Primary rectal cancer local staging

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Abstract The treatment of patients with a malignant rectal tumor has evolved over the past few years. The role of medical imaging techniques, notably MRI, has become increasingly important in the preoperative assessment of rectal tumors. Radiologists are finding that their presence is requested more and more frequently at multidisciplinary team meetings for decision-making on the treatment of these tumors and therefore they must have a grounding in the therapeutic issues involved. Locoregional assessment of malignant rectal tumors may be performed prior to initiating treatment or as a re-evaluation following neoadjuvant therapy. We are interested in the assessment of the initial locoregional extension of these rectal tumors and we place much emphasis on the ability to identify MRI criteria which determine the patient’s prognosis and treatment. We will also examine the advantages of MRI as well as its limits in this assessment.

During the past decades, the management of patients with rectal cancer has evolved with a significant reduction in local recurrence rate due to advances in surgical techniques and adjuvant therapies. Radiologist is now part of the decision-making process during multidisciplinary team meetings, both giving an anatomic definition of the tumor for surgical planning and differentiating between good and bad prognosis tumors. This review explains the role of the radiologist in patient management and describes the clinically relevant points radiologists have to notify during primary local staging of rectal cancer patients. It also gives the evidence for the use of magnetic resonance imaging (MRI) in staging these patients, reviews MRI performances in identifying several clinically relevant features, and gives some recommendations for how to perform rectal MR examinations.

Keywords Rectum; MRI; Tumor

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Local staging modalities

The two imaging modalities that are currently being used for local rectal tumor staging are endorectal ultrasonography (ERUS) and magnetic resonance imaging (MRI).

ERUS

Unlike with MRI, using ERUS, all layers of the bowel wall can be examined, with high accuracies reported for T staging [1]. True performances of ERUS are difficult to evaluate because in many initial studies, the patients with stenosing tumors were excluded. However, it is well admitted that ERUS remains the imaging method of first choice for differentiating between T1 and T2 tumors and also for the assessment of T1 tumors before local excision, but that it performs less well in cases of advanced and polypoid lesions [2,3]. The fascia recti and peritoneum cannot be correctly visualized by ERUS so that the circumferential resection margin (CRM) status and degree of peritoneal involvement cannot be assessed accurately (Fig. 1).

As far as T2 versus T3 tumors differentiation is concerned, although sensitivity of ERUS (90–96%) is high, specificity is lower (75–90.6%) [1,2,4], respectively, with the same difficulties as those observed with MRI to discriminate between T2 and small T3 tumors and interpret T2 with desmoplastic stranding in the mesorectal fat. For lymph node involvement, results are comparable to those obtained with MRI [1,2].

Further downside of ERUS is that it is subject to operator’s skill and that surgeons or radiotherapists cannot read the images as easily as with MRI or CT.

The use of endorectal ultrasonography is variable throughout Europe, with Holland being one of the countries where it is least widely used. In France, its use depends on its availability and on the preferences of oncologists, but recommendations still advise ERUS as a first-step imaging modality for local staging of rectal cancer, when the tumor is not bulky and/or located in the upper rectum and/or fixed.

MRI

A group of 14 abdominal imaging experts from the European Society of Gastrointestinal and Abdominal Radiology (ESGAR) in a recent article [5], as well as ESMO clinical practice guidelines [6] and European rectal cancer consensus conference [7] recommend MRI as crucial for staging the primary rectal cancer. Beets-Tan et al. [5] further report a consensus reached by the panel of European experts that MRI is the imaging technique of first choice for primary staging of rectal cancer but that ERUS remains the first choice imaging modality when local resection is being considered.

In a recent meta-analysis including 21 studies from 2000 to 2011 excluding patients who underwent preoperative long-course radiotherapy or chemoradiotherapy, Al-Sukhni et al. [8] found a good accuracy of MRI for both CRM and T category (sensitivities and specificities of 77% [57–90%; 95% CI] and 94% [88–97%; 95% CI] for CRM and 87% [81–92%; 95% CI] and 95% [91–99; 95% CI] for T, respectively). In contrast to its performance for T category and CRM, MRI performance was more consistently poor for the assessment of lymph node metastases.

