Clin Transl Oncol (2017) 19:135–148
DOI 10.1007/s12094-016-1518-9

SPECIAL ARTICLE

SEOM/SERAM consensus statement on radiological diagnosis, response assessment and follow-up in colorectal cancer

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Received: 23 February 2016 / Accepted: 30 April 2016 / Published online: 20 May 2016

Abstract Colorectal cancer (CRC) is one of the world's most common cancers, and has one of the highest mortality rates. The last few decades have seen great progress in preventing, diagnosing and treating this disease, providing undeniable impact on patients' prognosis and quality of life. At all these stages of CRC management, imaging techniques play an essential role. This article reviews some important issues concerning the use of various radiological techniques in the screening, diagnosis, staging, assessment of treatment response, and follow-up of patients with CRC. It also includes a number of practical recommendations on indications for use, technical requirements, minimum information required in the radiology report, evaluation criteria for the response to various drugs, and the recommended frequency at which different examinations should be performed. This consensus statement is the result of cooperation between the Spanish Society of Medical Oncology (SEOM) and the Spanish Society of Radiology (SERAM).

Keywords Colorectal cancer · Imaging techniques · Staging · Response evaluation · Follow-up · CT · MRI · Endorectal ultrasound

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Introduction

In Spain, malignant tumours of the colon and rectum are the third most common cause of cancer deaths, exceeded only by lung and stomach cancer. In terms of incidence rates, colorectal cancer (CRC) comes third in men, behind lung and prostate cancer. In women, its incidence is second only to breast cancer. Taking both sexes into account, however, CRC has the highest incidence of any cancer, representing 15 % of tumours diagnosed in this country. It is calculated that 32,240 new patients will be diagnosed every year in Spain, resulting in 14,700 deaths, with a 5-year prevalence of 89,705 cases [1].

This consensus statement will consider cancer of the colon and rectum as two separate entities, as the patterns of presentation, diagnostic tests and treatment are different. Thanks to diagnostic and therapeutic progress in the past decade, patients' prognosis and quality of life have improved significantly [2]. In particular, the various imaging modalities have proved essential for improving diagnosis, therapeutic decision-making, response assessment, and correct measurement of the efficacy of current therapies.

Caring for patients with cancer demands cooperation by the various professionals involved, working together in a coordinated multidisciplinary team with the sole aim of benefiting the patient and with specific protocols agreed between the different specialists in the team. Accordingly, the Spanish Society of Radiology (SERAM) and the Spanish Society of Medical Oncology (SEOM) decided to produce the first ever national consensus statement, written by 10 experts (5 radiologists and 5 medical oncologists), in order to make recommendations for the radiological diagnosis and assessment of treatment response in patients with cancer of the colon and rectum, based on the scientific evidence. In short, this document's raison d'être is to improve care for patients with colon or rectal cancer, and to minimise variability in routine clinical practice, using the best available radiological techniques in an optimal manner in order to achieve the best possible oncological outcome.

Radiological diagnosis of colorectal cancer

Technical issues concerning the radiological examinations available

Screening for colorectal cancer: computed tomographic (CT) colonography

In general and in our setting, screening of the population or individuals at risk of CRC begins with an immunological test for faecal occult blood, followed by colonoscopy when the result is positive [3]. CT colonography or virtual colonoscopy can be an alternative to colonoscopy when this is unfeasible or inadvisable for clinical reasons, or when incomplete because of the presence of obstructing lesions. In this case, it is best to perform it on the same day, to take advantage of the patient's bowel preparation [3–7]. The requirements for performing CT colonography are [5–8]:

- Hydration and low-residue diet from at least 48 h before the test is done. Liquid diet from the start of bowel preparation the day before, and nil by mouth from midnight the night before the test. Although some guidelines recommend using laxatives the day before, it is advisable to avoid cathartic laxatives at least.
- Faecal tagging 24 h before the examination, according to preference.
- Use of a thin, flexible rectal tube, uninflated in at least one acquisition.
- Automated CO_2 insufflation with pressure monitoring is preferred, although manual use of ambient air is also acceptable according to tolerance and insufflation as seen on the scan.
- Use of multi-detector CT (MDCT) with more than 4–16 rows.
- If there is a risk of perforation, a low-dose CT scan should be acquired first.
- The test should be performed in at least two positions. It should be done in the prone position first, in case staging is required.
- Low-dose acquisitions (<5.7 mSv): ≤50–80 mA except in obese patients; iterative reconstruction if available. If staging is required, the test is done in the supine position with a standard dose, including the thorax, administering an intravenous contrast agent.
- Use collimation of less than or equal to 1.25–2.5 mm.
- The whole colon and rectum should be scanned.
- It is recommended that an experienced reader should perform multiplanar 2D and 3D readings, according to preference. A computer-aided detection system (CADS) can be used as an optional tool.
- Illustrative axial images of 3 mm or more (e.g., target lesions) should be sent to the picture archiving and communications system (PACS), along with volumetric reconstructions for planning surgery.

