

Clinical Investigation: Gastrointestinal Cancer

# Australasian Gastrointestinal Trials Group (AGITG) Contouring Atlas and Planning Guidelines for Intensity-Modulated Radiotherapy in Anal Cancer

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## Summary

Chemoradiation is the standard of care for patients with anal canal SCC. IMRT is increasingly used to reduce treatment-associated toxicity. Critical to its use is accurate and consistent volume contouring. This publication represents the AGITG consensus recommendations of tumor, nodal and organ at risk volume delineation in anal cancer. Provided are detailed guidelines and a high resolution atlas which

**Purpose:** To develop a high-resolution target volume atlas with intensity-modulated radiotherapy (IMRT) planning guidelines for the conformal treatment of anal cancer.

**Methods and Materials:** A draft contouring atlas and planning guidelines for anal cancer IMRT were prepared at the Australasian Gastrointestinal Trials Group (AGITG) annual meeting in September 2010. An expert panel of radiation oncologists contoured an anal cancer case to generate discussion on recommendations regarding target definition for gross disease, elective nodal volumes, and organs at risk (OARs). Clinical target volume (CTV) and planning target volume (PTV) margins, dose fractionation, and other IMRT-specific issues were also addressed. A steering committee produced the final consensus guidelines.

**Results:** Detailed contouring and planning guidelines and a high-resolution atlas are provided. Gross tumor and elective target volumes are described and pictorially depicted. All elective regions should be routinely contoured for all disease stages, with the possible exception of the inguinal and high pelvic nodes for select, early-stage T1N0. A 20-mm CTV margin for the primary, 10- to 20-mm CTV margin for involved nodes and a 7-mm CTV margin for the elective pelvic nodal groups are recommended, while respecting anatomical boundaries. A 5- to 10-mm PTV margin is suggested. When using a simultaneous integrated boost technique, a dose of 54 Gy in 30 fractions to gross disease and 45 Gy to elective nodes with chemotherapy is appropriate. Guidelines are provided for OAR delineation.

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will be useful to the practicing radiation oncologist.

**Conclusion:** These consensus planning guidelines and high-resolution atlas complement the existing Radiation Therapy Oncology Group (RTOG) elective nodal ano-rectal atlas and provide additional anatomic, clinical, and technical instructions to guide radiation oncologists in the planning and delivery of IMRT for anal cancer. © 2012 Elsevier Inc.

**Keywords:** Anal cancer, IMRT, Chemoradiation, Atlas, Guidelines

## Introduction

With the advent of computed tomography (CT) planning and conformal radiation techniques including intensity-modulated radiotherapy (IMRT), comes the prerequisite for accurate and consistent contouring of target volumes.

Conformal radiotherapy for anal cancer allows the ability to spare surrounding organs at risk (OAR). Normal tissues such as small bowel, femoral heads, perineum, and external genitalia often receive high doses of radiation with more conventional techniques, which can result in significant acute and late toxicity. The use of IMRT provides an opportunity to spare OAR and to reduce toxicity in anal cancer patients.

The implementation of IMRT requires a clear understanding of target volume definition for the complex elective nodal regions in anal cancer. During the early conduct of the Radiation Therapy Oncology Group (RTOG) 0529 Phase II study investigating IMRT for anal cancer, it became necessary to create an atlas because many initial target volumes submitted for quality assurance required contouring revision (1). However, this atlas provided contouring guidance for elective nodal volumes only and did not provide instruction in the contouring of gross disease and OAR.

As such, an international workshop was convened at the 2010 Australasian Gastrointestinal Trials Group (AGITG) annual meeting to develop detailed contouring and planning guidelines for the IMRT treatment of anal cancer, supplemented by a high-resolution atlas. This article reports the AGITG recommendations.

## Methods and Materials

The AGITG is a national cooperative trials group that consists of radiation oncologists, surgeons, and medical oncologists who conduct clinical trials in gastrointestinal malignancies. In 2010, the Radiation Oncology Committee of AGITG organized a contouring workshop with member radiation oncologists to discuss radiotherapy target and OAR volume delineation for anal cancer, with the aim of developing consensus guidelines. Dr. Lisa Kachnic (L.K.), principal investigator of the RTOG 0529 study of IMRT in anal cancer, was invited to participate in the workshop.

To facilitate discussion and productivity at the workshop, a draft set of IMRT contouring and planning guidelines was sent to all 19 workshop participants before the meeting. These were based on anal canal IMRT guidelines previously developed in 2009 by the Gastrointestinal Unit at the Peter MacCallum Cancer Centre (PMCC). The aim of the PMCC guidelines, building off of previous publications describing clinical target volume (CTV) delineation for ano-rectal cancer (2, 3), was to standardize CTVs among radiation oncologists.