MRI protocol

Some teams use spasmolytic agents (e.g. Buscopan or Glucagon). Routine rectal filling, predominantly with ultrasound gel, is still a matter of debate. It allows better delineation of the lower pole of the tumor, particularly for readers with less experience and reduces artifacts on diffusion-weighted acquisitions. Conversely, it may compress the mesorectal fat and hamper evaluation of CRM [9] and may be uncomfortable to the patient.

The importance of rectal cancer MRI protocols on interpretation accuracy has been reported [10], particularly in terms of accuracy regarding assessment of anterior organ involvement for low rectal tumors. MR protocol includes 2D T2-weighted sequences acquired in sagittal, axial and oblique planes, with the sagittal sequence being used to determine the longitudinal tumor axis in order to angle the axial and coronal planes as perpendicular and parallel to the tumor axis, respectively. Incorrect plane obliquity leads to blurring of the muscularis propria or to a pseudospiculated appearance. For low rectal tumors, coronal planes should also be angled parallel to the anal canal in order to better evaluate relationship between the tumor and the anal sphincter [11]. Three-dimensional (3D) T2-weighted sequences permit the use of 1–2 mm thin sections with no intersection gap. They are theoretically able to compensate for difficulties to angulation of tumor such as tortuosity and redundancy of the rectum. However, evidence with respect to their superiority compared to 2D T2-weighted sequences is still lacking with contradictory results mainly in terms of contrast resolution and tumor conspicuity, due to many factors such as the type of MR unit used, section thickness and use of parallel imaging [12–14] (Fig. 2). Moreover, multiplanar reformatted images obtained away from the plane of acquisition are frequently blurred and small-FOV images are difficult to obtain.

As far as diffusion-weighted imaging is concerned, although more and more authors use it to improve the

Figure 1. Endorectal ultrasonography (ERUS) image of T3 rectal tumor (arrows). Note the small field of view of the ERUS image.
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diagnostic performance of MRI for the evaluation of tumoral response after chemoradiotherapy, there is so far no evidence that it is of some help for primary staging apart from improving tumoral and lymph node detection [5,15] (Fig. 3). They are thus not recommended for primary staging. In the consensus paper [5], the use of additional unenhanced T1-weighted sequence to T2-weighted FSE was supported by only 25% of the panelists, mainly for the help that it may provide characterizing coincidental pelvic findings. The authors did not either recommend the use of contrast-enhanced dynamic or steady state T1-weighted sequences, relying on their experience and on the lack of available evidence supporting the adjunct of contrast-enhanced sequences [5,16]. Some teams, mainly in France, somehow use fat-suppressed MR sequences in order to facilitate assessment of relationships of a low rectal tumor to the anal sphincters, particularly to the internal sphincter that enhances after gadolinium administration.

MR image interpretation

Location of the tumor

Detection of rectal tumor relies on clinical examination and/or endoscopy. The tumor is generally detected and located during digital rectal examination but may remain difficult to feel and/or locate for the physician, particularly in case of upper rectal tumors. Rectal tumor is most often well depicted on T2-weighted MR images.

There are different means of determining the height of the tumor. Rectal tumor level can be given with respect to its peritoneal or subperitoneal location, knowing that tumors located entirely above the peritoneal reflection, i.e. upper rectal tumor, will generally be treated like colonic tumors, i.e. without any neoadjuvant chemoradiotherapy unless they are considered T4 tumors. The anterior wall of the upper rectum is covered by the peritoneal reflection and the point of peritoneal attachment occurs at a

Figure 2. Coronal 2D T2-weighted MR image (a) shows better conspicuity of the tumor and of its extension in the mesorectum than coronal 3D T2-weighted MR image acquired in the same patient at the same time (b) (arrows).

Figure 3. Axial high b value (b = 1000) diffusion-weighted MR image (a) increases detection of the low rectum tumor which is hardly depicted on the corresponding T2-weighted MR image (b) (arrows).
variable height, particularly in women. In Gollub et al.’s study [17], median distances from the anorectal junction to the anterior peritoneal reflection was 67 to 69 mm (range 41–128 mm, 35–130 mm) and the average length of the anal canal was 41 and 36 mm for women. Both readers analyzing MR images indicated that the anterior peritoneal reflection was “probably” or “definitely” visible in 134 of 180 pelvic MR examinations (74.4%), as a thin T2 hypointense line 1 mm or less in thickness in most cases, in the midsagittal plane. Anatomic landmarks for identification of the most inferior portion of the peritoneal membrane were tip of seminal vesicles in men and the uterocervical angle in women (Fig. 4). Limitations for identification of this line included postoperative status, motion artifact, retroversion of the uterus, paucity of pelvic fat planes or large exophytic tumors. As the peritoneal reflection proceeds posteriorly, laterally and superiorly towards the anterior portion of the rectum, it is noteworthy that the peritoneal reflection will appear higher if visualized off midline.

