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Jiade J. Lu *Editors*

Target Volume Delineation and Field Setup

A Practical Guide for Conformal and Intensity-Modulated Radiation Therapy

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Contents

Nasopharyngeal Carcinoma

1

Nancy Y. Lee, Quynh-Thu Le, Brian O'Sullivan, and Jiade J. Lu

General Principles of Planning and Target Delineation

- Intensity-modulated radiation therapy (IMRT) is the standard technique for definitive radiation therapy for nasopharyngeal cancer (NPC). In addition to thorough physical examination, adequate imaging studies should be obtained for diagnosis, staging, and planning. Unless contraindicated, all patients should undergo MRI of the nasopharynx and neck, preferably 3-mm slice thickness. A PET/CT scan is also preferable. However, including the PET-avid region only as gross tumor volume (GTV) is inadequate. The skull base, i.e., clivus, and the nerves are best seen on MRI. Marrow infiltration of disease is best seen on T1-weighted noncontrast MRI sequence. Fusion of the skull base portion of the MRI will aid in the delineation of the GTV.
- CT simulation with IV contrast should be performed to help guide the GTV target, particularly for the lymph nodes.
- A bite block can be placed during simulation and throughout radiation to push the tongue away from the high-dose nasopharynx region. If an all-in-one IMRT plan is done, a thermoplastic mask to immobilize the head and neck including the shoulders will be preferable to only immobilizing the head and neck region.

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- Target volumes include gross tumor volume (GTV); clinical target volume (CTV) should be delineated on every slice on the planning CT; accurate selection and delineation of the CTV for gross disease (i.e., CTV_{70}) and the CTV for high-risk region ($CTV_{59.4}$) are the most critical processes when implementing IMRT for NPC.
- Suggested target volumes at the GTV and high-risk CTV are detailed in Tables 1.1 and 1.2.

Table 1.1 Suggested target volumes at the gross disease region

Target volumes	Definition and description
GTV_{70*} (the subscript 70 denotes the radiation dose delivered)	Primary: all gross disease on physical examination and imaging (see above regarding the importance of MRI) (Figs. 1.1 and 1.3) Neck nodes: all nodes > = 1 cm in short axis or those with necrotic center, or those that are FDG PET avid; given the high likelihood of nodal involvement, contour the lymph node in doubt as GTV
CTV_{70*}	Usually same as GTV_{70} (no need to add margin) (Fig. 1.2); if a margin is needed due to uncertainty of the gross disease, add 5 mm so that $GTV_{70}+5\ mm=CTV_{70.}$ Around the brainstem and spinal cord, 1-mm margin is acceptable, as protection of these critical normal tissues is needed. If tumor involves one side where the patient may be blind as a result of the treatment, obtain informed consent and constrain only on the optic chiasm to ensure protection of the contralateral optic structure For nodes that are small (i.e., ~1 cm), lower dose of 66 Gy can be considered at the discretion of the treating physician. Gross retropharyngeal lymph nodes should receive 70 Gy
PTV_{70*}	CTV_{70} + 3–5 mm, depending on comfort level of daily patient positioning. Around the brainstem and spinal cord, 1-mm margin is acceptable (Figs. 1.4).

*Suggested gross dose disease is 2.12 Gy/fraction to 69.96 Gy

Table 1.2 Suggested target volumes at the high-risk subclinical region

Target volumes	Definition and description
$CTV_{59.4*}$	$CTV_{59.4}$ should encompass the entire GTV_{70} Primary: entire nasopharynx ensuring inferior coverage of soft palate, clivus, skull base (ensuring coverage of foramen ovale where V3 resides), pterygoid fossae, parapharyngeal space, sphenoid sinus, posterior 1/3 of the maxillary sinuses (ensuring coverage of pterygopalatine fossae where V2 resides), posterior 1/3 of the nasal cavity, posterior ethmoid sinuses (if necessary to allow adequate coverage of subclinical region, i.e., pending distance from GTV so that a sharp dose fall-off does not occur) (Figs. 1.1, 1.2, 1.3, 1.4, and 1.5); cavernous sinus to Meckel's cave for advanced T3–T4 lesions (Fig. 1.3). Importance of reviewing bone window while contouring on CT scan to ensure coverage of skull base foramens (Figs. 1.2 and 1.5) Neck: Include retropharyngeal nodal regions, levels IB–V (Fig. 1.6); patients with N0 neck can omit level IB nodal region.
$PTV_{59.4*}$	$CTV_{59.4}$ + 3–5 mm, depending on comfort level of daily patient positioning but can be as small as 1 mm when near critical normal tissues (Fig. 1.4)

*High-risk subclinical dose: 1.8 Gy/fraction to 59.4 Gy; lower risk subclinical regions *excluding the nasopharynx/skull base regions where they are always considered high risk* can consider 1.64 Gy/fraction to 54 Gy, i.e., N0 neck or low neck (levels IV and VB) at the discretion of the treating physician. This is known as the PTV_{54}