The draft guidelines described seven elective regions to be considered when treating anal cancer, including the mesorectum, presacral space, internal iliac lymph nodes, external iliac lymph nodes, obturator lymph nodes, ischio-rectal fossa, and inguinal

lymph nodes. Each elective region was described individually, including borders for CTV delineation. The guidelines also contained recommendations for contouring target volumes for gross disease and instructions for standardized contouring of OAR. Planning target volume (PTV) margins, dose fractionation, and other IMRT-specific issues were also addressed.

The AGITG workshop was coordinated by two chairs, A.K. and M.N., and three radiation oncologists (T.L., S.Ca. and L.K.) who were invited to form a discussion panel. Before the meeting, each panelist was sent an anonymized CT dataset of a female patient with a T2N0 anal cancer. The gross tumor volume (GTV) was already defined, and panelists were asked to delineate the above target volumes and OAR. These volumes were then displayed, serving as discussion points for the development of consensus guidelines and an atlas (Fig. 3–5: Atlas Panels 1,2,3 respectively). Where available, references are provided with these final recommendations.

## Results

### Elective nodal volumes

#### *Mesorectum*

The mesorectum is not well visualized on CT, and if fat-saturated T2 magnetic resonance imaging cannot be obtained, neighboring structures can be used to delineate this volume.

**Cranial:** The level of the recto-sigmoid junction; best identified where the rectum runs anteriorly to join the sigmoid colon (Atlas 4b).

**Caudal:** The ano-rectal junction, defined by where the levator muscles fuse with the external sphincter muscles, where mesorectal fat/space is no longer seen tapering inferiorly (Atlas 10a). Often this level can be identified by a plane drawn from the caudal edge of the pubic symphysis to the coccyx transecting the rectum (Fig. 1).

**Posterior:** The presacral space (Atlas 5b).

**Anterior:** For males, the boundary is formed by the penile bulb and prostate in the lower pelvis, and by the posterior edge of the seminal vesicles (SV) and bladder in the mid pelvis (Atlas 6b). In females, the boundary is formed by the bladder, vagina, cervix, and uterus. An internal margin of 10 mm should be added to this anterior mesorectal border on axial slices containing bladder, SV, or uterus to account for the effect of bladder volume variation (Atlas 5c–8c) (4).

**Lateral:** In the lower pelvis, the border is the medial edge of the levator ani (Atlas 9b). In the upper pelvis, it is the internal iliac lymph node group (Atlas 4b).

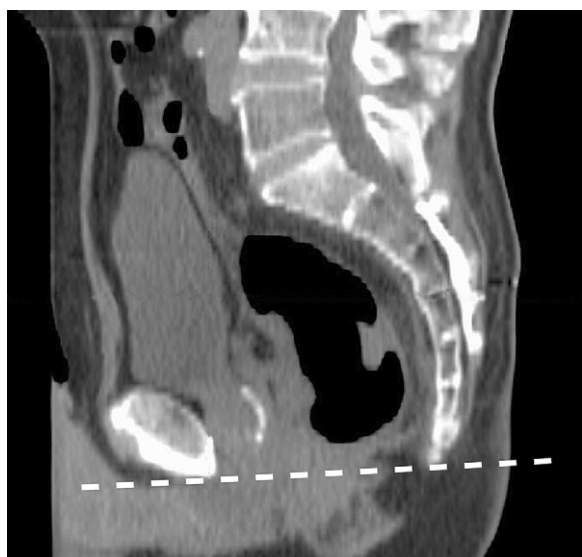
#### *Presacral space*

The presacral space lies posterior to the mesorectum and contains lymph nodes that may harbor micro-metastatic disease.

**Cranial:** The sacral promontory, defined at the L5–S1 interspace (Atlas 1b).

**Caudal:** The inferior edge of the coccyx (Atlas 8b).

**Lateral:** The sacro-iliac joints (Atlas 3b).



**Fig. 1.** Caudal level of mesorectum clinical target volume (CTV).

Anterior: Ten mm anterior to the anterior sacral border encompassing any lymph nodes or presacral vessels (Atlas 2b) (5).

Posterior: The position at the anterior border of the sacral bone. The sacral hollows should be included in this volume (Atlas 3a).

#### *Internal iliac lymph nodes*

This group of nodes lies lateral to the mesorectum and presacral space and are associated with the internal iliac vessels.

Cranial: Bifurcation of the common iliac artery into the external and internal iliac arteries (usually corresponds to the L5–S1 interspace level) (Atlas 1a).

Caudal: This volume typically ends caudally where the fibers of the levator ani insert into the obturator fascia and obturator internus, and can be demarcated either at the level of the obturator canal, or at the level where there is no space between the obturator internus muscle and the midline organs (bladder, SV) (Atlas 8b).