The level of the rectal tumor may also be given from the anal verge, which is the distal end of the anal canal, as it is a reference point for physicians (Fig. 5). According to this reference, the rectum is divided into three thirds. Tumors of the lower third have a lowest edge, which is located less than 5 cm from the anal verge. It corresponds to the level where mesorectum tapers sharply (Fig. 6). The anorectal junction is held forward by the puborectal sling. The anorectal junction is an important landmark and it is seen as transition from low T2 signal (the superior border of the internal sphincter and the puborectalis complex = upper edge of the surgical anal canal) to intermediate T2 signal (rectal wall) (Fig. 7). It is the point where the internal layer of the muscularis propria thickens and becomes the internal sphincter. The external sphincter complex is composed of the puborectalis sling and then caudally of the external sphincter. Between these two sphincters, there is a plane called the intersphincteric plane.

Tumors are considered in the middle rectum if their lowest edge is located between 5 and 10 cm from the anal verge. At this level, the rectum is surrounded by mesorectum, itself limited by mesorectal fascia, forming the surgical plane of dissection for total mesorectal excision. Anteriorly the mesorectal fascia fuses caudally with the remnant of the urogenital septum forming a dense fascia band called rectovaginal septum in females and rectoprostatic fascia in men. Upper rectal tumors are located more than 10 cm from the anal verge, above the inferior point of the peritoneal reflection. Level of the tumor may also be given with respect to the upper pole of the internal sphincter.

**T staging and depth of tumor spread beyond the muscularis propria**

On T2-weighted images, stage T1 tumors are confined to the submucosa, which manifests as a hyperintense layer; stage T2 tumors extend into, but not beyond, the muscularis propria, which is seen as a hypointense layer; and stage
T3 tumors extend beyond the muscularis propria into the mesorectal fat [18]. T4 disease corresponds to spread of tumor into the visceral peritoneum (T4a) (Fig. 8) or adjacent organs (T4b). The structures most commonly involved by primary rectal cancer are the uterus, vagina, prostate gland and seminal vesicles. The assessment of tumor abutment of the presacral fascia and involvement of sacral nerve roots is also important for surgical planning as tumor extension into the proximal sacrum or nerve root involvement above the S2 vertebral level renders the tumor unresectable.

The relationship between tumor and the peritoneal reflection is important to assess in order to warn the surgeon to perform careful dissection to minimize the risk of tumor spillage in case of T4 a tumor.

T stage assessment depends on course of optimization of the MRI protocol but also on the experience of the reader [19]. It is known to be difficult to distinguish between T2 and small T3 tumors, particularly to differentiate between desmoplastic reaction and true mesorectal invasion, although the latter is known to form intermediate signal intensity linear bands, thicker than what is usually seen with desmoplasia.

However, it is much more important to measure the depth of extramural spread in the mesorectal fat than to give the T stage, since a T2 tumor has the same prognosis as a T3 tumor with less than 1 mm spread. T3 tumors with more than 5 mm mesorectal invasion (Fig. 9) have a cancer specific 5-year survival rate of approximately 54% versus 85% for tumors with less than 5 mm mesorectal invasion [20,21] (Fig. 10). The depth of extramural spread must be measured in millimeters beyond the outer edge of the longitudinal muscular layer and recorded according to Smith and Brown [21]. The MERCURY Study Group showed that there was excellent correlation between the depth of extramural spread and histopathologic results [22].

Low rectal tumors deserve special consideration because conventional staging systems are insufficient in these cases, because anatomy is different than for mid- and upper rectum and because three different types of surgery can be performed depending on tumoral stage [23].
continuity is not maintained. This applies to tumors extending into the internal sphincter (partial invasion) but not extending to the full thickness of muscularis propria or to the intersphincteric plane or beyond.

