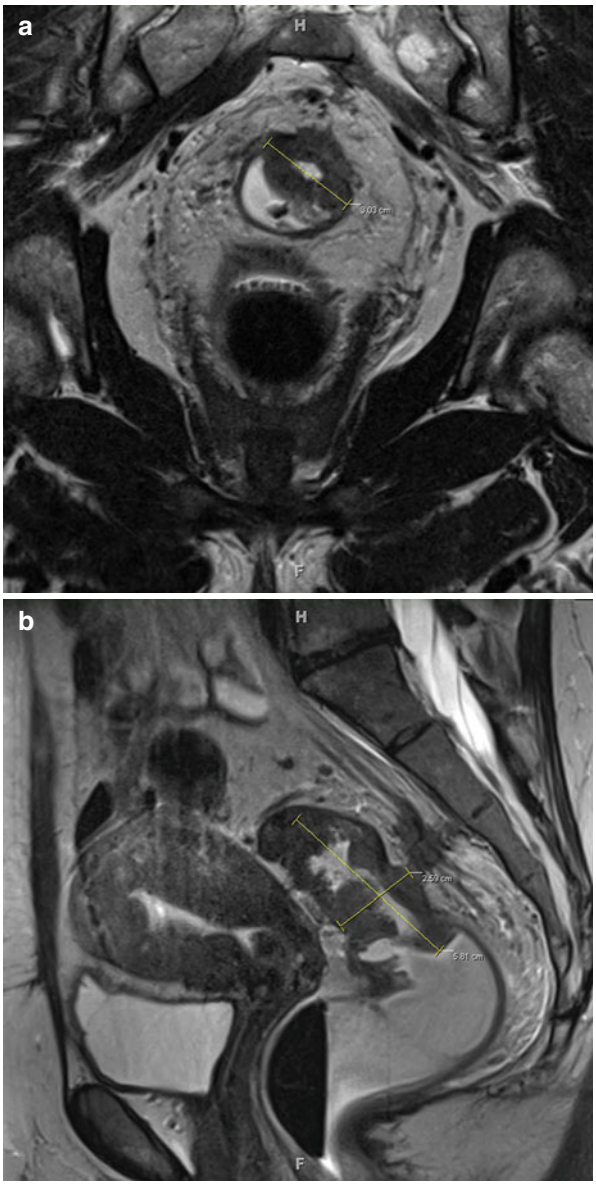

Fig. 42.2 (**a** and **b**). The main concept in the use of MRI to stage rectal cancer is to obtain high-resolution images within small field-of-view thin sections with fast/turbo spin echo (FSE/TSE) T-2-weighted axial and coronal views of the rectum.

- The common imaging modality used today to detect liver metastasis pre-operatively is computerized tomography (CT); however, MRI and PET/CT are being used more frequently (Tables 42.3 and 42.4).

Table 42.3 Sensitivity and specificity for EUS, CT, and MRI in the preoperative staging of rectal cancer

Stage	Imaging modality	Sensitivity % (95 % CI)	Specificity % (95 % CI)
T2	EUS	94 (90–97)	86 (80–90)
	MRI	94 (89–97)	69 (52–82)*
	CT	–	–
T	EUS	90 (88–92)	75 (69–81)
	MRI	82 (74–87)*	76 (65–84)
	CT	79 (74–84)*	78 (73–83)
T4	EUS	70 (62–77)	97 (96–98)
	MRI	74 (63–83)	96 (95–97)
	CT	72 (64–79)	96 (95–97)
Node positive	EUS	67 (60–73)	78 (71–84)
	MRI	66 (54–76)	76 (59–87)
	CT	55 (43–67)	74 (67–80)

Modified from Bipat S, van Leeuwen M, Comans E, Pijil M, Bossuyt P, Zwinderman A, Stoker J. Colorectal liver metastases: CT, MR Imaging, and PET for diagnosis – meta-analysis. Radiology. 2005:237;123–31.29

EUS endorectal ultrasound, *CT* computed tomography, *MRI* magnetic resonance imaging, *CI* confidence interval

*$p < 0.05$ EUS to other

Table 42.4 Accuracy of nodal staging in preoperative evaluation of rectal cancer with MRI pelvic phased-array coil

References	No. of patients	Accuracy (%)
Ferri (2005)	29	59
Matsuoka (2003)	19	89.5
Brown (2003)	60	85
Gagliardi (2002)	26	69
Blomqvist (2000)	47	47
Kim (2000)	217	63
Hadfield (1997)	28	76

Modified from Skandarajah A and Tjandra J. Preoperative loco-regional imaging in rectal cancer. ANZ J Surg. 2006;76:497–504

MRI magnetic resonance imaging

- A recent meta-analysis reported by Bipat et al. that evaluated the use of CT, MRI, or PET found that 18-fluorodeoxyglucose positron emission tomography (FDG-PET) was the more accurate method to detect liver metastasis on a per-patient basis.
  - When evaluating different lesions, MR imaging at 1.5 T and FDG-PET were comparable and significantly more accurate than CT.
  - Sensitivity estimates for all imaging modalities studied for lesions less than 1 cm were much less than for lesions ≥1 cm (11.6–29.3 % vs. 65.7–90.2 %).
  - They reported an accuracy rate of 95 % on the depth of invasion for MDRCT vs. 100 % for MRI, whereas lymph node accuracy was 70 % vs. 61 % for MDRCT and MRI, respectively.