Lateral: The medial edge of the obturator internus muscle (or bone where the obturator internus is not present) in the lower pelvis (Atlas 7b); iliopsoas muscle in the upper pelvis. (Atlas 2b)

Medial: The mesorectum and the presacral space in the lower pelvis (Atlas 8b). In the upper pelvis, a 7-mm medial margin is recommended from the internal iliac vessels (5).

Anterior: The obturator internus muscle or bone in the lower pelvis. In the upper pelvis, a 7-mm margin around the internal iliac vessels (Atlas 1b).

#### *Ischioanal fossa (IRF)*

Cranial: The apex of the IRF is formed by the levator ani, gluteus maximus, and obturator internus (Atlas 9b).

Caudal: There exists no anatomical structure that delineates the most inferior level of the IRF, and we suggest that this corresponds with the level of the anal verge (Atlas 12a).

Lateral: The lateral walls of the IRF are formed by the ischial tuberosity, obturator internus, and gluteus maximus muscles (Atlas 10a).

Anterior: The level where the obturator internus muscle, levator ani, and anal sphincter muscles fuse (Atlas 10b). Inferiorly, at least 10- to 20-mm anterior to the sphincter muscles.

Posterior: A transverse plane joining the anterior edge of the medial walls of the gluteus maximus muscle (Atlas 10b).

#### *Obturator nodes*

These nodes lie along the obturator artery, a branch of the internal iliac artery that usually starts at the level of the acetabulum. This branch travels inferiorly and anteriorly, exiting the pelvis via the obturator canal. The target volume for the obturator nodes is small, being 3- to 5-mm in the cranio-caudal axis (Atlas 6b).

Cranial: Three to 5 mm cranial to the obturator canal where the obturator artery is sometimes visible.

Caudal: The obturator canal (Atlas 7a), where the obturator artery has exited the pelvis.

Anterior: The anterior extent of the obturator internus muscle.

Posterior: The internal iliac lymph node group.

Lateral: The obturator internus muscle.

Medial: The bladder.

#### *External iliac lymph nodes*

The draining lymphatics are associated with the external iliac vessels.

Cranial: Bifurcation of the common iliac artery into the external and internal iliac arteries (Atlas 1a).

Caudal: The level where the external iliac vessels are still located within the bony pelvis (Atlas 5a) before continuing as the femoral artery. This transition usually occurs between the acetabulum's roof and the superior pubic rami (Fig. 2).

Lateral: The iliopsoas muscle (Atlas 4a).

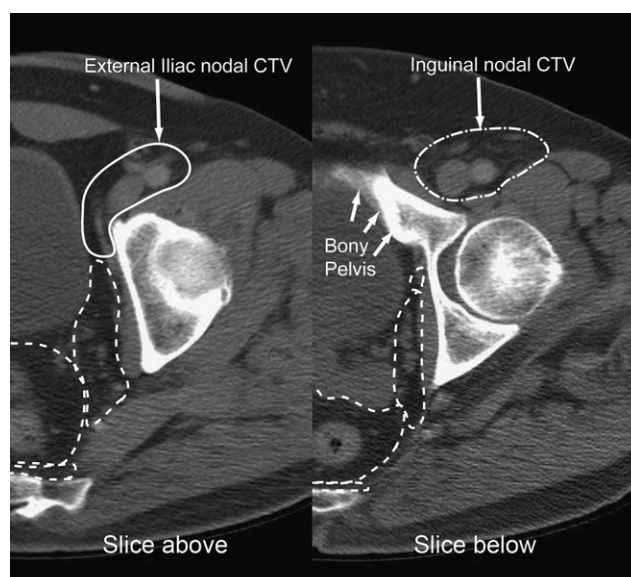
Medially: Usually, the bladder forms the medial wall; otherwise a 7-mm margin around the vessels (Atlas 5b).

Anterior: A 7-mm margin anterior to the external iliac vessels (Atlas 3b).

Posterior: The internal iliac lymph node group (Atlas 4b).

#### *Inguinal lymph nodes*

There is a lack of evidence to define the borders of the inguinal lymph node group. Both superficial and deep inguinal lymph nodes of the femoral triangle, and any visible lymph nodes or lympho-coles outside the following boundaries, should be included.