Lastly, in case of low rectal tumors extending within 1 mm of circumferential resection margin or in the intersphincteric plane (Fig. 11) and/or extending into or beyond the levator muscles, extralevator abdominoperineal excision is performed: the abdominal part of surgery follows the plane of total mesorectal excision (TME) dissection, as described above, but mobilisation is stopped at the upper border [11]. Recently, Shihab et al. [11,24] proposed a specific T staging for low rectal tumors to better define the tumor free margin. This staging is based on the coronal and axial T2-weighted images and includes precise assessment of the involvement of muscularis propria, of the intersphincteric plane and of the external sphincter.

Assessment of circumferential resection margin (CRM)

Identification of tumors with a potentially positive CRM by MRI is necessary for aggressive preoperative treatment and prevention of local recurrence [25] (Fig. 12).

A recent prospective multicenter study consisting of follow-up of 374 patients with rectal cancer assessed with MRI, of which 216 (57.8%) underwent primary surgery, confirms that MRI assessment of CRM status is superior to TNM-based criteria for assessing risk of local recurrence, disease-free survival and overall survival. Interestingly, it also demonstrates that CRM involvement is significantly associated with distant metastatic disease. When correlated with pathologic specimens, it has been shown that the risk of local recurrence is significantly increased with clearances...
of 1 mm or less, which are thus considered a positive CRM [26]. Using this 1 mm cut-off, specificity and negative predictive values are of 92 and 94%, respectively, for predicting involvement of the CRM by MRI [8,27]. The measured distance is the distance to the mesorectal fascia and/or to the levator ani muscles for low rectal tumors from either the tumor margin, tumor thrombus within a vessel, malignant node or tumor deposit. Limitations of assessment of the CRM include patients with low and anterior rectal tumors and thin patients with little perirectal fat.

**Extramuscular vascular invasion (EMVI)**

EMVI is invasion of large vessels directly by tumor, which are located deep to the muscularis propria. The presence of tumor signal intensity within an expanded vascular structure is highly suggestive of extramural vascular invasion (Fig. 13). The possibility of EMVI should be considered whenever tumor is seen to lie close to a vessel [28]. EMVI is considered by some authors as an important prognostic factor that should be identified on MRI [29,30]. A recent study [31] even reported that patients who presented a significant response of EMVI to neoadjuvant chemoradiation therapy showed improved disease-free survival.

**Nodal staging**

Nodal spread occurs via the mesorectal lymph nodes and along the superior rectal vessels as well as laterally along the internal and external iliac chains. They are typically at the level of the primary tumor or above. External iliac lymph nodes and obturator lymph nodes are consistent with metastases. Size criteria that are used to detect lymph node involvement are insufficient, as using a 5 mm short axis as a cut-off has proven to provide a sensitivity of 66% and a specificity of 76% [32]. Morphological criteria such as irregularity of the contours and heterogeneous internal signal intensity have been evaluated and better predict involvement than size alone [32,33]. Patients with 4 or more involved regional lymph nodes are known to have a worse prognosis [34]. These patients are somehow likely to present with other more easily recognizable poor prognostic MR features such as important depth of extramural spread or CRM involvement.

It is also important to identify involved lymph nodes located outside mesorectal fascia, as they will not be resected during standard anterior resection with total mesorectal excision and may for some authors benefit from additional treatment, as they may be responsible for local recurrence.

A recent study that matched lymph nodes seen on MRI with their precise histologic counterparts after total mesorectal excision reported that of the 341 nodes harvested, 120 were too small (<3 mm) to be depicted with MRI, and 15% of these contained metastases, with a node-by-node sensitivity and positive predictive value of 58 and 61.7%, respectively [35]. Moreover, there was no difference in the diagnostic accuracy between the primary surgery subgroup and preoperative radiation subgroups. Given the low performances of conventional criteria for assessment of lymph node status, the use of superparamagnetic iron oxide particles [36,37] or Gadofosveset [38] has been evaluated and yielded promising results. However, these specific agents have been withdrawn from the market and are currently not available. As far as diffusion-weighted MR imaging is concerned, it has been proved that although it improves detection of lymph nodes, it cannot help to accurately differentiate between benign and malignant lymph node [39] (Fig. 14).