Locoregional staging of colon cancer and distant staging of colorectal cancer: computed tomography

In order to establish the locoregional and distant spread of a CRC, a CT scan of the chest, abdomen and pelvis should be performed [3, 9–11]. The requirements for CT staging of CRC are as follows [3, 9–13]:

- No bowel preparation is required.
- Intravenous contrast is essential, with portal-phase acquisition (60–75 s). If this is contraindicated or unavailable, magnetic resonance imaging (MRI) of the liver and/or contrast-enhanced ultrasonography should be performed [3, 9, 11].
- An oral contrast agent is recommended, according to preference.
- Some authors recommend an enema first, with 2 L of warm water for 3 min, to achieve greater diagnostic accuracy if neoadjuvants are being considered. This also allows better planning of laparoscopic surgery [12, 14].
- Scan from the domes of the diaphragm to the ischial tuberosities.
- The use of MDCT is highly advisable.
- The use of low doses should be considered (iterative reconstruction and low kilovoltage in thin patients).
- Collimation should be 5 mm or less, preferably with acquisition of isotropic voxels.
- Multiplanar reading.

- Representative axial and coronal images 3 mm thick or less (e.g. target lesions) should be stored in the PACS.

Locoregional staging of rectal cancer: magnetic resonance imaging and endorectal ultrasound

Scientific societies recommend locoregional staging of rectal cancer by MRI [3, 9, 10, 15, 16]. Endorectal ultrasound (ERUS) is a useful alternative for early stages at which local excision is being considered [9, 15, 16], or for anterior low tumours [3]. The technical requirements for local staging by MRI in rectal cancer are as follows [3, 9, 10, 16]:

- No bowel preparation is required.
- The MRI scanner should be at least 1T.
- Rectal insufflation is not advisable.
- Administer antispasmodics on occasions (high rectum and 3T).
- Use phased-array surface coils.
- Use 2D T2-weighted sequences without fat saturation.
- Inclusion of a diffusion-weighted sequence is recommended.
- Thickness of 3–4 mm or less.
- The planes used should be pure sagittal, transverse and coronal parallel to the tumour. In the low rectum, a coronal plane parallel to the anal canal is used.

The technical requirements for ERUS are as follows [17]:

- Administer a cleansing enema 2 h before the test.
- Place the patient in a left lateral decubitus position with legs bent.
- Do a digital rectal examination before performing the test.
- Use a multi-frequency circumferential rigid probe (5–15 MHz).
- Use a balloon filled with 30–60 cc of fluid, with no gas.
- Take care when passing the lesion.
- 3D acquisition and multiplanar and volumetric post-processing.

TNM staging of colorectal cancer: structured report

Rectal cancer

Current recommendations for treating rectal cancer at clinical stage II (cT3–T4N0) or clinical stage III (any T, N+) include preoperative chemoradiotherapy or short-course radiotherapy treatments, followed by surgery with total excision of the mesorectum. Preoperative treatment reduces the risk of local relapse and improves patient survival. Also, giving radiotherapy prior to surgery is considerably less toxic than administering it after surgery. In any case, however, neoadjuvant therapy is also associated with worse bowel and sexual function, compared with treatment by surgery alone. Thus, understaging might mean effective treatment is not given, but overstaging might lead to treatment that entails excessive, unnecessary toxicity for the patient. Correct clinical and radiological staging is, therefore, needed before planning the treatment that provides the best therapy in each case.

The most important radiological data, which need to be reported in preoperative investigations because of their prognostic implications or for planning treatment, are as follows: longitudinal extent and depth penetration of the tumour (the T descriptor), lymph node status (the N descriptor), extramural vascular invasion (EMVI), relationship of the tumour to the mesorectal fascia (MRF) and distance from the lower pole of the tumour to the anal verge [18].

Endorectal ultrasound Rectal cancer has the appearance of a hypoechogenic lesion disrupting the normal layered structure of the rectal wall. The accuracy of ERUS for T staging ranges from 80 to 95 %, slightly better than MRI (75–85 %) [19–21]. The limitations of ERUS include understaging of T3 tumours (because its limits of resolution mean it cannot detect microscopic invasion), operator expertise, tumour level (less diagnostic accuracy for low rectal tumours; difficult access for high rectal tumours), its application to highly stenosing tumours, and inability to evaluate the MRF [22–24]. Staging accuracy is greater for T2 tumours, although overstaging may occur as a consequence of inflammation around the tumour, which is indistinguishable from malignant tissue. Accuracy for detecting mesorectal lymph node involvement is approximately 70–75 %, comparable with MRI (70–77 %) [19].

Magnetic resonance imaging High-resolution MR images look similar to histopathology sections, with excellent representation of the rectum, mesorectum, MRF, levator muscles and other tumour-related anatomical structures. This imaging modality yields data of prognostic importance with crucial implications for treatment planning, to supplement the T and N descriptors, such as EMVI [23–26], and the relationship of the tumour or mesorectal tumour deposits to the MRF and anal sphincter (Fig. 1).