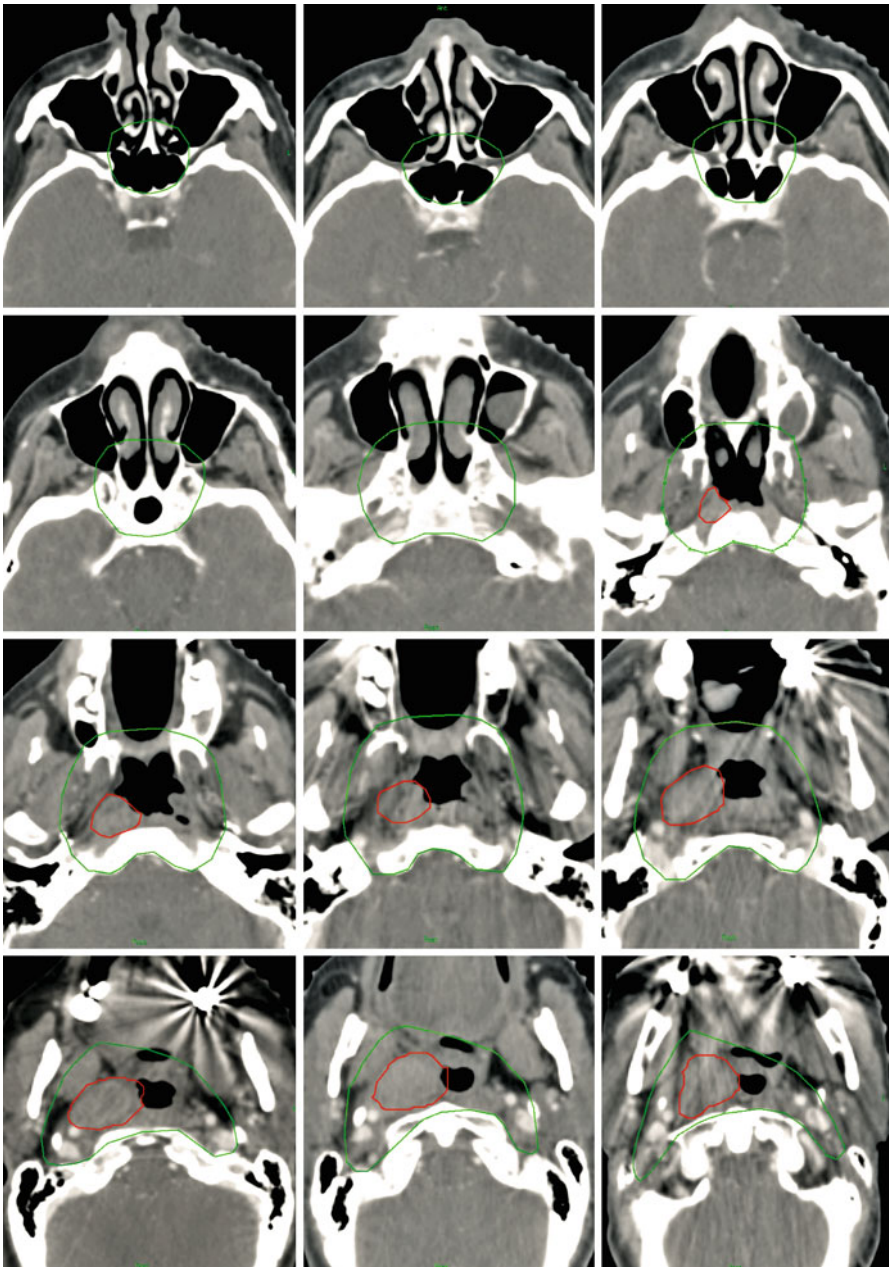

Fig. 1.1 A patient with T1N1 nasopharyngeal carcinoma with retropharyngeal and level II nodes in a cranial to caudal direction. This patient was simulated using PET/CT simulation with a 2.5-mm thickness on each slice. Notice the difference in the target delineation of the N+ versus N0 neck. Please note that these are representative slices and not all slices are included. Light green line indicates CTV59.4 and light blue line indicates CTV54