**Fig. 2.** Transition of external iliac clinical target volume (CTV) to inguinal CTV.



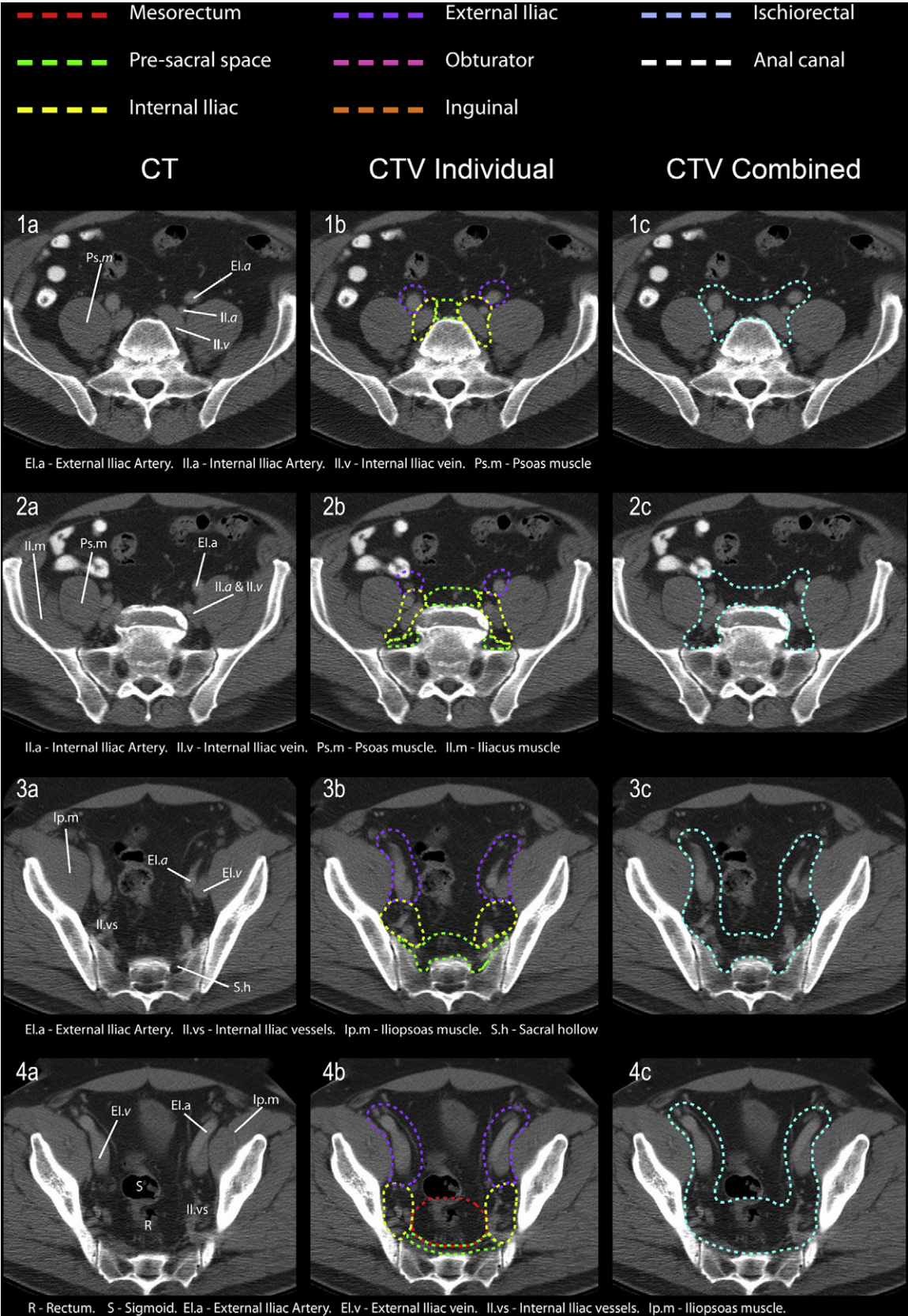
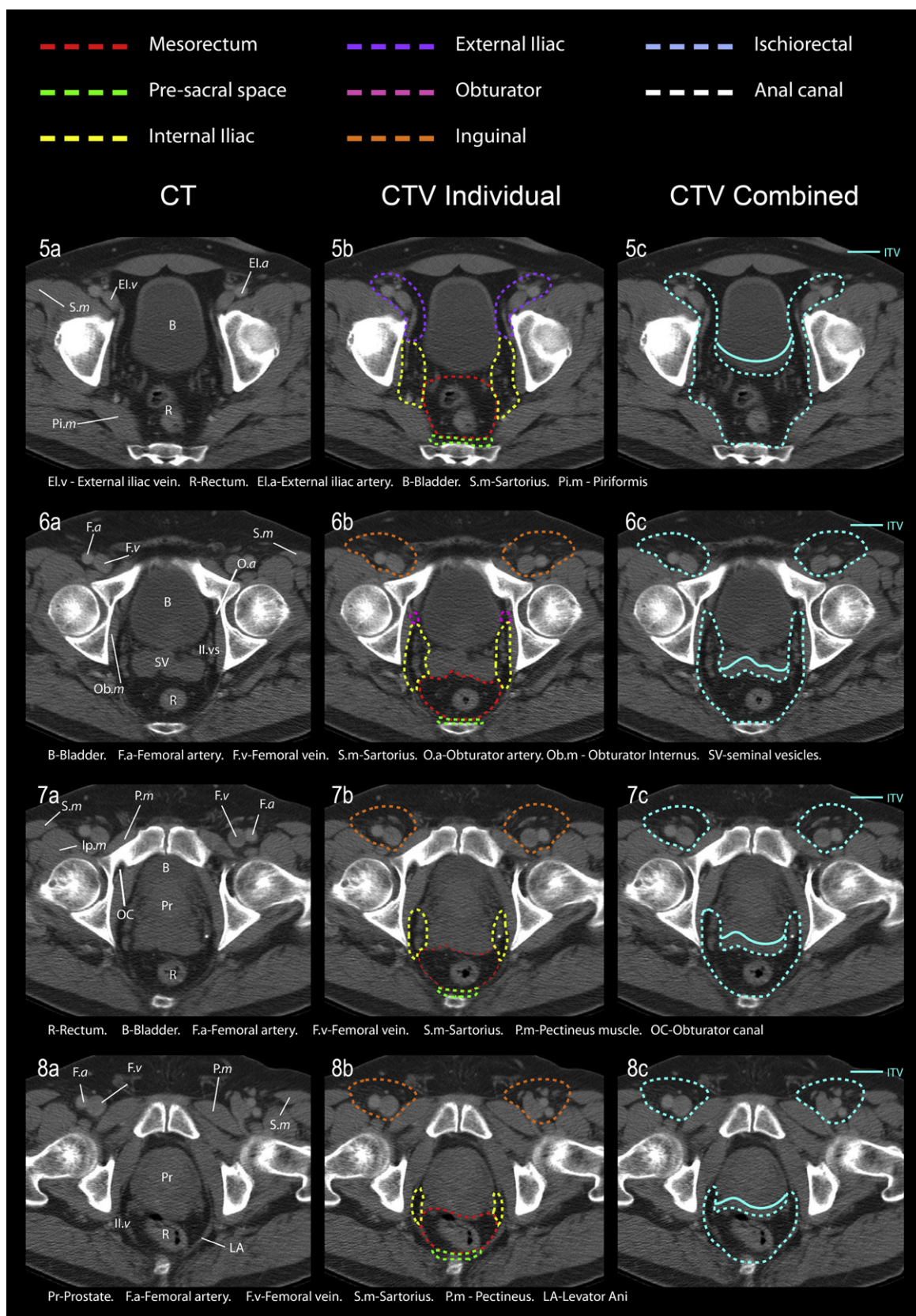