Distance from the tumour to the MRF is currently one of the most important parameters for the preoperative evaluation of rectal cancer. The sensitivity of MRI for predicting MRF involvement is 77 %, with 94 % specificity, according to a recent meta-analysis [27]. All these details of therapeutic/prognostic importance should be properly recorded in the initial radiology reports. Table 1 shows a

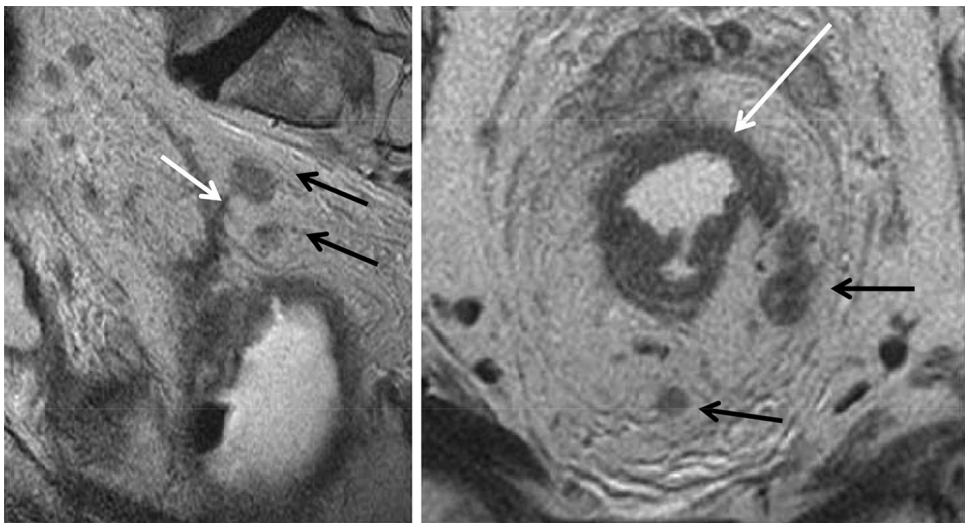

Fig. 1 Rectal cancer staging by magnetic resonance imaging. High-resolution T2-weighted sagittal and axial images showing a T4aN2 rectal tumour with extramural venous invasion. The axial plane shows tumour penetration of the peritoneal reflection, which is thickened (*large arrow*). Also, the middle rectal vein is occupied by tumour (*white arrows*) and there are several mesorectal lymphadenopathies of heterogeneous signal intensity and irregular border (*black arrows*)

structured MRI staging report incorporating the recommendations by the Spanish Society of Abdominal Imaging (SEDIA) [28], the European Society of Gastrointestinal and Abdominal Radiology (ESGAR) [16] and the Canadian Cancer Society [29].

Evaluation of the T descriptor is controversial. The ESGAR consensus statement says spiculation in the perirectal fat may be a desmoplastic reaction or tumour. On the other hand, the Canadian group recommends regarding it as early T3, in contrast to SEDIA, which follows the Mercury group and regards it as T2. Low rectal tumours carry a greater risk of perforation and local recurrence, and warrant special mention; when the lower margin of the tumour is at or below the top edge of the anorectal angle, the depth of invasion should be detailed as shown in Table 1 [29].

Accurate characterization of lymph nodes remain a challenge at MR. Suspicious lymph nodes demonstrate heterogeneous signal intensity and irregular margins. No universal agreement upon optimal size cut-off exists. Comparing MR to histological results, using irregular morphology and signal characteristics to determine nodal status, MR had 64 % accuracy for node positive disease. In addition to assessing whether a lymph node is suspicious of metastatic disease, it is important to accurately describe lymph node location [30].

Colon cancer

Investigating the extent of colon cancer Diagnostic investigation and assessment of the extent of colon cancer essentially require a full colonoscopy and a CT scan of the chest, abdomen and pelvis [3, 11]. Some recent studies question the need for routine thoracic CT because of the low incidence of lung metastases in low-risk patients (e.g., stage I–IIA colon cancer with no liver metastases, particularly if located in the right colon) [31, 32]. In this case, CT could be replaced by a chest radiograph [3]. Performing a radioisotope bone scan or CT brain scan is not indicated in the absence of symptoms suggestive of tumour involvement of the bones or central nervous system. If diagnostic colonoscopy was incomplete, CT colonography with intravenous contrast agent may be considered. This might serve both to rule out synchronous colonic lesions, and to stage distant disease. At sites where CT colonography is unavailable, a barium enema may be considered, to rule out synchronous colonic lesions in obstructing tumours of the colon that prevented full endoscopic examination, as this might affect the surgical technique to be used.

Table 2 shows a structured report for staging colon cancer, which should be done according to the current TNM classification (7th Edition) [33].

Locoregional staging of colon cancer Firstly, the location of the tumour must be narrowed down to one of the six classical segments of the colon: the caecum, ascending colon, transverse colon, descending colon, sigmoid colon or rectum [34]. CT or CT colonography are more accurate tools than endoscopy for locating the tumour.

Although T and N parameters are more accurately determined by histopathology tests on the surgical specimen, CT can provide a preoperative approximation. CT cannot distinguish between T1 tumours (invading the submucosa) and T2 tumours (invading the muscularis propria layer), but it can identify invasion of the mesenteric fat typical of T3 tumours (invading through the muscularis propria layer into pericolonic tissues). It is more difficult to tell by CT whether the tumour is invading the visceral peritoneum (T4a), although it is possible to detect invasion of neighbouring organs (T4b) [33]. A recent meta-analysis

Table 1 Structured MRI staging report for rectal cancer [16, 28, 29]