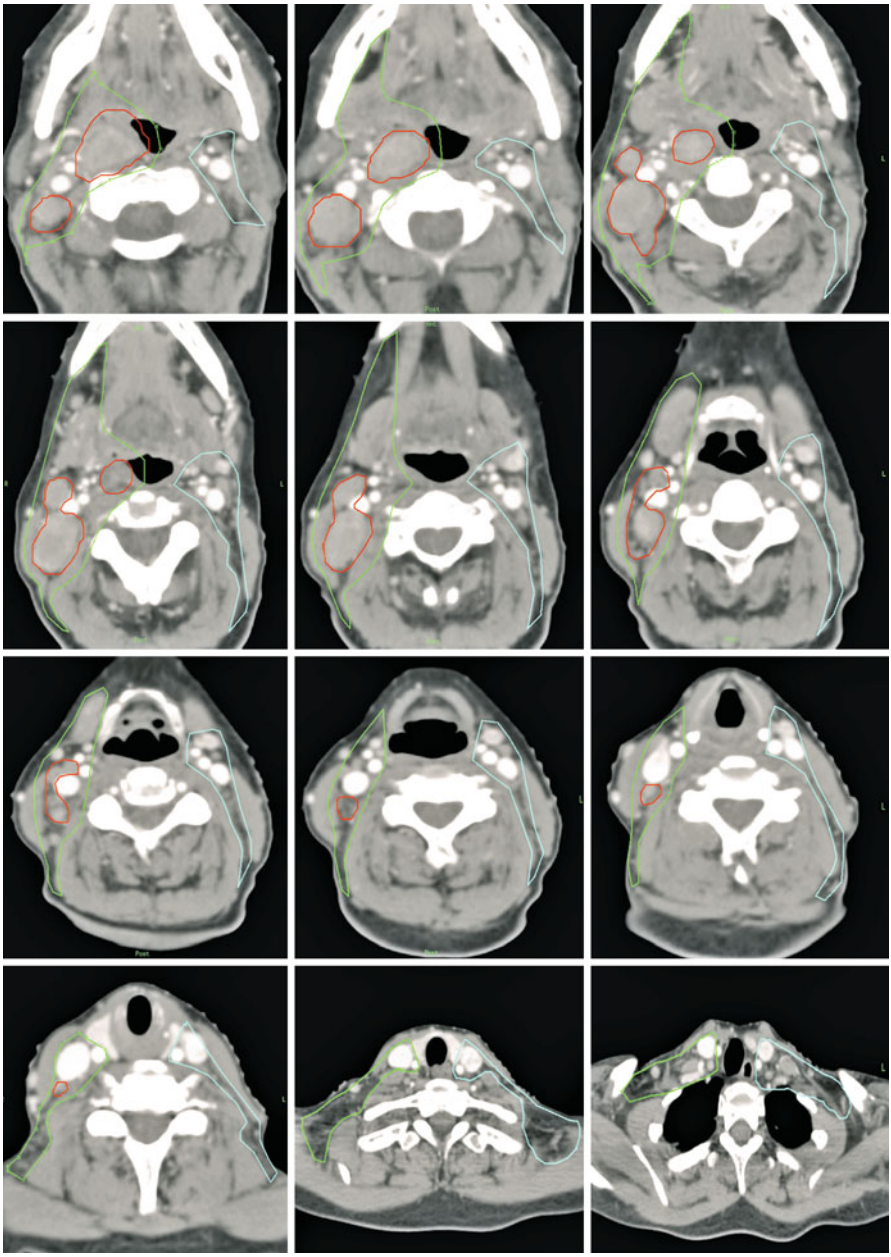

Fig. 1.1 (continued)