Fig. 3. Atlas panel 1.



**Fig. 4.** Atlas panel 2.



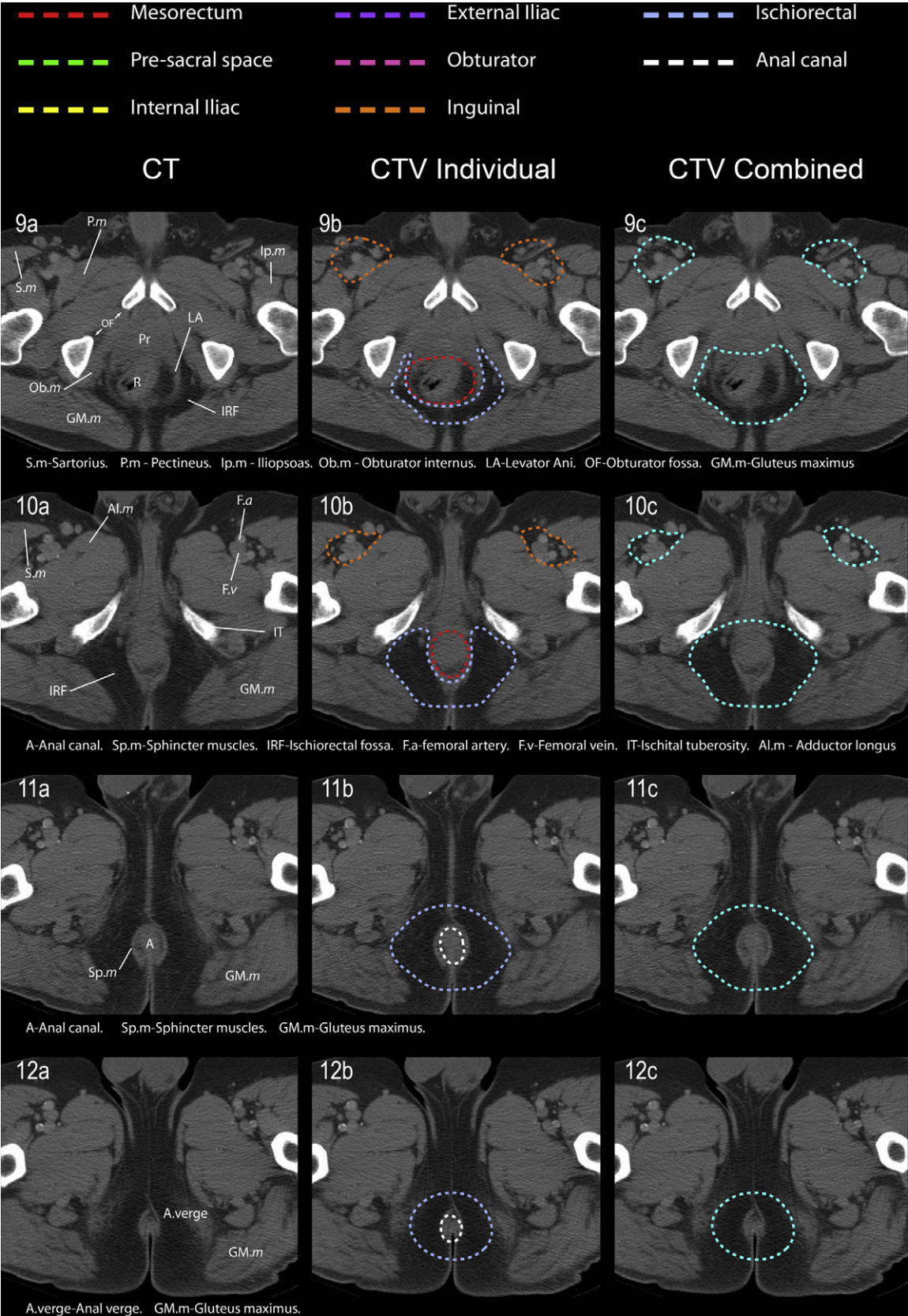


Fig. 5. Atlas panel 3.

**Cranial:** The level where the external iliac artery leaves the bony pelvis to become the femoral artery (Fig. 2).

**Caudal:** There is no consensus on the definition of the inferior extent. Some publications have recommended (a) the position where the great saphenous vein enters the femoral vein with a margin (2), or (b) where the muscles of sartorius and adductor longus cross (6). A compromise is the lower edge of the ischial tuberosities, which lies between (a) and (b) as defined above and is an identifiable landmark (Atlas 10a).

**Posterior:** The bed of the femoral triangle is formed by the iliopsoas, pectineus, and adductor longus muscles (Atlas 10a).

**Anterior:** A minimum 20-mm margin on the inguinal vessels, inclusive of any visible lymph nodes or lymphocoeles (Atlas 7b).

**Lateral:** The medial edge of sartorius or iliopsoas (Atlas 7a).

**Medial:** A 10- to 20-mm margin around the femoral vessels. The medial third to half of the pectineus or adductor longus muscle serves as an approximate border (Atlas 7b).

## Elective nodal volumes to be covered per stage of disease

All nodal volumes described should be covered for all stages. In patients with select early T1N0 cancers, particularly those patients with major comorbidities, it may be appropriate to omit elective nodal irradiation superior to the caudal edge of the sacro-iliac joints, and the inguinal nodes (low risk of failure, <5%) (7).

## Clinical target volumes for gross disease

### Primary tumor

- **GTV:** The GTV should be delineated as a separate structure based on all available clinical and imaging information.
- **CTV:** This volume must encompass (1) the GTV, (2) the entire anal canal from the ano-rectal junction to the anal verge, and (3) the internal and external anal sphincters. A further 20-mm isotropic margin should be added to items (1), (2), and (3) above, to account for microscopic disease, while respecting anatomical boundaries. Attention must be given, especially for anal verge and perianal lesions, that a 20-mm radial and caudal margin is used to ensure coverage of perianal skin.

### Involved nodes

- **GTV:** The involved node(s).
- **CTV:** The involved node(s) or nodal region(s) with a 10- to 20-mm margin, respecting anatomical boundaries.

## Planning target volumes

An isotropic 10-mm expansion is recommended on CTVs to generate PTVs. Daily image guidance is recommended for IMRT, especially prone patients, which may allow CTV–PTV margin reduction to 5- to 7-mm.

## Dose and fractionation with IMRT

Dose and fractionation for radical treatment depends on the following: disease stage; whether excisional biopsy has been performed; use of concurrent chemotherapy; macroscopic vs. microscopic disease; and the use of a simultaneous integrated boost (SIB) technique. We prefer

a SIB technique because of the reduced planning complexity compared with a sequential approach.

In general, gross disease should be treated to 54 Gy over 30 fractions when using chemotherapy. However, for T1 and non-bulky T2 tumors, a dose of 50.4 Gy in 28 fractions is appropriate. Involved nodes/regions should receive 50.4 to 54 Gy, depending on size.

