

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com



Rectal cancer guidelines

International consensus guidelines on Clinical Target Volume delineation in rectal cancer



Vincenzo Valentini ^a, Maria Antonietta Gambacorta ^{a,*}, Brunella Barbaro ^b, Giuditta Chiloiro ^a, Claudio Coco ^c, Prajnan Das ^d, Francesco Fanfani ^e, Ines Joye ^f, Lisa Kachnic ^g, Philippe Maingon ^h, Corrie Marijnen ⁱ, Samuel Ngan ^j, Karin Haustermans ^f

^a Università Cattolica del Sacro Cuore, Radiation Oncology Department; ^b Università Cattolica del Sacro Cuore, Department of Radiological Sciences; ^c Università Cattolica del Sacro Cuore, Department of Surgical Science, Rome, Italy; ^d University of Texas MD Anderson Cancer Center, Department of Radiation Oncology, Houston, USA; ^e University G. D'Annunzio, Gynecologic Oncology Department of Medicine and Aging Sciences, Chieti, Italy; ^f KU Leuven – University of Leuven, Department of Oncology and University Hospitals Leuven, Radiation Oncology, Belgium; ^g Boston Medical Center, Department of Radiation Oncology, USA; ^h Centre Georges-François Leclerc, Department of Radiation Oncology, Dijon, France; [†] Leiden University Medical Center, Department of Radiation Oncology, The Netherlands; [†] Peter MacCallum Cancer Centre, Division of Radiation Oncology and Cancer Imaging, Melhourne, Australia

ARTICLE INFO

Article history:
Received 23 May 2016
Received in revised form 7 July 2016
Accepted 23 July 2016
Available online 12 August 2016

Keywords: Consensus guidelines Rectal cancer Clinical Target Volume delineation

ABSTRACT

Introduction: The delineation of Clinical Target Volume (CTV) is a critical step in radiotherapy. Several guidelines suggest different subvolumes and anatomical boundaries in rectal cancer (RC), potentially leading to a misunderstanding in the CTV definition. International consensus guidelines (CG) are needed to improve uniformity in RC CTV delineation.

Material and methods: The 7 radiation oncologist experts defined a roadmap to produce RC CG. Step 1: revision of the published guidelines. Step 2: selection of RC cases with different clinical stages. Step 3: delineation of cases using Falcon following previously published guidelines. Step 4: meeting in person to discuss the initial delineation outcome, followed by a CTV proposal based on revised and if needed, adapted anatomical boundaries. Step 5: peer review of the agreed consensus. Step 6: peer review meeting to validate the final outcome. Step 7: completion of RC delineation atlases.

Results: A new ontology of structure sets was defined and the related table of anatomical boundaries was generated. The major modifications were about the lateral lymph nodes and the ischio-rectal fossa delineation. Seven RC cases were made available online as consultation atlases.

Conclusion: The definition of international CG for RC delineation endorsed by international experts might support a future homogeneous comparison between clinical trial outcomes.

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Clinical Target Volume (CTV) and Organs at Risk (OARs) delineation is a fundamental step in modern radiotherapy. Despite this awareness, CTV contouring between radiation oncologists (ROs) still remains inhomogeneous, leading to systematic errors with standard deviations up to 1 cm, as demonstrated in some reports [1–5].

To decrease the inter- and intra-observer variability in rectal cancer (RC) CTV delineation, guidelines for contouring of pelvic regions at risk in RC have been published [1-2,6-8]. All these

E-mail addresses: vincenzo.valentini@unicatt.it (V. Valentini), magambacorta@rm.unicatt.it (M.A. Gambacorta), bbarbaro@rm.unicatt.it (B. Barbaro), vchiloiro@gmail.com (G. Chiloiro), coco_claudio@rm.unicatt.it (C. Coco), PrajDas@mdanderson. org (P. Das), francesco.fanfani@unich.it (F. Fanfani), ines.joye@uzleuven.be (I. Joye), lisa.kachnic@bmc.org (L. Kachnic), PMaingon@cgfl.fr (P. Maingon), c.a.m.marijnen@lumc.nl (C. Marijnen), Sam.Ngan@petermac.org (S. Ngan), karin.haustermans@uz.kuleuven.ac.be (K. Haustermans).