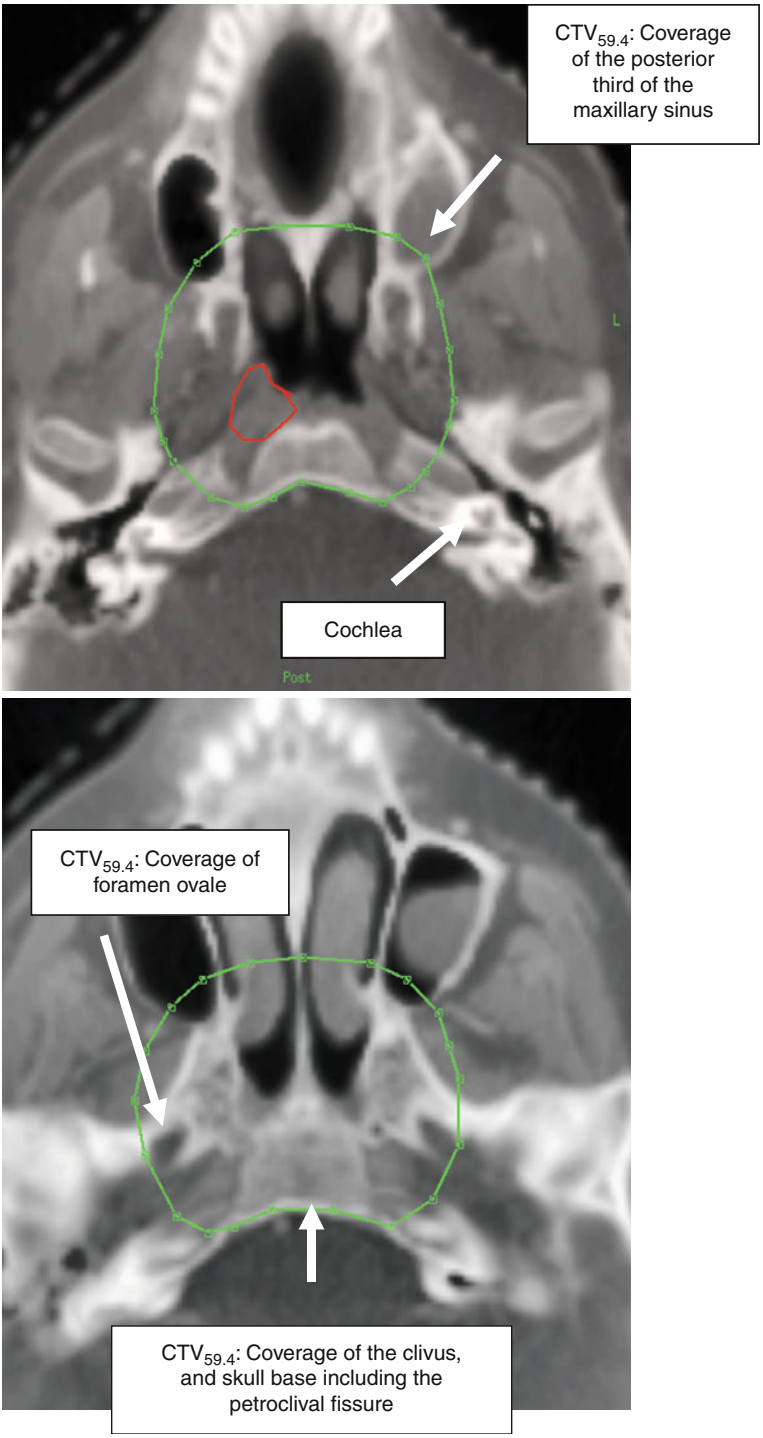

Fig. 1.2 Example of CTVs displayed on bone windows

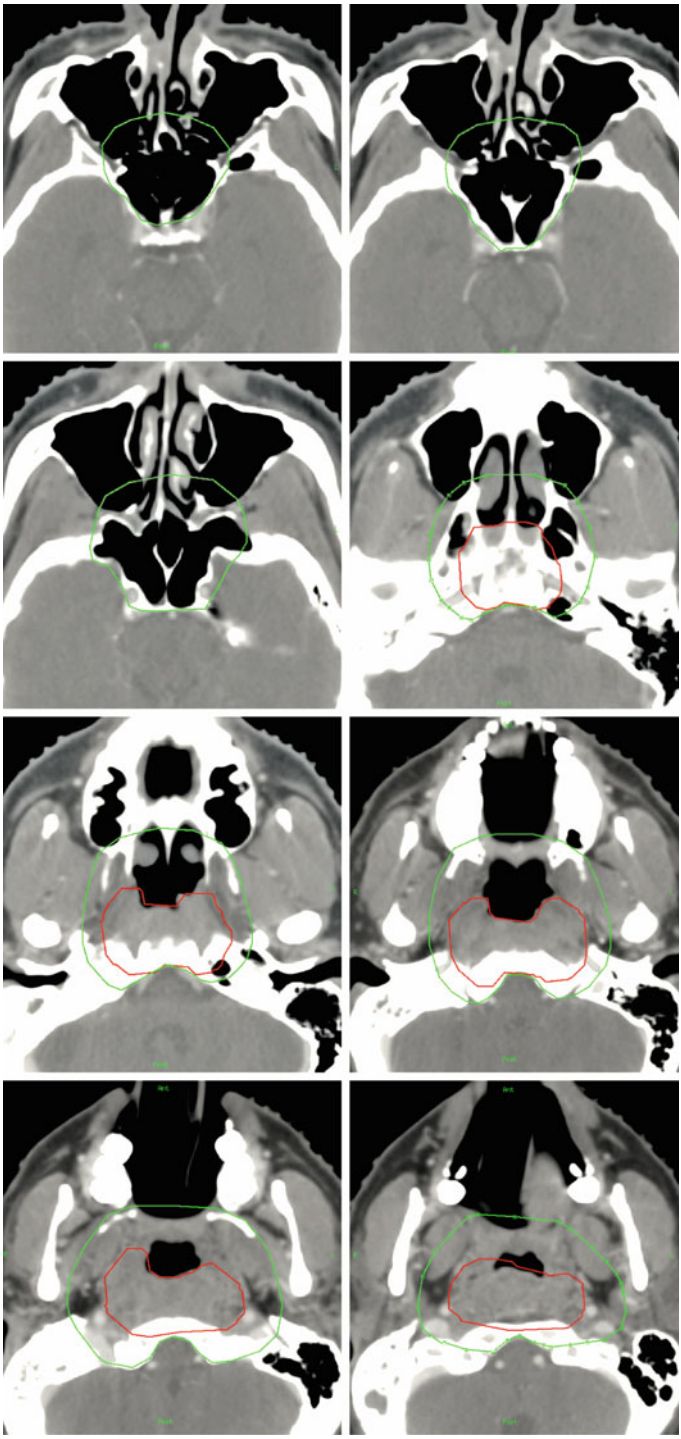