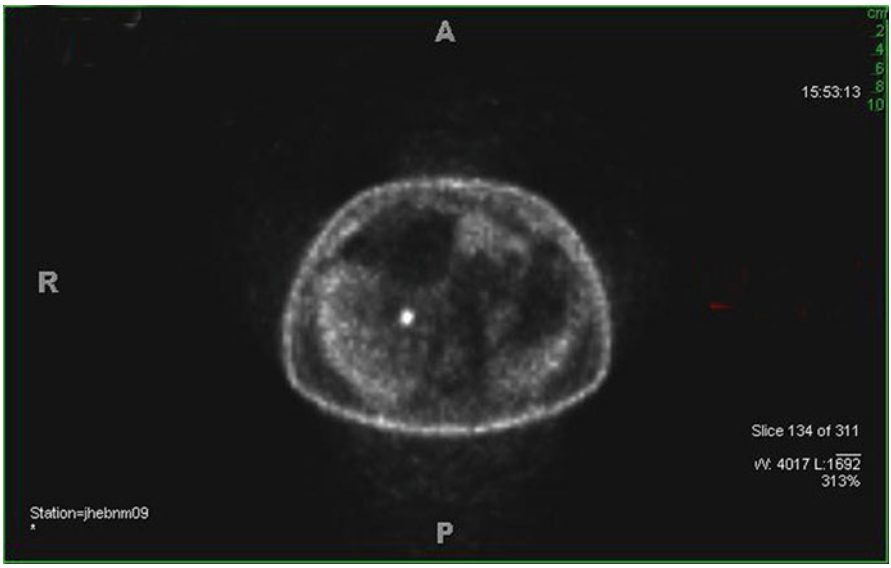

Fig. 42.3 PET scan

- At the present time, FDG-PET is primarily used for the diagnosis of local and distant recurrence after curative surgery for colorectal cancer (Fig. 42.3).
- The impact of FDG-PET and FDG-PET/CT in the preoperative staging and management of rectal cancer patients has been studied by Heriot et al. in a series of 46 patients who were assessed with FDG-PET scans at the time of their initial diagnosis. The surgical management was changed in 17 % of the patients because of positive FDG-PET scan findings that upstaged the disease.
- Furthermore, Gearhart et al. demonstrated in 37 patients that FDG-PET/CT was able to demonstrate additional significant findings in 38 % of patients with a known primary rectal cancer resulting in an alteration in the treatment planning for 27 % of patients. These changes in management included canceling surgery and changing the field of administered radiation.
- Preoperative radiation of rectal cancer causes various degrees of tumor regression resulting in scarring and fibrosis that impairs accurate imaging.
- The value of EUS in restaging rectal cancer following radiation is limited.
- The limitation of MR imaging in rectal cancer has been its inherent inability to differentiate fibrosis from residual tumor following treatment. For this reason, conventional MRI has not been shown to be useful in determining response to therapy.
- However, functional MR imaging has been demonstrated to be useful in the evaluation of the response of rectal cancer to neoadjuvant therapy.

- The components of functional MR include spectroscopy, diffusion, and contrast enhancement.
  - Further studies to validate promising early results are necessary.
- The use of serial FDG-PET/CT in predicting response to neoadjuvant therapy has been evaluated by several investigators.
  - The reported specificity for predicting a near-complete or complete pathologic response to therapy with serial FDG-PET/CT is 60–95 % (Table 42.5).
  - The timing of serial FDG-PET appears to be important in that FDG-PET/CT after 2 weeks of treatment can predict pathologic response with similar specificity to FDG-PET/CT performed at the end of treatment. This earlier time period may be advantageous for determining if the neoadjuvant regimen should be modified in patients that appear not to be responding.

Table 42.5 Specificity of FDG-PET to predict near-complete or complete pathologic response following chemoradiation for primary rectal cancer

Author	Year	*N*	Specificity (%)	Parameter	Endpoint
Guillem	2004	10	80	VRS	pCR (TRG 1)
Amthauer	2004	20	86	RI	R1
Capirci	2004	78	76	VRS	TRG 1–2
Chessin	2005	21	95	VRS	Response
Deneke	2005	23	60	RI	Major response
Melton	2007	21	81	RI	TRG 1–2
Cascini	2006	33	87	RI	TRG 1–2
Caprici	2009	81	80	RI	TRG 1–2

Modified from Capirci C, Rubello D, Pasini F, et al. The role of dual-time combined 18-fluoridedoexyglucose positron emission tomography and computed tomography in the staging and restaging workup of locally advanced rectal cancer, treated with preoperative chemoradiation therapy and radical surgery. Int J Radiation Oncology Biol Phys. 2009;74:1461–69.51
VRS visual response score, *RI* response index, *TRG* tumor regression grade