http://dx.doi.org/10.1016/j.radonc.2016.07.017 0167-8140/© 2016 Elsevier Ireland Ltd. All rights reserved. guidelines provide boundaries, atlases and recommendations for pelvic CTV's delineation, but they differ in target definition (CTV versus subsites), in subsites nomenclature and in anatomical boundaries. The lack of a "common language" may lead to a complexity of interpretation of the RC CTV and difficulties in the comparison of clinical and dosimetric outcomes between different RC trials. To reduce this variation in target volume interpretation we attempted to define a consensus guideline, which integrates convergencies and overcomes divergencies present in the different published guidelines.

In this manuscript, the method and the final outcome of the consensus are reported. In addition to the delineation guidelines, the table of boundaries and recommendation for CTV modulation presented in this article, an online set of clinical cases delineated and peer reviewed by the consensus panel, is described and available on Falcon platform.

^{*} Corresponding author.

Materials and methods

Participants

A working group (WG) of seven skilled ROs, reviewed the current guidelines and proposed consensus guidelines for RC CTV delineation. All ROs were authors of at least one of the published delineation guidelines and all of them were members of the principal radiation oncology societies: the European Society of Radiotherapy & Oncology (ESTRO), the American Society for Radiation Oncology (ASTRO), the Trans Tasman Radiation Oncology Group (TROG) and the European Organization for Research and Treatment of Cancer (EORTC).

Surgeons and radiologists specialized in RC and gynecological cancer were involved in the discussion of the anatomical boundaries of the different CTV subsites. The working group focused on the definition and delineation of the elective nodal CTV. Delineation of the gross tumor volume (GTV) was beyond the scope of this project.

Falcon, the educational web-based multifunctional platform for delineation endorsed by ESTRO, was used to support the consensus process and to facilitate the validation process by teleconference discussions.

Consensus process

During a kick-off meeting, the seven delegates defined a road-map to develop consensus guidelines on RC CTV delineation.

Following steps of the process were defined:

- Step 1: comparison of the current and available published guidelines.
- Step 2: selection of RC cases with different clinical stages and tumor location for delineation agreement exercises on the Falcon platform.
- Step 3: selection of CT scan slices considered significant in terms of potential disagreement for each case and delineation of RC cases following previously published guidelines.
- Step 4: meeting to discuss the results of the first delineation round, followed by a CTV proposal based on new anatomical boundaries. During this meeting, the pelvic anatomy was reviewed with the aid of a surgeon and a radiologist, both experts in rectal and gynecological cancer.
- Step 5: peer review of the agreed consensus.
- Step 6: meeting to validate the final consensus guidelines.
- Step 7: completion of RC delineation atlases for publication on the Falcon platform.

The degree of agreement on RC CTV delineation among the seven observers was evaluated through the EduCause ${}^{\text{TM}}$ STAPLE algorithm.

Results

Consensus was obtained for delineation of the CTV for elective irradiation of all regional lymph node levels. Seven subsites at risk were identified: presacral space (PS), mesorectum (M), lateral lymph nodes (LLN), external iliac nodes (EIN), inguinal nodes (IN), ischiorectal fossa (IRF) and sphincter complex (SC).

Timeframe

A kick-off meeting was held in August 2014. Step 1 was at the ASTRO meeting 2014: an overview of RC structure sets was made. In Table 1 provides an overview of the subsites defined in the available RC delineation guidelines. Details on their individual boundaries can be found in the Supplementary material. In December 2014, seven rectal cancer cases were selected (Step 2). Step 3 required 2 months to enable each participant to delineate the selected CT scan slices on Falcon. In April 2015, a meeting was organized in Rome and an agreement on subsites, anatomical boundaries and CTV definition according to stage and tumor location was achieved (Step 4) (Table 2). In the following months, four of the delegates completed Step 5: delineation of the CT slices according to the new guidelines, and in July 2015 the other three delegates reviewed them. During the ASTRO meeting held in September 2015 a general consensus was reached (Step 6) and three months later, seven atlases illustrating the delineation for the different clinical stages at presentation were published on Falcon (Step 7). The entire process to develop final consensus guidelines, a table of boundaries and delineation atlases took 17 months.