Tumour location, size and morphology
Flat mass measuring ___ mm in length: • Invasive • Ulcerated • Stenotic
Growth: • Circumferential • Eccentric in left/right anterior/posterior quadrant(s)
Polypoid mass measuring ___ mm • Ulcerated
Growth in left/right anterior/posterior quadrant(s)
The lower margin of the lesion is located ___ cm from the anal verge (high/mid/low third) and ___ mm from the puborectalis muscle • More than 10 cm from the anal verge (high rectum) • Between 5 and 10 cm from the anal verge (mid rectum) • Less than 5 cm from the anal verge (low rectum)
The tumour is located below, at, or above the peritoneal reflection
The tumour displays areas of hyperintensity (≥ 50%) suggestive of mucinous adenocarcinoma
Local invasion
Local extent: T • Tumour not visible (Tx) • Tumour invades submucosa (T1) • Tumour invades muscularis propria (T2) • Tumour invades ≤ 5 mm into the mesorectal fat (superficial T3) • Tumour invades > 5 mm into the mesorectal fat (deep T3) • Tumour penetrates the peritoneum (T4a) • Tumour invades adjacent organ(s) (please state which, including levator ani muscle) (T4b)
Low rectal tumours only (0-5 cm) Is the distal margin of the tumour at or below the puborectalis muscle?: No Yes* *Yes: please complete the following section for the most penetrating component of the tumour • Possibly confined to the submucosa; no involvement of the internal sphincter (suspected T1)

Table 1 continued

• Confined to the internal sphincter; no involvement of the intersphincteric fat or external sphincter (early T2) • Through the internal sphincter and intersphincteric fat; possible or definite involvement of the external sphincter (advanced T2) • Through the external sphincter and into surrounding soft tissues; no organ involvement (T3) • Through the external sphincter and possible involvement of adjacent organs (e.g. prostate, vagina) (T3/T4) • Through the external sphincter and definite involvement of adjacent organs (e.g. prostate, vagina) (T4)
Extramural vascular invasion (EMVI): Yes/No (tumour thrombosis of veins in the mesorectal fat)
Satellite tumour deposit: Yes/No (tumour nodules in the mesorectal fat < 3 mm)
Locoregional lymphatic spread
Perirectal lymphadenopathies: • Negative: No lymphadenopathies seen, or lymph nodes with smooth border and homogeneous signal intensity seen (N0) ≤ 3 mm • Suspicious: x lymphadenopathies > 3 mm (short axis) seen, with smooth border and heterogeneous signal intensity • Positive: - ≤ 3 lymphadenopathies seen, with irregular border and heterogeneous signal intensity (N1) - ≥ 4 lymphadenopathies seen, with irregular border and heterogeneous signal intensity (N2)
Lateral pelvic lymphadenopathies: • Negative: No lymphadenopathies seen, or lymphadenopathies < 5 mm (short axis) seen, with smooth border and homogeneous signal intensity • Suspicious: Lymphadenopathies > 5 mm (short axis) seen, with smooth border and heterogeneous signal intensity • Positive: Lymphadenopathies > 5 mm (short axis) seen, with irregular border and heterogeneous signal intensity Note. Lateral pelvic lymphadenopathies are: internal iliac, obturator, internal pudendal and external iliac
Circumferential resection margin (CRM): Clear/Invaded
CRM Invaded: distance* to mesorectal fascia ≤ 1 mm CRM Clear: distance to mesorectal fascia > 1 mm

Table 1 continued

* the shortest of any of the following distances is to be recorded in the report: • Shortest distance from tumour to MRF is ___ mm • Shortest distance from satellite deposits to MRF is ___ mm • Shortest distance from positive lymph nodes to MRF is ___ mm • Shortest distance from EMVI to MRF is ___ mm
Metastasis
• Not evident in staging MRI for rectal cancer (Mx) • Tumour involvement in common iliac or external iliac lymphadenopathies (M1a) • Distant metastasis in a single organ (M1a) (please state) • Metastases in more than one organ (please state) or peritoneal carcinomatosis (M1b)
Additional remarks

Table 2 Structured report for colon cancer staging

Tumour location (caecum, ascending colon, transverse colon, descending colon, sigmoid colon or rectum)
Size (longest diameter)
Signs of mesenteric fat invasion
Signs of invasion of neighbouring organs
Signs of invasion of the visceral peritoneum
Presence of locoregional lymphadenopathies of pathological size
Presence of synchronous lesions (if investigation involves CT colonography)
Presence of distant lymphadenopathies of pathological size
Presence of liver metastases. Number, size and location by segment. Relationship to main vascular structures (vena cava, portal vein, hepatic veins). Possibility of volumetry study
Signs of peritoneal carcinomatosis. Peritoneal cancer index if potentially amenable to peritonectomy
Presence of lung metastases. Number, size and location
Metastases elsewhere (bone, subcutaneous tissue)

found the sensitivity and specificity of CT for distinguishing between T1–T2 and T3–T4 to be 86 and 78 %, respectively [34].

Investigation of lymph nodes (the N descriptor) by CT is limited to criteria of size. This is an unreliable parameter for determining whether lymph nodes are really involved. Most errors will be due to undetected micrometastases and false positives caused by inflammation. The TNM system (7th Edition) defines N1 as 1 to 3 positive lymph nodes detected (N1a if 1 node and N1b if 2–3 nodes); N2a as 4 to 6 lymph nodes involved; N2b as 7 and above; and N2c as tumour deposits detected other than in lymph nodes.

Distant staging of colon and rectal cancer For most patients with CRC, a CT scan of the chest, abdomen and pelvis is enough to provide adequate distant staging. For the time being, positron emission tomography (PET)-CT is not accepted as part of the initial investigation of extent in any published consensus statements [3, 11], although it is indicated when CT or MRI findings are inconclusive but raise suspicions of metastasis, particularly if that affects management [11].