**Prognostic risk factors**

There is a current trend to use MRI for identification of prognostic risk factors, thereby potentially allowing the
selection of low risk patients whose indication is primary surgery and the high-risk patients who will benefit from intensified neoadjuvant treatment [40]. Stratification of patients include mainly determination of the depth of tumor spread beyond the muscularis propria, EMVI, CRM, but also location of the tumor, nodal status, and presence of peritoneal perforation. The latest and seventh edition of the TNM has made changes based on recurrence and survival data.

Good prognosis patients are those whose tumor has a CRM >1 mm, T1—T2 or T3 tumors with extramural extension <5 mm, absence of extramural vascular invasion, N0/N1, tumors located in the middle or upper third [29,41–44]. The Mercury Study Group [42] in a prospective and multicenter study reported that for patients who were considered to have a good prognosis on the basis of a potentially negative CRM (>1 mm of the mesorectal fascia), of absence of extramural invasion, of tumors staged T1, T2 or T3 with extramural extension <5 mm and low rectal tumors not compromising the intersphincteric space or levator ani muscles, whatever the N stage, overall survival and disease-free survival were 68 and 85%, respectively and local recurrence rate was of 3%. Conversely, poor prognosis tumors include tumors with potentially positive CRM, a committed intersphincteric space, an extramural extension >5 mm and presence of extramural vascular invasion.

**Conclusion**

Endorectal ultrasonography and pelvic MR imaging are the two main imaging modalities for preoperative assessment of rectal tumor. Preoperative MR imaging of rectal cancer is now well defined and is part of the multidisciplinary team discussion. Preoperative MR imaging of rectal cancer implies optimization of MR technique and sequence parameters as well as familiarity of the reader with anatomy, limitations of the technique and understanding of how preoperative imaging impacts the management of the patient. Some key points that are not currently part of the TNM staging should somehow be incorporated into all reports for prognostic implications.

**TAKE-HOME MESSAGES**

- A pelvic MRI provides the elements required for the assessment of locoregional extension of a rectal tumor as well as prognostic elements.
- An endorectal ultrasound is the preferred medical imaging technique for differentiating T1 and T2 tumors.
- T2-weighted sequences without fat suppression in the three planes and perpendicular to the axis of the tumor are essential and are generally sufficient.
- Sections on the tumor must be 4 mm maximum and a small field of view must be used.
- Elements to identify are:
  - localisation of tumor in relation to the anal margin as well as in relation to the peritoneal reflection line,
  - T and N staging,
  - distance to the circumferential resection margin,
  - relation with sphincters,
  - intravascular extramural extension.

**Clinical case**

A 70-year-old man is experiencing rectorrhagia. Following an endoscopy, a rectal tumor was diagnosed and a pelvic MRI was requested to assess the locoregional extension of this lesion (Fig. 15).

**Questions**

1. Knowing that the distance we can measure in this sagittal section (Fig. 15a) between the lower edge of the tumor and the anal margin is 10 cm, how would you situate this tumor? What anatomical element would enable you to define the highest point of this lesion?
2. How would you classify this lesion for stage T? Justify your answer.
3. During multidisciplinary meetings, is the distinction between the stages T2 and T3 fundamental in the case of this tumor? Why?
4. How would you evaluate the prognosis of this tumor?

**Answers**

1. A tumor whose lower edge is 10 cm from the anal margin is at the limit of the upper rectum. However, from the sagittal section, we can observe that the main part of the tumor is located below the anterior peritoneal reflection line. Furthermore, in the axial section, the lower part of the tumor is surrounded by mesorectum. It is therefore a tumor of the mid-rectum.
2. The lesion must be classified as T3. In fact, in both the sagittal and axial sections perpendicular to the tumor, there is an area where the muscular layer is no longer visible, with a discreet tumoral extension into the mesorectal fat.

3. No, the distinction is not fundamental because the pro- 

grosses of a T2 lesion of the mid-rectum and, as in this case, of a T3 lesion with a small extension into the mesorectum <1 mm, are similar.

4. In theory, this tumor has a good prognosis because it is a tumor of the mid-rectum at stage T3 with an associated extension into the mesorectum <5 mm, a clear circumfer- 

tential resection margin, and no signs of an intravascular extramural extension or suspicious lymph nodes.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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