Subsite boundaries

Consensus boundaries are provided as Table 2 and Supplementary material. The following subsites were identified: Presacral nodes (PN), Mesorectum (M), Lateral lymph nodes (LLN), External iliac nodes (EIN), Ischio-rectal fossa (IRF), Sphincter complex (SC), Inguinal Nodes (IN).

Presacral nodes (PN): PN are lymph nodes located within a thin space between the rectum and the sacrum. We suggest to divide this space into two sub-volumes: the abdominal and the pelvic PN. The abdominal PN start at the bifurcation of the aorta or 5 mm above the positive node and end at the sacral promontory. At the level of the sacral promontory, the pelvic PN start, ending at the level of the caudal border of the M. Since the PN is a thin structure, which is often difficult to identify on CT scan as a separate structure, the WG suggests to enclose this subsite in the M and the LLN when the PN are at the level of these two structures.

Mesorectum (M): The M is the fat around the rectum, bounded by the mesorectal fascia (MRF). In the mid-low pelvis, the M is

 Table 1

 overview of different subsites described in the available guidelines.

Name	Subsite	Fuller CD ¹	Valentini V ²	Roels S ⁸	Ng M ⁶	Myerson RJ ⁷
PS	Presacral space (PS)	X	X	X	X	
M	Mesorectum (M)	X	X	X	X	
LLN	Lateral Lymph Nodes (LLN)			X		
IIN	Internal Iliac Nodes (IIN)	X	X		X	
ON	Obturator Nodes (ON)	X	X		X	
EIN	External Iliac Nodes (EIN)	X	X		X	
IRF/IPS	Ischiorectal Fossa (IRF)		X	X	X	
	Inferior Pelvic Subsite (IPS)					
CTV A	CTV A					X
CTV B	CTV B					X
CTV C	CTV C					X

 Table 2

 Definition of subsites: anatomical boundaries and clinical recommendations.