Fig. 1.3 A patient with T3N2 nasopharyngeal carcinoma

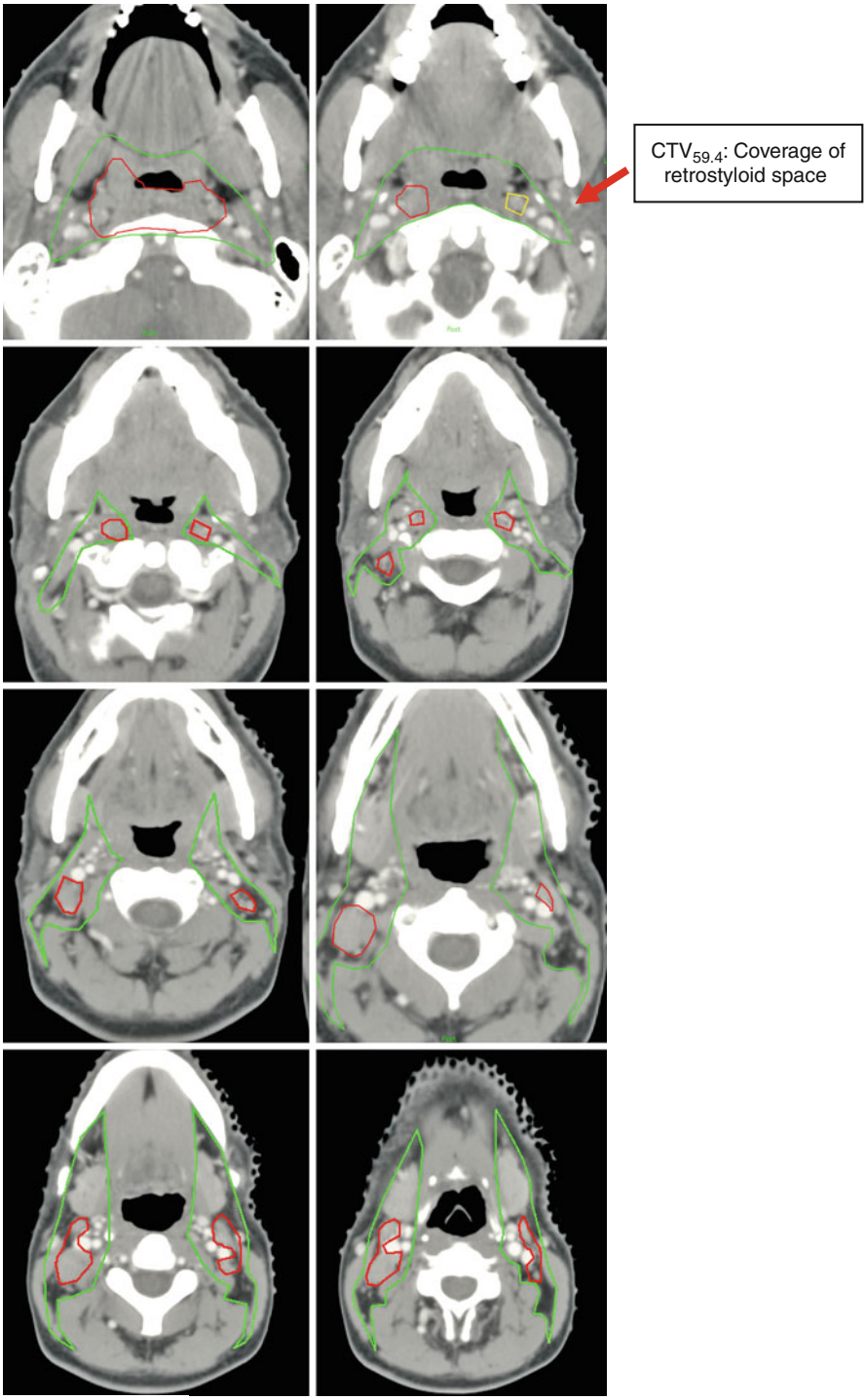

Fig. 1.3 (continued)