Higher doses to treat elective nodal regions must be considered when using SIB techniques to account for longer treatment duration. For total doses of 54 Gy or more over 30 fractions, the recommended elective dose is 45 Gy. If using 50.4 Gy in 28 fractions, the recommended elective dose is 42 Gy (8). When using a sequential technique, an initial elective dose of 30 to 36 Gy, followed by a boost to macroscopic disease totaling 50.4 to 60 Gy, is appropriate (9).

## Organs at risk (OAR)

**Femoral head and neck:** The entire femoral head and neck should be contoured. The inferior extent is the cranial edge of the lesser trochanter.

**Urinary bladder:** The entire external outline of the bladder wall should be contoured.

**Bowel:** Although many descriptions for contouring the “bowel” exist, only one publication has correlated dose to the bowel with gastrointestinal toxicity in anal cancer patients (10). We have therefore followed the recommendations in this report. Small bowel and large bowel, opacified or nonopacified, should be delineated from 15-mm superior to the cranial aspect of the PTV, extending inferiorly to the recto-sigmoid junction. In the anterior–posterior direction, the bowel will be contoured from the anterior abdominal wall to the most posterior extent of bowel. In the lateral direction, the borders are bowel edge to bowel edge.

**External genitalia and perineum:** There are no established recommendations for contouring this volume. In males, this volume will include the penis, scrotum, and area including skin and fat anterior to the pubic symphysis. In females, this volume will include the clitoris, labia majora and minora, and area including skin and fat anterior to pubic symphysis. The cranial extent of this volume is the caudal edge of the pubic symphysis.

**Bone marrow:** Both iliac crests will be used to define “bone marrow.” Delineation will extend cranially from the top of the iliac crests to the superior part of the acetabulum caudally. The left and right iliac crests are combined into one volume (8, 11).

No recommended dose constraints are provided, given the lack of data specific to anal cancer and the variation among different institutions. Guidelines on dose constraints may be found per the RTOG 0529 closed study protocol (<http://www.rtog.org>).

## Discussion

The implementation of IMRT in anal cancer requires accurate CT contouring of clinical target volumes. Roels *et al.* originally highlighted the need for guidelines in contour delineation in radiotherapy for rectal cancer (3). Subsequently, the RTOG released an atlas and guidelines for ano-rectal cancer that was driven by the need to improve contouring quality in the RTOG 0529 trial (2). With the early implementation of IMRT in Australia, the AGITG meeting provided a unique opportunity for GI radiation oncologists to develop detailed contouring and planning consensus guidelines for IMRT in anal cancer.

This document aims to address the important points that need to be considered when implementing IMRT for anal cancer. We have attempted to provide clear descriptions of individual nodal groups complementary to the RTOG ano-rectal IMRT directives, and these are supplemented with a high-resolution atlas. The determination of CTV borders for individual nodal groups has been based on a combination of anatomical landmarks (when unambiguous), descriptions available in the published literature, and traditional field borders based on bony landmarks. In addition, we have provided detailed instruction in the contouring of gross disease and OAR, as well as considerations for planning parameters.

There were specific issues for which we did not automatically reach consensus during the meeting. For example, defining the lateral and inferior boundaries of the IRF was difficult. It was believed that microscopic disease was unlikely to be found at these lateral edges; however, without supporting evidence, we conservatively recommended treating the entire IRF. The RTOG guidelines do not consider the IRF to be an area at risk. However, because traditional 2D pelvic fields from previous randomized controlled trials encompassed the entire IRF (intentionally or unintentionally) (9), we have recommended including the IRF. Patterns of failure data from RTOG 0529 will help to clarify whether the IRF is at risk.

The inguinal lymph node group was another region where consensus was difficult to achieve. Some publications have recommended using a uniform radial margin around the pelvic vessels to encompass lymph nodes (5, 12). However, applying a “margin rule” for femoral vessels has its limitations, given that there is no clear anatomical compartment and that variation is seen with different body habitus. To account for body habitus, our recommendations use a combination of landmark-based boundaries and margins when no anatomical boundaries exist. The inferior edge of the ischial tuberosity was selected as the caudal level for contouring the inguinal fossa. As there is no anatomic landmark, the tuberosity level provided acceptable caudal coverage and is easily identifiable.

We also provided some recommendations for delineation of the CTV for gross disease. The group acknowledged that traditional two-dimensional fields have recommended a 20- to 30-mm margin for the field edge around gross disease for the “boost” volume. The consensus for this boost volume was to include the entire anal canal and sphincter muscles with a further margin. There was variation in this expansion margin during the meeting, with a range of 10- to 20-mm. With no published pathology data to help clarify the microscopic extent, we conservatively recommended a 20-mm margin. Similarly, there was a variation of 10- to 20-mm for the CTV margin around involved nodes to account for extracapsular extension (ECE). A minimum of 10-mm was based on pathological studies on ECE of metastatic lymph nodes in head-and-neck squamous cell carcinoma (13).