PS Abdominal above the most cranial positive lymph-node above and the most activation of the lumbar vertebrae positive lymph nodes. Pelvic (Candal: bifurcation of the common iliac arterises into the external and internal iliac artery)scarcial promotory and aniemal iliac artery iscarcial points above of the M anterior: 1 cm ventral to the lumbar vertebrae positive: 1 cateral: sacrolilac joints and positive lymph nodes. Midingerior: 1 cm ventral to the lumbar vertebrae positive: 1 cateral: 2 candal: 1 cateral: 2 candal: 1 cateral: 2 candal: 1 cateral: 2 cardal: 3 candal: 3
delineation of M and LLN subsites, when the PS is at the let these 2 structures. In all other cases the PS must be control to the lumbar vertebrae medial: — Luteral: sacroiliac joints M Cranial: bifurcation of the IMA in SA and SRA Caudal: insertion of the IMA in SA and SRA Caudal: insertion of the lewtor ani muscle into the external sphincter muscles (disappearing of the mesorectal fat around the rectum) Anterior Superior: 7 mm beyond SRA excluding bowel structures Mid/inferior: mesorectal fascia, posterior border of the anterior pelvic organs Posterior: Anterior surface of the sacrum and coccyx to the level of IRF (including the medial part of the PS) Medial: — Lateral: Upper/mid: Mesorectal fascia if visible or medial border of the LLN and EIN Lower: medial edge levator ani muscle into the external sphincter muscles (pelvic floor) Upper pelvis: 7 mm around the vessel. Mid pelvis: a virtual coronal plane crossing the anterior wall of the ureters when they join the bladder and the posterior aspect of the external iliac arteries (orresponding to the culmit of the bifurcation of the common iliac arteries in to in all iliac and external iliac arteries (corresponding to the culmit of the bifurcation of the common iliac arteries in to in all iliac and external iliac arteries (corresponding to the culmit of the bifurcation of the common iliac arteries in to in all iliac and external iliac arteries (corresponding to the culmit of the bifurcation of the common iliac arteries in to in all iliac and external iliac arteries (corresponding to the culmit of the bifurcation of the common iliac arteries in to in all iliac and external iliac arteries (corresponding to the culmit of the bifurcation of the common iliac arteries in to in all iliac and external iliac arteries (corresponding to the culmit of the bifurcation of the common iliac arteries in to in all iliac and external iliac arteries (corresponding to the culmit of the bifurcation of the common iliac arteries in to in all iliac and external iliac arteries (correspo
Consider anisotropic CTV-PTV margins anteriorly to account for Caudal: insertion of the levator ani muscle into the external sphincter muscles (disappearing of the mesorectal fat around the rectum) Anterior Superior: 7 mm beyond SRA excluding bowel structures Mid/inferior: mesorectal fascia, posterior border of the anterior pelvic organs Posterior: Anterior surface of the sacrum and coccyx to the level of IRF (including the medial part of the PS) Medial: - Lateral: Upper/mid: Mesorectal fascia if visible or medial border of the LLN and EIN Lower: medial edge levator ani muscle LLN Posterior (ex internal iliac arteries nodes) Posterior (ex internal iliac arteries Caudal: insertion of the levator ani muscle into the external sphincter muscles (pelvic floor) Anterior Upper pelvis: 7 mm around the vessel. Mid pelvis: a virtual coronal plane crossing the anterior wall of the external iliac arteries in to inal iliac and external iliac arteries (corresponding to the colimit of the bifurcation of the common iliac arteries in to inal iliac and external iliac arteries (corresponding to the colimit of the LLN) Inferior pelvis: posterior limit of the obturator fossa Posterior: Lateral edge of the sacro-iliac joint Medial: Cranial limit: (1) In cT3N0, MRF-, the cranial limit may be lowered at the of the bifurcation of the inferior mesenteric artery in sig artery and superior rectal artery (corresponding to the colimit of the M) (2) In all other cases (MRF+ or cT4 or N+) consider the anato limit of the bifurcation of the common iliac arteries in to in all iliac and external iliac arteries (corresponding to the colimit of the LLN)
LLN Posterior (ex internal iliac arteries (1) In cT3N0, MRF-, the cranial limit may be lowered at the condes) Caudal: insertion of the levator ani muscle into the external sphincter muscles (pelvic floor) Anterior Upper pelvis: 7 mm around the vessel. Mid pelvis: a virtual coronal plane crossing the anterior wall of the ureters when they join the bladder and the posterior aspect of the external iliac arteries (corresponding to the condition of the limit of the blifurcation of the common iliac arteries in to it is nal iliac and external iliac arteries (corresponding to the condition of the limit of the blifurcation of the common iliac arteries in to it is nal iliac and external iliac arteries (corresponding to the condition of the limit of the LLN) Inferior pelvis: posterior limit of the obturator fossa Posterior: Lateral edge of the sacro-iliac joint Medial:
anatomic structures Mid/lower: Mesorectal fascia, pelvic organs Lateral Upper: iliopsoas, pelvic bones Mid-lower: medial edge of the pelvic wall muscles (pyriform and internal obturator muscles)
Anterior (ex obturator modes) Anterior Mid pelvis: posterior wall of the EIN Low pelvis (when external iliac vessels leave the pelvis): anterior surface of obturator artery Anterior Mid pelvis: posterior wall of the EIN Low pelvis (when external iliac vessels leave the pelvis): anterior surface of obturator artery Include in case of: (1) positive nodes in the posterior LLN (internal iliac) (2) cT4 (3) numerous mesorectal nodes (cN2)
EIN Cranial: bifurcation of common iliac artery into internal and external iliac arteries Caudal: where the deep circumflex vein crosses the external iliac artery. Alternatively (if difficult detection on CT images) between the acetabulum roof and the superior pubic rami Anterior: 0.7 cm anterior to the vessels. 1.5 cm antero-laterally along the iliopsoas muscle to include the antero-lateral nodes Posterior: posterior border of the external iliac vein Medial: 7 mm medial to the vessel, excluding pelvic organs Lateral: the iliopsoas muscle
IN Cranial: where the deep circumflex vein crosses the external iliac artery. Alternatively (if difficult detection on CT images) between the acetabulum roof and the superior pubic rami Caudal: where the great saphenous vein enters the femoral vein Anterior: at least 20 mm margin around inguinal vessels including any visible lymph nodes or lymphoceles Posterior: the femoral triangle formed by iliopsoas, pectineus and abductor longus muscles Medial: 10-20 mm margin around the femoral vessels including any visible lymph nodes or lymphoceles
Lateral: medial edge of the sartorius or iliopsoas muscles