Therefore, in patients with potentially resectable metastases, generally in the liver or lung, PET-CT is advisable in order to confirm whether or not the patient is eligible for radical treatment.

In patients with potentially resectable metastatic liver disease, investigation of spread should also include a contrast-enhanced hepatic MRI scan. MRI is more sensitive than CT and can detect previously unknown metastases that may change the indication or surgical technique [11]. This MRI scan should consider T1-weighted, T2-weighted, diffusion-weighted, and T1-weighted 3D gradient-echo sequences following administration of contrast agent, which may be an extracellular gadolinium chelate or a liver-specific contrast agent. The best results are obtained when analysis combines diffusion-weighted sequences with sequences following the administration of a liver-specific contrast agent [35], but there is still no published consensus on the matter. PET-CT is needed to rule out metastatic disease not detected by CT that would contraindicate hepatic surgery.

The surgeon may sometimes require a liver volumetry calculation to ensure enough liver parenchyma is left. The

calculation may be done by CT or MRI. At the time of surgery, intraoperative ultrasound imaging is advisable to confirm previous findings. This may even detect lesions not previously identified in preoperative investigations.

Treatment response assessment criteria in colorectal cancer

Locally advanced rectal cancer: assessing the response to neoadjuvant therapy

Neoadjuvant chemoradiotherapy is standard practice today in the locoregional treatment of locally advanced rectal cancer. Many studies demonstrate that it reduces size, tumour stage and local recurrence. It also improves survival, with histopathological complete responses in 25 % of cases [36].

The response must be assessed by MRI 6–8 weeks after completion of therapy, which is when the greatest neoadjuvant-induced reduction in tumour volume can be detected [37]. The protocol is the same as for baseline MRI, and if possible it should be done with the same angulation. It is essential to compare both MRI scans in order to locate the treated tumour (Fig. 2). The Mercury group recommends that the response report should include the following points, most of which are also recommended by ESGAR (Table 3) [16, 38]:

- Changes in tumour morphology: (a) fibrosis, which appears hypointense in T2-weighted images, similar to the muscularis propria layer; (b) desmoplastic response, in which T2-weighted images show hypointense fine spicules radiating from residual tumour towards fat; and (c) tumour necrosis with mucinous degeneration, indicating a response to treatment: T2-weighted images show hyperintense pools of acellular mucin inside a non-mucinous tumour, or in a mucinous tumour, not present in the baseline MRI scan; these pools are of higher signal intensity than cellular mucin. Desmoplastic response and fibrosis must not be confused with residual tumour, which is of intermediate signal intensity and has a nodular advancing margin. High-resolution T2-weighted sequences are therefore essential.
- Tumour length: this must be compared against the baseline MRI scan. According to Response Evaluation Criteria in Solid Tumours (RECIST), a complete response is defined as no tumour, partial response as a decrease of at least 30 %, progression as an increase of at least 20 %, and stable disease as neither progression nor partial remission.
- Tumour regression grade: the Mercury group uses the pathologic tumour regression grading system of Dworak et al., adapted to MRI [39]:
  - Grade 1—complete response: tumour not visible.
  - Grade 2—good response: dense fibrosis, minimal residual tumour.
  - Grade 3—moderate response: more than 50 % fibrosis or minimal mucin. Intermediate signal intensity.
  - Grade 4—minimal response: minimal fibrosis. Mostly of intermediate signal intensity.
  - Grade 5—no response: intermediate signal intensity, similar to the original tumour.

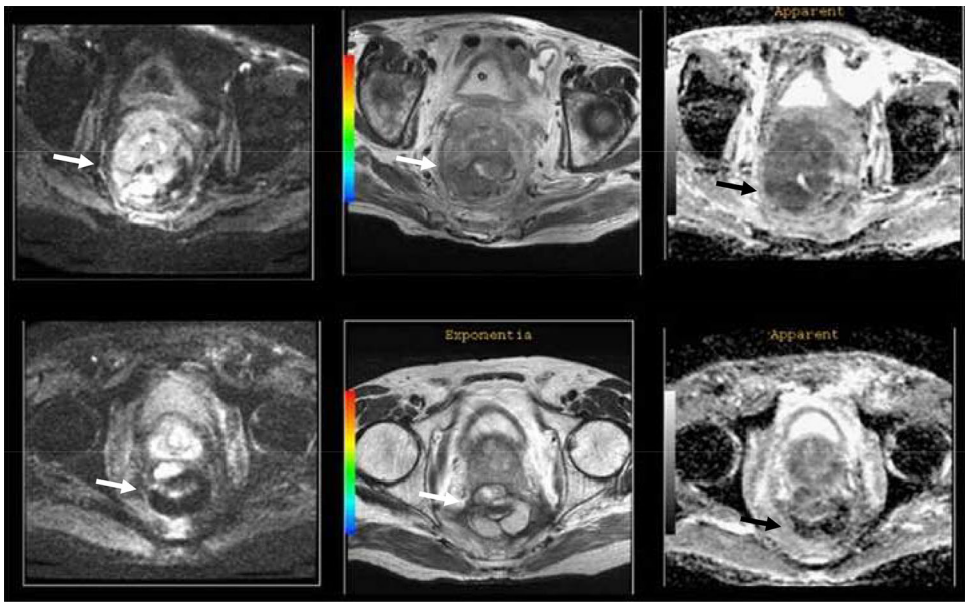

Fig. 2 Rectal cancer restaging following neoadjuvant therapy. The *top row*, from *left to right*, shows a diffusion-weighted image, a T2-weighted image and an ADC map of the tumour before treatment (*arrows*). The *bottom row* shows the corresponding images following neoadjuvant therapy. The initially bulky tumour (*arrows*) has shrunk, leaving a focus of residual tumour that restricts the diffusion-weighted signal (*arrow*)