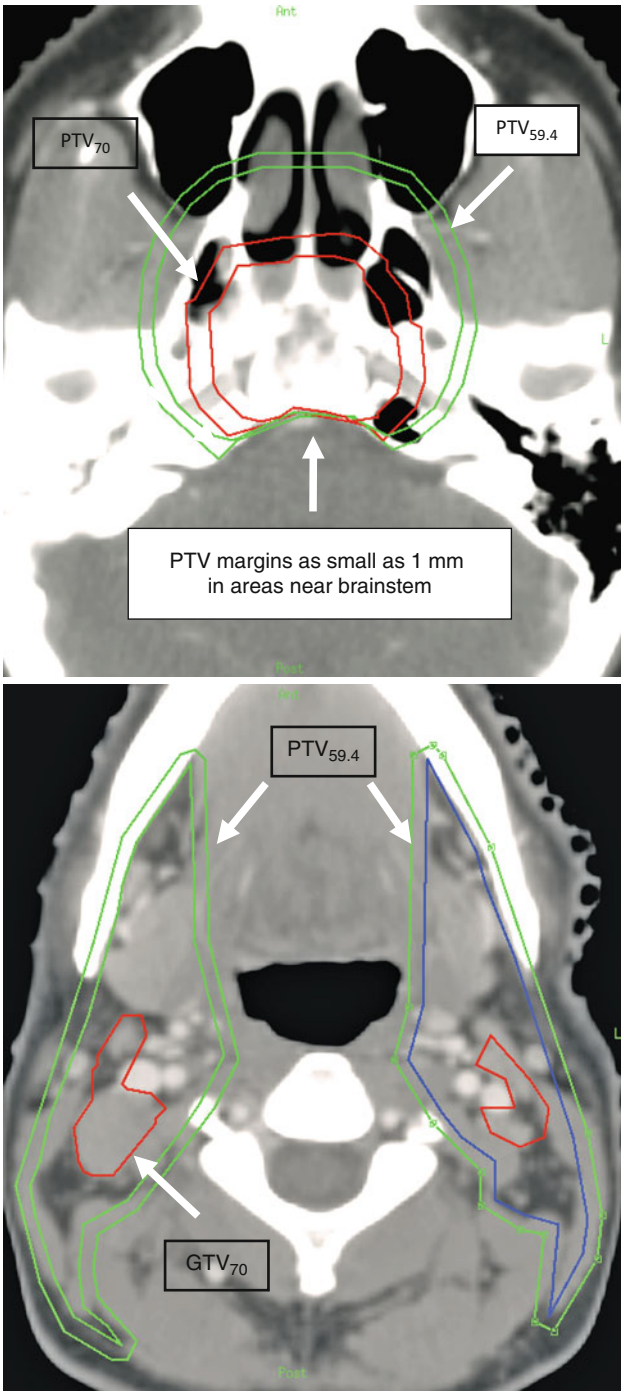

Fig. 1.4 An example of the final PTV images

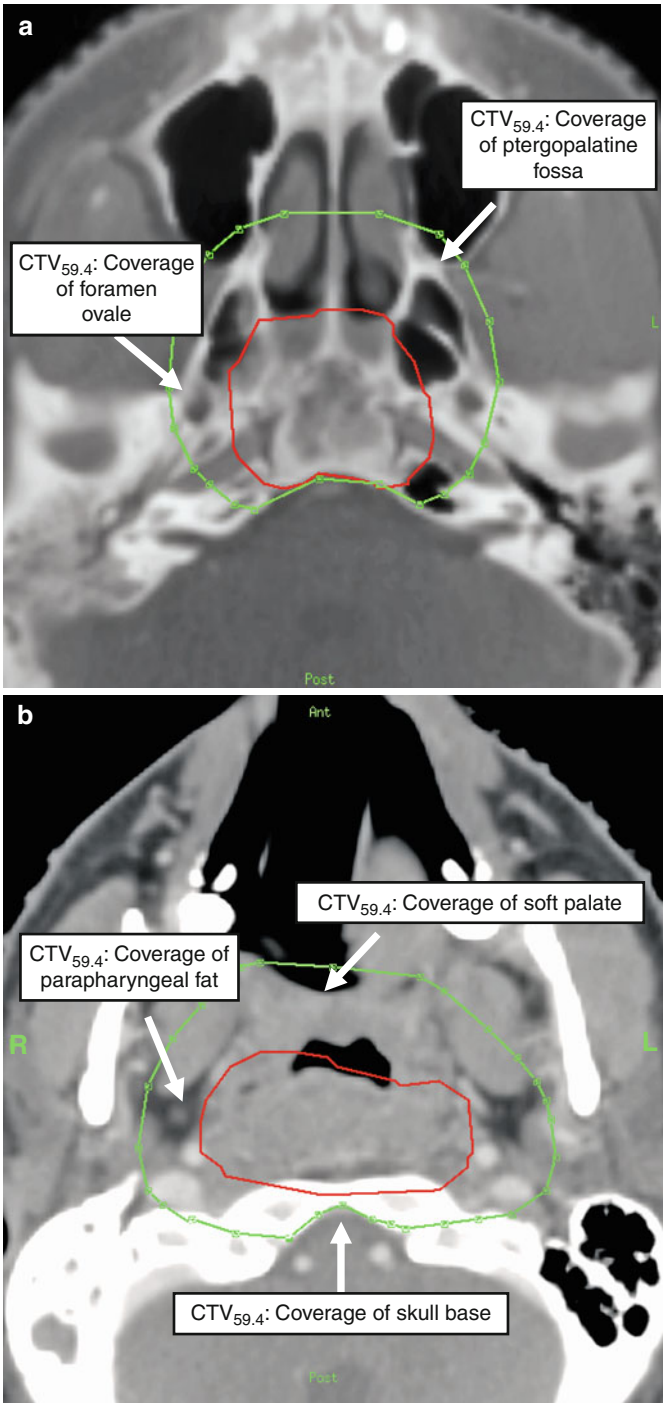

Fig. 1.5 An example of GTV and CTV: (**a**) bone window, (**b**) soft tissue window

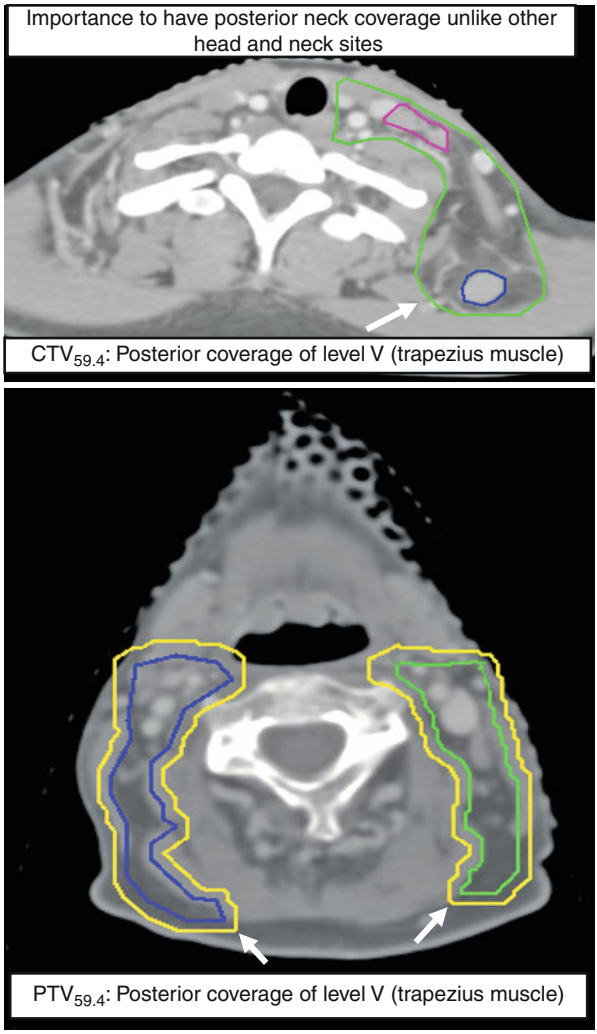

Fig. 1.6 An example of a NPC with a very posterior level V gross nodal involvement

Further Reading

1. Lee N, Harris J, Garden AS, et al. Intensity-modulated radiation therapy with or without chemotherapy for nasopharyngeal carcinoma: radiation therapy oncology group phase II trial 0225. J Clin Oncol. 2009 Aug 1;27(22):3684–90. Epub 2009 Jun 29.

Oropharyngeal Carcinoma

2

Ian Poon, Nadeem Riaz, Kenneth Hu, and Nancy Y. Lee

General Principles of Planning and Target Delineation

- The oropharynx has extensive but orderly lymphatic drainage. The most common involved nodes include retropharyngeal nodes and levels 2–4. Level 1b is less frequently involved but should be included in the microscopic volume if the primary tumor extends anteriorly. Level 5 should be covered in node-positive cases. Lymphatic drainage is bilateral with the exception of early primary tonsil without extension to the midline, to the soft palate, or to the base of the tongue. Ipsilateral nodal involvement increases the risk of contralateral involvement.
- The physical examination as well as imaging should be considered for gross tumor delineation. Visual inspection ± endoscopy as well as palpation to define mucosal (low bulk) contiguous extension within the oropharynx and/or to oral cavity is critical to accurate GTV delineation. Visual documentation of disease (using a dental camera with a ring flash) that is not well visualized on imaging because of low bulk and/or imaging artifacts can be beneficial (Fig. 2.1a). MRI fusion to define primary soft tissue extent and involvement of retropharyngeal lymph nodes is recommended for all subsites of oropharynx (Tables 2.1 and 2.2, Figs. 2.2, 2.3, 2.4, and 2.5).
- Human papilloma virus (HPV) status should be defined currently to assist in the discussion of prognosis with modern-day treatment. Future trials may define a low-risk, HPV-positive cohort that can be considered for a de-intensification treatment scheme.