(continued on next page)

Table 2 (continued)

Sub	osites	Limits	Recommendations
		Caudal: oblique plane joining the inferior level of SC and the ischial tuberosity. Posterior: Mid-superior: major gluteus muscle Inferior: a virtual line tangent to the posterior level of the sphincter Medial: levator ani muscle Lateral: ischial tuberosity, internal obturator muscle, Gluteus maximus muscle	
SC		From the anal-rectal junction. Around the sphincter	To include in case of sphincter infiltration

PS: Presacral space, M: Mesorectum, LLN: Lateral Lymph Nodes, EIN: External Iliac Nodes, IN: Inguinal Nodes, IRF: Ischio-Rectal Fossae, SC: Sphincter Complex, IMA: inferior mesenteric artery, SA: sigmoid artery, SRA: superior rectal artery.

anteriorly bound by the MRF and by the posterior border of the anterior pelvic organs (prostate, seminal vesicles, bladder and penis bulb in men and vagina and uterus in women). An anterior anisotropic internal margin is recommended to account for bladder, uterus and seminal vesicles motion and/or volume variation [6,9]. This subsite is posteriorly bounded by the anterior surface of the sacrum. The WG suggests to include the medial part of PN into the M.

Lateral lymph nodes (LLN): The LLN correlate with a triangular lymph-vascular area located between the pelvic wall and the M, containing the lymphatic vessels and the nodes along the internal iliac and obturator vessels [8]. In the present guidelines this subsite has been divided into two sub-volumes: the posterior and the anterior lateral nodes. The posterior lateral nodes have as anterior border a virtual coronal plane crossing the anterior wall of the ureters when they join the bladder and the posterior aspect of the external iliac vessels cranially (Fig. 1). The anterior lateral nodes have as the anterior border the posterior wall of the external iliac vessels lying anteriorly to the virtual coronal plane crossing the anterior wall of the ureters when it joins the bladder, till external iliac vessels leave the pelvis.

External iliac nodes (EIN): EIN are located around the external iliac vessels. The cranial boundary corresponds to the upper limit of LLN. This region extends caudally to the level of the acetabulum roof and of the superior pubic rami where the deep circumflex vein crosses the external iliac artery (Fig. 2). For the antero-lateral boundary, in the upper pelvis a 7 mm margin should be considered around the external iliac vessels, while in the mid-low pelvis we suggest to take a 15 mm margin, along the ilio-psoas muscle [10].

Ischio-rectal fossa (IRF): IRF is the fatty triangular area formed between the framed by the levator ani muscles, the obturator and gluteus muscles and the ischial tuberosity. It starts where the inferior pudendal artery leaves the pelvis going into the Alcock's canal (Fig. 3) and ends by an oblique plane joining the inferior level of SC and the ischial tuberosity (Fig. 4).