Table 3 Standard MRI restaging report for rectal cancer following neoadjuvant therapy. ESGAR consensus statement [16]

Points to be included in the report (with over 80 % consensus)
Distance from lower pole of tumour to anal verge or anorectal junction
Tumour length
Presence or absence of residual tumour
Presence or absence of fibrosis
Post-treatment T stage (yT) and any residual tumour deposit in the mesorectum
yN stage and number of suspicious residual lymph nodes
Presence of any suspicious residual lymph node outside the mesorectum
Persistence or regression of MRF involvement
Shortest distance (mm) between residual tumour and MRF, and its location
Points for which inclusion is recommended, although not unanimously
Circumferential location of tumour in wall (lateral, anterior, posterior)
Morphological pattern of tumour growth (annular, polypoid, mucinous, ulcerated, perforated)
In the case of yT3, extent (mm) of extramural growth
Points with no consensus regarding routine inclusion in the report
Residual tumour volume
Circumferential growth
Extramural venous invasion

- Restaging of the primary tumour following neoadjuvant therapy (yT): depth of maximum extramural spread should be given separately for post-treatment tumour (yT) and fibrosis.
- Distance to the circumferential resection margin (CRM), which may be clear or invaded. Response is reflected in a reduction in total tumour volume and an increase in CRM. This is of great importance in low rectal cancer as it sometimes allows sphincter preservation and/or radical surgical resection with clear margins (R0).
- Distal resection margin: it is important to state the relationship between the residual tumour and the anal sphincter and adjacent structures with a view to planning surgery. Endoanal ultrasound does not distinguish tumour from fibrosis, and is not recommended for sphincter reassessment.
- Extramural venous invasion: this may disappear completely with treatment, exhibiting fibrous cords.
- Lymph node restaging following neoadjuvant therapy (yN): the lateral pelvic lymph nodes should be included. This currently still poses a challenge. The diagnostic accuracy of MRI is 65 % using size criteria and 85 % using irregular border and heterogeneous signal intensity [40].
- Peritoneal reflection: it should be stated whether or not this is involved.
- Functional imaging: the usefulness of MRI for restaging rectal cancer after neoadjuvants is limited. Its diagnostic accuracy is 50 % for yT and 77 % for predicting CRM involvement [36, 37]. Various studies have assessed contrast-enhanced dynamic MRI, but this is not recommended for routine restaging [37]. Diffusion-weighted MRI enables residual tumour to be distinguished from post-neoadjuvant changes. ESGAR recommends it, especially for yT [16]. Some authors think it improves lymph node characterisation, although this is unclear [40–42]. The use of ultrasmall superparamagnetic iron oxide (USPIO) particles to assess lymph node involvement is being investigated, with promising results. PET results in this context are contradictory, so more studies are needed [37].

Metastatic colorectal cancer: radiological criteria for response evaluation

The efficacy of cancer treatment for metastatic CRC, in both routine clinical practice and clinical trials, can be evaluated by various parameters: tumour response, progression-free survival (PFS) and overall survival. The criteria usually used to determine tumour response and PFS are those of RECIST [43]. The RECIST criteria are based on changes in the size of malignant lesions in response to treatment, and have the advantage of being simple, reproducible, universally accepted standard criteria. Nevertheless, beyond RECIST, a number of other radiological and measurement parameters are proving very useful for evaluating the therapeutic effect of certain drugs. Thus, the speed or depth of response obtained may be relevant when using therapies directed against epidermal growth factor receptor (EGFR), or certain morphological changes not necessarily associated with shrinkage, may indicate a substantial treatment effect when using antiangiogenic therapies, as discussed below.

RECIST criteria

In the baseline radiological examination, a number of target lesions representative of the organs involved should be selected, consisting of up to five lesions in total and two per organ. Evaluable radiological disease should also be identified. This includes non-measurable disease and measurable disease not selected as a target lesion. The response is evaluated by adding up the longest diameters of the target lesions in the baseline CT scan and successive CT scans performed throughout treatment; these measurements are compared and the relative change experienced is

calculated. A treatment response is considered complete if all target and non-target lesions disappear, and partial if the sum of diameters decreases by at least 30 %. The disease is regarded as stable if the sum of diameters decreases by ≤30 % or increases by ≤20 %. Lastly, the disease is considered to have progressed when the sum increases by more than 20 % compared with the smallest sum achieved or if new metastatic lesions appear.

Beyond RECIST criteria: speed, depth and duration of response

Speed of response can be taken as time to tumour response, time to RECIST response, or early tumour response or shrinkage rate (percentage of patients with a 20 or 30 % decrease in the sum of target lesion diameters 6 or 8 weeks after starting therapy). This response criterion has been correlated with greater depth of response, with a higher rate of R0 resections and longer progression-free and overall survival, in patients with metastatic CRC treated with either chemotherapy alone [44], or anti-EGFR [45, 46], and with bevacizumab [47]. Nevertheless, a meta-analysis cast doubt on its value as a surrogate efficacy end-point [48] (Fig. 3).