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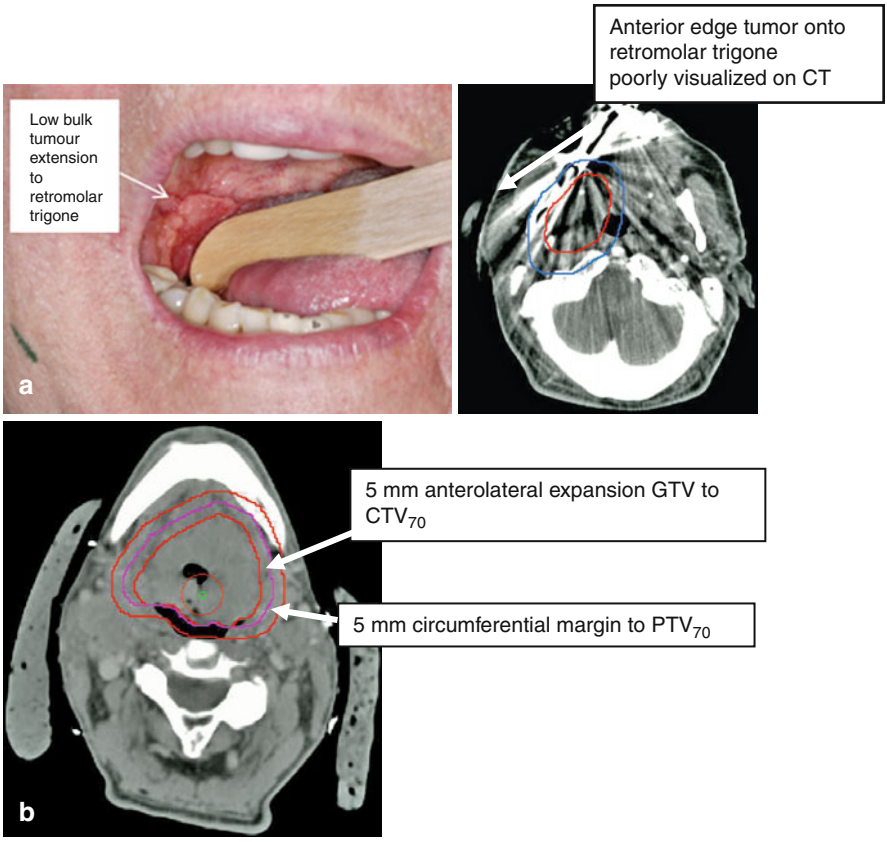

Fig. 2.1 (**a**) Anterior extension of tumour may be poorly visualized on axial imaging but seen on clinical exam (**b**) Anterolateral CTV_{70} expansion from GTV when tumour edges not clearly defined

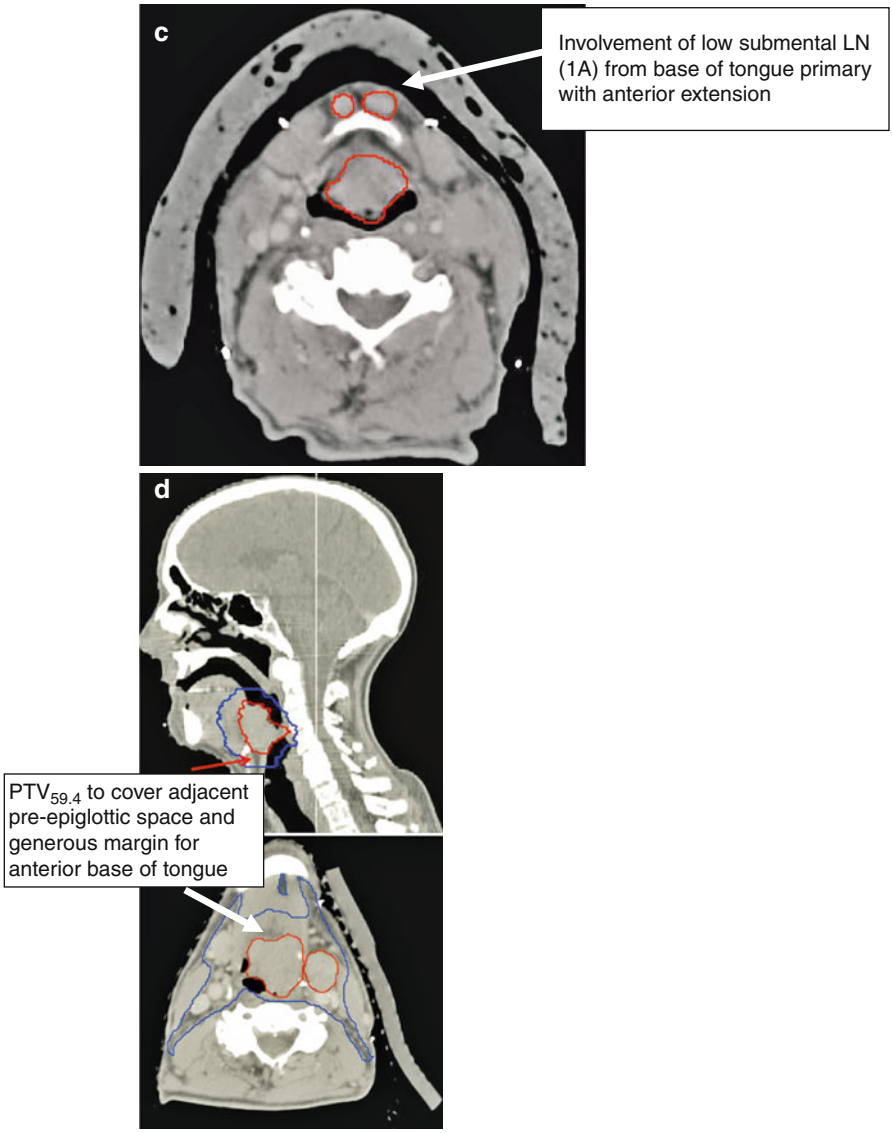

Fig. 2.1 (**c**) Involvement of level 1A with BOT SCC with anterior extension to oral tongue (**d**) Expanded microscopic expansion of $PTV_{59.4}$ with BOT SCC

Table 2.1 Suggested target volumes for gross disease

Target volumes	Definition and description
GTV_{70*}	Primary: all gross disease on physical examination with endoscopy and imaging Neck nodes: all suspicious (>1-cm or numerous small nodes) but not clearly involved nodes should at least receive an intermediate dose (66 Gy in 33 fractions)
CTV_{70*}	Usually same as GTV_{70} (no added margin) where the delineation between malignant and normal tissue is clear. In areas where there is less edge clarity, i.e., anterior edge of a base of tongue mass, glossotonsillar sulcus (Fig. 2.1b), a margin may be added (5 mm) so that $GTV_{70}+5\ mm=CTV_{70}$
PTV_{70*}	CTV_{70} + 3–5 mm, depending on comfort level of daily patient positioning and availability of cone beam CT