One minor area of contention was how to describe the anterior CTV of the mesorectum. Nuytens *et al.* reported that the anterior wall of the mesorectum can vary by 10-mm (4). The RTOG atlas accounts for the 10 mm of motion by contouring into the bladder and describing this as the CTV (2). Roels *et al.* defined the anterior CTV border of the mesorectum behind the bladder or SV, and did not address potential organ motion (3). We have addressed this issue by using ICRU63 definitions where we describe an internal margin of 10-mm to be added to the CTV at the levels of the bladder to form an internal target volume.

This report does not discuss other important IMRT issues in anal cancer, such as patient setup and immobilization, supine vs. prone position, use of fiducials, and bolus. These issues need to be considered by the clinician, but are beyond the scope of this article.

These anal cancer IMRT guidelines are based on recommendations from a consensus working group. When there were differences in opinion and lack of supporting evidence, we have generally been more conservative in our recommendations. As such, these consensus guidelines should be continuously re-evaluated as centers gain more clinical experience and as new evidence is reported.

## Conclusion

IMRT for anal cancer has significant potential to benefit patients. These detailed guidelines, supplemented with a high-resolution atlas, aim to improve the understanding of target volume definition and IMRT planning for anal cancer.

## References

1. Kachnic LA, Winter K, Myerson RJ, *et al.* RTOG 0529: A phase II evaluation of dose-painted IMRT in combination with 5-fluorouracil and mitomycin-C for reduction of acute morbidity in carcinoma of the anal canal. *Int J Radiat Oncol Biol Phys* 2009;75:S5.
2. Myerson RJ, Garofalo MC, El Naqa I, *et al.* Elective clinical target volumes for conformal therapy in anorectal cancer: A Radiation Therapy Oncology Group consensus panel contouring atlas. *Int J Radiat Oncol Biol Phys* 2009;74:824-830.
3. Roels S, Duthoy W, Haustermans K, *et al.* Definition and delineation of the clinical target volume for rectal cancer. *Int J Radiat Oncol Biol Phys* 2006;65:1129-1142.
4. Nuytens JJ, Robertson JM, Yan D, *et al.* The variability of the clinical target volume for rectal cancer due to internal organ motion during adjuvant treatment. *Int J Radiat Oncol Biol Phys* 2002;53:497-503.
5. Taylor A, Rockall A, Reznick R, *et al.* Mapping pelvic lymph nodes: Guidelines for delineation in intensity-modulated radiotherapy. *Int J Radiat Oncol Biol Phys* 2005;63:1604-1612.
6. Portaluri M, Bambace S, Perez C, *et al.* Clinical and anatomical guidelines in pelvic cancer contouring for radiotherapy treatment planning. *Cancer Radiother* 2004;8:222-229.
7. Tomaszewski JM, Link E, Leong T, *et al.* Twenty-five-year experience with radical chemoradiation for anal cancer. *Int J Radiat Oncol Biol Phys* 2011 Oct 21. [Epub ahead of print]. PMID: 22019078.
8. Kachnic L, Winter K, Myerson R. RTOG 05-29: A phase II evaluation of dose-painted IMRT in combination with 5-fluorouracil and mitomycin-C for reduction of acute morbidity in carcinoma of the anal canal. 2005. Available at [www.rtog.org](http://www.rtog.org). Accessed February 15, 2011.
9. Ajani JA, Winter KA, Gunderson LL, *et al.* Fluorouracil, mitomycin, and radiotherapy vs fluorouracil, cisplatin, and radiotherapy for carcinoma of the anal canal: A randomized controlled trial. *JAMA* 2008;299:1914-1921.
10. Devisetty K, Mell LK, Salama JK, *et al.* A multi-institutional acute gastrointestinal toxicity analysis of anal cancer patients treated with concurrent intensity-modulated radiation therapy (IMRT) and chemotherapy. *Radiother Oncol* 2009;93:298-301.
11. Menkarios C, Azria D, Laliberte B, *et al.* Optimal organ-sparing intensity-modulated radiation therapy (IMRT) regimen for the treatment of locally advanced anal canal carcinoma: A comparison of conventional and IMRT plans. *Radiat Oncol* 2007;2:41.
12. Chao KS, Lin M. Lymphangiogram-assisted lymph node target delineation for patients with gynecologic malignancies. *Int J Radiat Oncol Biol Phys* 2002;54:1147-1152.
13. Apisarnthanarax S, Elliott DD, El-Naggar AK, *et al.* Determining optimal clinical target volume margins in head-and-neck cancer based on microscopic extracapsular extension of metastatic neck nodes. *Int J Radiat Oncol Biol Phys* 2006;64:678-683.