Duration of response can be measured using a survival curve that only includes patients who achieve at least a partial response, in which the event is progression. Depth of response can be evaluated in terms of percentage reduction in the sum of target lesion diameters. It can be expressed as a single parameter, maximum reduction achieved throughout the entire treatment, or as a curve in which the x-axis shows time and the y-axis shows percentage reduction on that treatment at each time point. Depth of response curves for various treatments can be plotted in the same graph and comparisons made. Several studies have established a correlation between depth of response and survival [45–47].

Alternative response evaluation criteria: morphological criteria

The survival benefits achieved with bevacizumab are not always accompanied by higher tumour response rates in conventional terms. Response evaluation by RECIST criteria is not well correlated with survival [49, 50]. Also, these criteria may offer misleading measures for antiangiogenic activity, which may not be accompanied by tumour shrinkage [51]. After bevacizumab therapy, liver metastases tend to become homogeneous hypodense lesions with well-defined borders. Chun et al. proposed a set of response criteria based on morphological changes seen by CT in patients treated with bevacizumab for hepatic metastases of colorectal cancer [52]. Radiological features evaluated by CT were as follows: overall density (heterogeneous, mixed, or homogeneous and hypodense; groups 3, 2 and 1, respectively); the interface between the metastasis and the liver parenchyma (ill-defined, variable or sharp; groups 3, 2 and 1, respectively); and the presence or absence of increased contrast uptake at the peripheral rim of the lesion (presence was considered a group 3 characteristic, and its partial or complete resolution over time reclassified it into group 2 or 1, respectively). Morphological response criteria were defined as optimal if metastases changed from group 3 or 2 to group 1; incomplete if they changed from 3 to 2; and no response if the group neither increased nor decreased. In patients with

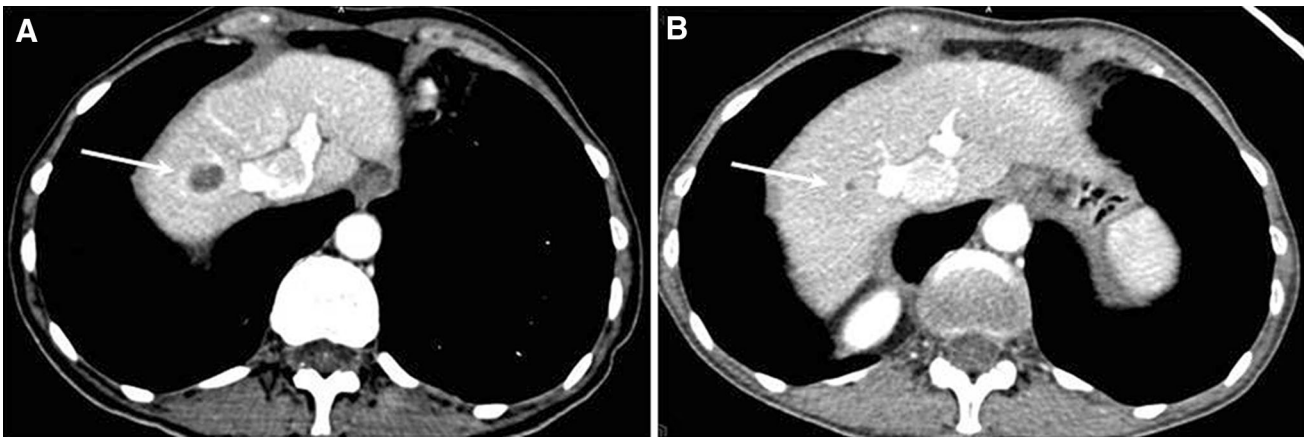

Fig. 3 **a** Colorectal cancer metastasis measuring 14 mm in the dome of the liver following anti-EGFR therapy. **b** Repeat scan showing over 30 % reduction in metastasis diameter and partial radiological response at 12 weeks. Intraoperative ultrasound detected a single 8 mm nodule in segment VIII. Right hepatectomy (segment VIII) revealed an 8 mm adenocarcinoma nodule with histological tumour regression grade of over 50 % residual tumour cells

multiple lesions, response evaluation was based on the behaviour observed in the majority of lesions. Both CT-based morphological criteria and pathological response markers described in patients with liver metastases treated with bevacizumab have proved to be better correlated with survival than RECIST criteria [52].

Radiological response evaluation frequency

It is advisable for baseline CT to be performed within 4 weeks prior to starting cancer therapy in a patient with metastatic disease. This CT scan should be repeated periodically during treatment to evaluate its results, preferably under the same technical conditions. There is no universally accepted rule about how often these CT scans for evaluating radiological response should be done, although the panel's consensus is to do them every 8–12 weeks until tumour progression. It is important to evaluate response at the right frequency, especially in potentially resectable patients, because induction treatment should last for as short a time as possible, to allow the tumour to respond and become resectable without causing unnecessary liver toxicity that might hinder resection. If complete surgical resection of metastases proves possible, leaving the patient disease-free, a radiological follow-up should be performed according to the recommendations set out in "Follow-up of patients with CRC with no evidence of disease". It should also be remembered that not evaluating response at the right frequency might mean a delay in detecting progression, resulting in continued administration of ineffective treatment entailing needless toxicity and cost.