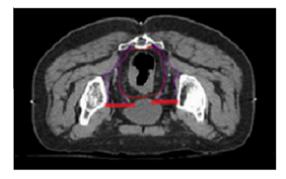


Fig. 1. Anterior border of the posterior lateral node (purple), when the ureters join the bladder (red line).

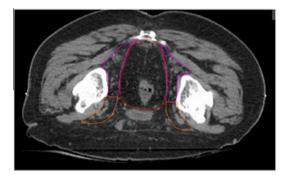


Fig. 2. Caudal border of the external iliac nodes (orange), where the deep circumflex vein crosses the external iliac artery.

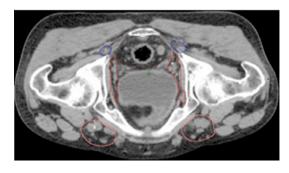


Fig. 3. Cranial border of the ischio-rectal fossa (blue), where the inferior pudendal artery leaves the pelvis going into the Alcock's canal.

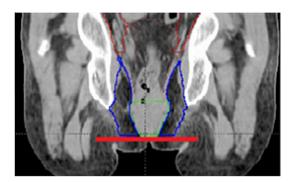


Fig. 4. Caudal border of the ischio-rectal fossa (blue), at the inferior level of the sphincter complex and the ischial tuberosity.

Sphincter complex (SC): The SC consists of the internal and external anal sphincter muscles which enclose the anal canal.

Table 3Elective nodes subsites to include in the CTV according to the tumor stage and location.

	M	PS		LLN		EIN	IRF	IN	SC
		Pelvic	Abdominal	Post	Ant				
cT3	+	+	When LN+	+	+ (in case of numerous mesorectum nodes (N2)				
cT4 (anterior pelvic organ)	+	+	When LN+	+	+	+		+ (in case of infiltration of inferior third of vagina)	
cT4 (anal sphincter)	+	+	When LN+	+	+	+	+ (when direct tumor infiltration of IRF or external anal sphincter)	+	+
cT3 with extra mesorectal node	+	+	When LN+	+	+	+	• •		

M: mesorectum, PS: Presacral Space LLN: Lateral Lymph Nodes, EIN: External iliac Nodes, IRF: Ischiorectal Fossa,IN: Inguinal Nodes, SC: Sphincter Complex.

Inguinal nodes (IN): IN start below the EIN and end where the great saphenous vein enters the femoral vein. An antero-medial margin of at least 20 mm around the inguinal vessels is recommended, including any visible lymph nodes or lymphoceles.

CTV definition: subsite inclusion and modulation according to tumor stage and location

Besides, consensus for nomenclature and delineation of the CTV for elective irradiation of all regional lymph node levels was obtained. Consensus on elective nodes subsites to include in the CTV was achieved: Table 3 demonstrates how the CTV should be tailored according to the tumor stage and location. In this perspective, the M, the pelvic PN and the posterior LLN must always be included in the CTV.

Abdominal PN must only be included when there are positive lymph nodes in this area. The WG proposed to consider the aorta bifurcation as its cranial limit, however at least 5 mm margin above the most cranial positive lymph node should be included.

Posterior LLN must always be included in the CTV. Although its cranial level is located at the bifurcation of the common iliac vessels into the internal and external iliac vessels, the cranial level can be modulated according to MRF and nodal status [8,11,19]. As reported in Table 2, the WG recommended to consider the cranial boundary at the level of the bifurcation of the superior rectal artery, in cT3N0 and MRF-cases. In all the other cases including cT4, cN+ and/or cT3 MRF+, the upper limit remains at the bifurcation of common iliac artery into internal and external iliac arteries.

Anterior LLN, which anatomically corresponds to the obturator nodes, must be enclosed in the CTV only in case of cT4 tumors, multiple positive lymph nodes in the mesorectum (N2-disease) and/or positive nodes in the posterior LLN.

EIN should be included if the primary tumor invades adjacent organs (cT4) or if the anterior LLNs (or obturator nodes) are involved [7,13].

The entire *IRF* should be included in the CTV when the primary tumor directly invades the *IRF* or when the external anal sphincter is infiltrated.

IN are not commonly involved in rectal cancer. The WG proposed to include this sub-site in the CTV in case of positive inguinal nodes, massive tumor extension into the internal or external anal sphincter or when the lower third of the vagina is infiltrated [14].

RC cases atlases

As RC CTV delineation depends on tumor stage and location, seven RC cases were chosen as delineation atlases:

- cT3 mid-rectum MRF—: rectal lesion starting at 4 cm above the ano-rectal junction and extending over 4 cm cranially with evidence of early infiltration of mesorectal fat. Three mesorectal nodes are observed (clinical stage: cT3N1M0).
- cT3 low-rectum MRF-: rectal lesion above the dentate line, cranially extending over 2 cm, with evidence of early infiltration of mesorectal fat. Multiple mesorectal nodes are observed (clinical stage: cT3N2M0).
- cT3 MRF+: a vegetating lesion of mid-rectum starting at 4 cm above the ano-rectal junction and extending cranially over 6.5 cm. The tumor infiltrates the mesorectal fat and reaches the MRF anteriorly. Three mesorectal nodes are observed (clinical stage: cT3N1M0 MRF+).
- cT4 with infiltration of anterior organ: a bulky circumferential vegetating lesion at the level of the anal canal and the low-rectum, cranially extending over 10 cm. The tumor infiltrates the prostate, both the seminal vesicles and obliterates the prostatic-bladder angle. The tumor infiltrates the mesorectal fat with a nodule reaching the MRF on the left. Multiple mesorectal nodes are observed (clinical stage: cT4N2M0).
- cT4 with infiltration of the internal anal sphincter: a wall thickening "plaque" at the level of the low-rectum and extending cranially over 4 cm. This lesion infiltrates the internal anal sphincter and the mesorectal fat. Multiple nodes were observed in the mesorectum and in the right obturator and internal iliac areas (clinical stage: cT4N2M0).
- cT4 with infiltration of the external anal sphincter: a vegetating lesion of low-rectum which extended caudally in the anal canal, infiltrating the internal and external anal sphincter and the mesorectal fat. Multiple nodes are observed in the Mesorectum, in the internal iliac and inguinal areas (clinical stage: cT4N2M0).
- LLN involvement: a circumferential lesion starting at 4 cm from the ano-rectal junction. The tumor anteriorly reaches the MRF and the right seminal vesicle. There are multiple nodes in the mesorectum and in the left obturator area (clinical stage: cT4N2M0).

Discussion

Consensus guidelines for RC CTV were developed based on a detailed analysis of local and nodal recurrences in the "TME era", on a review of the available RC delineation guidelines and on surgical and radiological pelvic anatomical knowledge.

This peer review process was conducted by seven ROs with recognized expertise in RC treatment, each of them author of at least one of the available guidelines and members of ESTRO, ASTRO, TROG and FORTC.

An unanimous degree of agreement was reached through teleconferences, live meetings and delineation exercises using the Falcon platform, the educational ESTRO web-based multifunctional platform for target volume delineation. The definition of a road map by a series of scheduled steps has allowed us to achieve a uniform consensus within 21 months. Our efforts led to the following deliverables: the consensus guidelines for RC sub-sites with the correlating table of boundaries, a recommendation about which subsites to include into the CTV according to tumor stage and location, and seven clinical RC cases which are available on the Falcon platform to illustrate the consensus guidelines and to offer health care practitioners the possibility to train themselves.