Technical issues when evaluating radiological response

The main ways of reducing errors in response evaluation are to ensure a reproducible technique and the right choice of target lesions. It is, therefore, very important for radiological examinations always to be performed, if possible, using the same imaging modality, contrast-enhanced acquisition phases, sequences, planes and imaging windows. On the other hand, it is important that target lesions, as far as possible, should be the largest, and easy to identify and pick out during follow-up. Lesions that coalesce over time should be taken as a single diameter for follow-up purposes, whereas lesions that fragment should be assigned the sum of diameters of both resultant lesions. New lesions must be unmistakable, not attributable to different techniques or benign pathology. If in doubt, treatment should be continued and the evaluation repeated again subsequently [43].

Follow-up of patients with CRC with no evidence of disease

Resected stages I–III

Between 30 and 50 % of patients who have tumours resected will experience a relapse. This will be amenable to rescue surgery in up to 20 % of cases, of whom 50 % will be cured and another 50 % will have a further relapse. Intensive follow-up of patients who undergo surgery for colon cancer has been shown to increase survival by 7–13 % compared with those who do not undergo such follow-up, essentially due to patients who are amenable to rescue surgery [53, 54]. The proportion of local recurrences that can be resected is clearly higher when intensive follow-up takes place. Much the same is true of liver and lung metastases. On the other hand, when unresectable disseminated disease is detected at an early, asymptomatic stage, chemotherapy offers better results in terms of survival and quality of life [55].

Accordingly, although this is a controversial issue, most recommendations support intensive follow-up in stage II and III colon cancer, especially in the first 2–3 years, which is when most (80 %) of these relapses occur [56]. Following the recommendations of the US and European guidelines, follow-up rules might be as follows [57, 58]:

- During the first 2–3 years after surgery, a medical history should be taken, a physical examination done, and CEA measured every 3 months [59]. Also, a CT scan of the chest, abdomen and pelvis should be done every 6–12 months, and is mandatory every year. Abdominal ultrasound could be performed annually, alternating with CT. No guidelines recommend chest radiography. When preoperative colonoscopy was complete, colonoscopy should be repeated a year after that surgery. If colonoscopy was incomplete, it is recommended that it be done within 6 months after surgery.
- For 2–5 years after surgery, as well as medical history, physical examination and CEA tests every 6 months, a CT scan of the chest, abdomen and pelvis should be done every 12 months, and colonoscopy should take place in year 3 or 4 post-surgery if the previous colonoscopy was normal.
- From year 6 post-surgery onwards, the patient only needs to undergo colonoscopy every 5 years. Other investigations are not recommended in the absence of suspicious clinical signs or symptoms.
- PET-CT is not recommended for routine follow-up, although it may be considered if relapse is suspected on clinical grounds or for biochemical reasons (elevated CEA) in the absence of CT findings.

Resected stage IV

- During the first 2–3 years after metastasis surgery, a medical history should be taken, a physical examination done, and CEA measured every 3 months, as well as a CT scan of the chest, abdomen and pelvis every 3–6 months, this being mandatory every 6 months. Abdominal ultrasound could be performed on a six-monthly basis, alternating with CT. Although no guidelines recommend chest radiography in the case of resected lung metastases, doing this plus abdominal ultrasound every 6 months alternating with CT might be recommended [30, 60].
- For 2–5 years after metastasis surgery, a medical history should be taken, a physical examination done, and CEA measured every 6 months. Also, a CT scan of the chest, abdomen and pelvis should be done every 6–12 months, and is mandatory every 12 months. Abdominal ultrasound could be performed annually, alternating with CT. Although no guidelines recommend chest radiography in the case of resected lung metastases, doing this plus abdominal ultrasound annually, alternating with CT, might be recommended [30, 60].
- PET-CT is not recommended for routine follow-up and should be done when clinical evidence and/or elevated CEA raise suspicions of a relapse not detected by CT. If a resectable relapse is detected by other imaging tests, a PET-CT scan before surgery is recommended [30, 60].

Conclusions

The last few years have seen great progress in the screening, diagnosis, treatment and follow-up of patients with CRC, all of which has undoubtedly improved the prognosis and quality of life of these patients. At all these stages of CRC management, imaging techniques play an essential role. In routine clinical practice, however, there is enormous variability in the use of these techniques. This document represents a consensus between medical oncology specialists from SEOM and diagnostic imaging experts from SERAM. It addresses several important issues concerning the use of various radiological techniques in the screening, diagnosis, staging, assessment of treatment response, and follow-up of patients with CRC. These include indications for use, technical requirements, minimum information required in the radiology report, evaluation criteria for the response to various drugs, and the recommended frequency at which different examinations should be performed. This document is intended as a simple way of providing the clinician with a number of recommendations to assist and standardise his or her decisions in routine clinical practice. It must be stressed that the document reflects issues on which there was majority agreement based on the available evidence at the time it was written.

Acknowledgments The authors are grateful for the editorial assistance of Fernando Sánchez-Barbero of HealthCo (Madrid, Spain) in the production of this manuscript.

Compliance with ethical standards

Conflict of interest SEOM and SERAM wish to thank to Bayer and Sanofi for the financial support of this project through no restriction grants.
The authors declare that, when writing and revising the text, they did not know the names of the pharmaceutical companies that provided financial support for this project, so this support has not influenced the content of this article.

Ethical statement The study has been performed in accordance with the ethical standards of the Declaration of Helsinki and its later amendments. This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent statement Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

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