In the CTV proposal, the M, the pelvic PN and the posterior LLN should always be included, whereas the inclusion of the anterior LLN, the SC, the IRF and the IN depends on tumor stage and tumor location. The major differences/changes compared to previous published guidelines are:

- The abdominal presacral nodes have been added as a new subvolume to the rectal CTV. This sub-volume should only be included when it harbors positive nodes. The advent of highly-conformal radiotherapy techniques such as intensitymodulated radiotherapy (IMRT) or volumetric-modulated arc therapy (VMAT) allows to irradiate larger volumes without a significant increase of toxicity [15,16].
- One of the major differences between these consensus guidelines and the previous ones, is the level of the LLN cranial border.
 In case of cT3, cN0 tumors without invasion of the MRF, the upper border of the LLN can be lowered to the cranial border of the M, corresponding with the bifurcation of the superior rectal artery.
 - In a recent update of Roel's guidelines, the authors discussed the opportunity to modify the cranial level of the CTV [11], based on literature data on local recurrences. This is consistent with the post-TME era data on local recurrences: the highest rate of recurrence has been reported in the posterior pelvis and the anastomotic area [17], whereas the radiological evidence of recurrence in the LLN is shown to be well below 5% [18]. In a large study investigating 99 cross-sectional imaging series, all local recurrences occurred in the lower pelvis, below the S1–S2 interspace [18]. Similar observations were made in an analysis of local recurrences of patients included in the Dutch TME trial, particularly in patients without primary nodal involvement and involvement of the MRF [19]. In the same study, it was demonstrated that lowering the cranial limit might reduce the small bowel exposure at dose levels from 15 to 35 Gy with 60% 3D-conventional radiotherapy and with 80% when IMRT was used [19].
- Another major difference is the modification of the position the anterior border of the LLN sub-site, according to local recurrences data [18,19]. The WG recommends inclusion of the obturator nodes, named as anterior LLN in the present guidelines, by moving forward the anterior border behind the external iliac vessels, only in case of cT4 with anterior organ infiltration and/or numerous mesorectal nodes (cN2) and positive nodes in the posterior LLN. In less advanced cases the WG suggests to include only the posterior LLN. Hence, a more posterior limit of the anterior LLN border is considered, corresponding to a virtual coronal plane crossing the anterior wall of the ureters when they join the bladder and the posterior aspect of the external iliac vessels cranially.
- Finally, another major difference with the other previously published guidelines is the definition of IRF and the criteria to include this subsite into the CTV.
 - The superior border is defined as the level where the inferior pudendal artery leaves the pelvis going into Alcock's canal. Caudally, the IRF ends at the caudal limit of SC. The WG suggests to include the IRF into the CTV when the tumor invades the

external anal sphincter. This recommendation is based on the vascular supply of the external anal sphincter by the inferior rectal artery which branches from the internal pudendal artery and the internal iliac artery. The second indication to include the IRF in the CTV is its infiltration by the tumor. It is now recognized that the levator ani muscles constitute an effective barrier against cancer spread into the ischio-rectal space and not a single case of nodal metastasis in the IRF has been reported in literature [13]. For these reasons, which have been debated before [8,11,13], the WG decided to omit the previous recommendation to include the IRF when tumors are located below 6 cm from the anal verge. Irradiation of the IRF subsite could increase the risk of acute skin toxicity and might result in delayed perineal wound healing after abdominal-perineal resection (APR) [13,20]. Therefore, the WG suggests to omit the IRF in preoperative radiotherapy schedules when patients undergo APR for tumors superficially infiltrating the IRF. Although recurrences in the IRF have frequently been reported in patients who underwent APR, these recurrences seem to be related to tumor spillage during inadequate surgical procedure rather than to tumor cells located in the IRF [11,13].

The goal of this international consensus was to provide reproducible guideline for RC CTV delineation in order to create a common language through the minimization of misinterpretation of CTV definition, creation of common nomenclature of different subsites, definition of shared anatomical boundaries, provision of detailed on-line atlases and an archive of case studies on the Falcon platform to utilized for individual training.

Uniform RC CTV delineation guidelines will likely decrease the inter-observer variability in CTV delineation and will facilitate outcome comparison between RC trials.

Future research should focus on validating the reproducibility and on investigating the dosimetrical and clinical impact of these guidelines.

Conflict of interest statement

All authors declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.radonc.2016.07. 017.

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Further reading

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