*Suggested gross disease dose is 2.12 Gy/fraction to 69.96 Gy

Table 2.2 Suggested target volumes at the high-risk subclinical region

Target volumes	Definition and description
General guidelines for primary $CTV_{59.4}$	Should encompass the entire GTV + a minimum 1 cm but respecting anatomical barriers to microscopic spread – skin, air, bone, muscle, etc.
Tonsil $CTV_{59.4*}$ (and soft palate)	Ipsilateral soft/hard palate to midline, anterior glossotonsillar sulcus/retromolar trigone, inferior glossotonsillar sulcus, ipsilateral base of tongue. Ipsilateral parapharyngeal space coverage for possible local extension and retro/parapharyngeal nodal involvement. Consider inclusion of pterygoid space and bilateral retropharyngeal nodes coverage with advanced primary disease
Base of tongue $CTV_{59.4*}$	Glossotonsillar sulcus and minimum 1.0 cm base of tongue mucosal margin for well-lateralized primary tumors. Consider a more generous anterior margin (1.0–1.5 cm) with advanced primary. (Fig. 2.1d), Pre-epiglottic space coverage with a 1–1.5-cm margin inferiorly from GTV Posterior pharyngeal wall – include minimum 1.5-cm margin in all directions
Neck $CTV_{59.4*}$	Higher risk nodal areas can receive 59.4 Gy. Includes retropharyngeal (RP) nodal regions, levels IB–V; cover all of IA/B if anterior extension into oral tongue/oral cavity (Fig. 2.1c)
	Exclusion of contralateral 1b in cases with ipsilateral neck involvement can be considered to reduce oral cavity dose
	T1, small well-lateralized T2 tonsil primary (not primary soft palate), N0 (possibly low bulk N1) with minimal or no extension to soft palate or base of tongue – nodal coverage can be limited to ipsilateral neck

Note: Contralateral node-negative neck cancer can receive 54–56 Gy in 1.64–1.7 Gy per fraction. In the node-negative contralateral neck, omit levels IB and V when the risk is deemed low at the discretion of the treating physician

*Subclinical dose is 1.8 Gy/fraction to 59.4 Gy

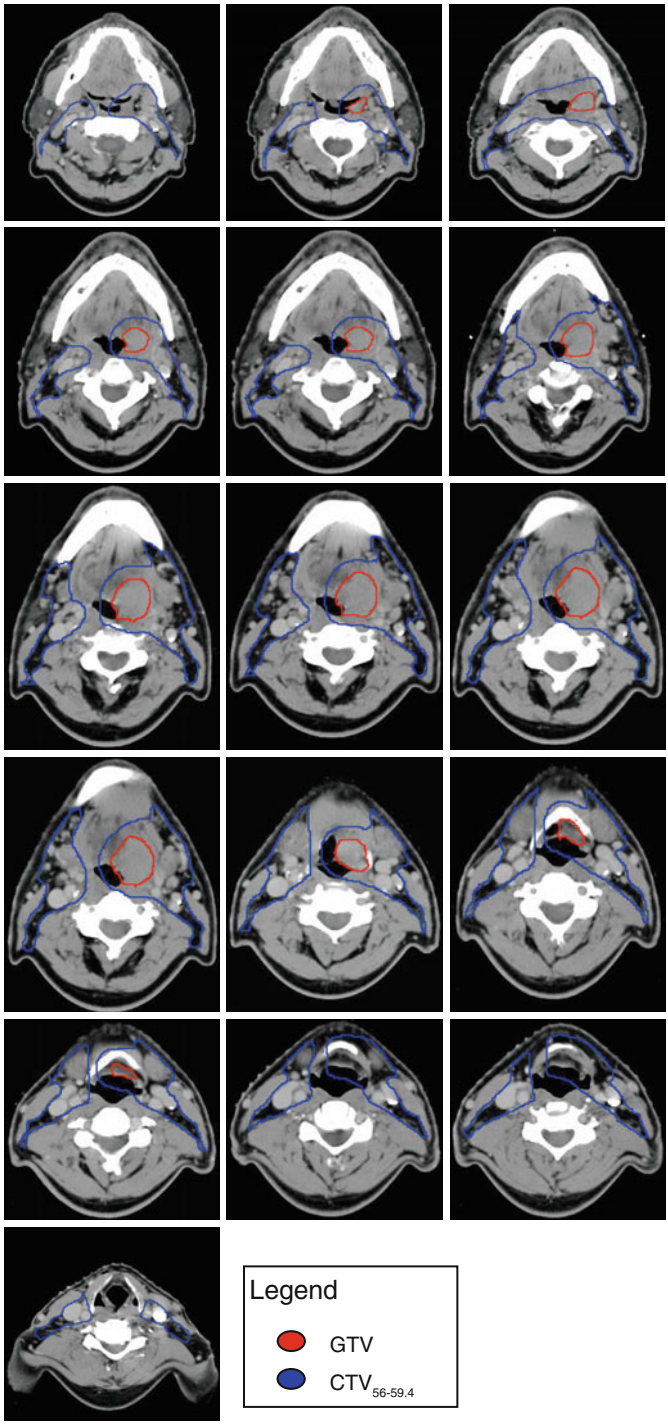

Fig. 2.2 Bulky T2N0 base of tongue SCC where the ipsilateral CTV that included the primary was treated to 59.4 Gy while the contralateral neck was treated to 56 Gy

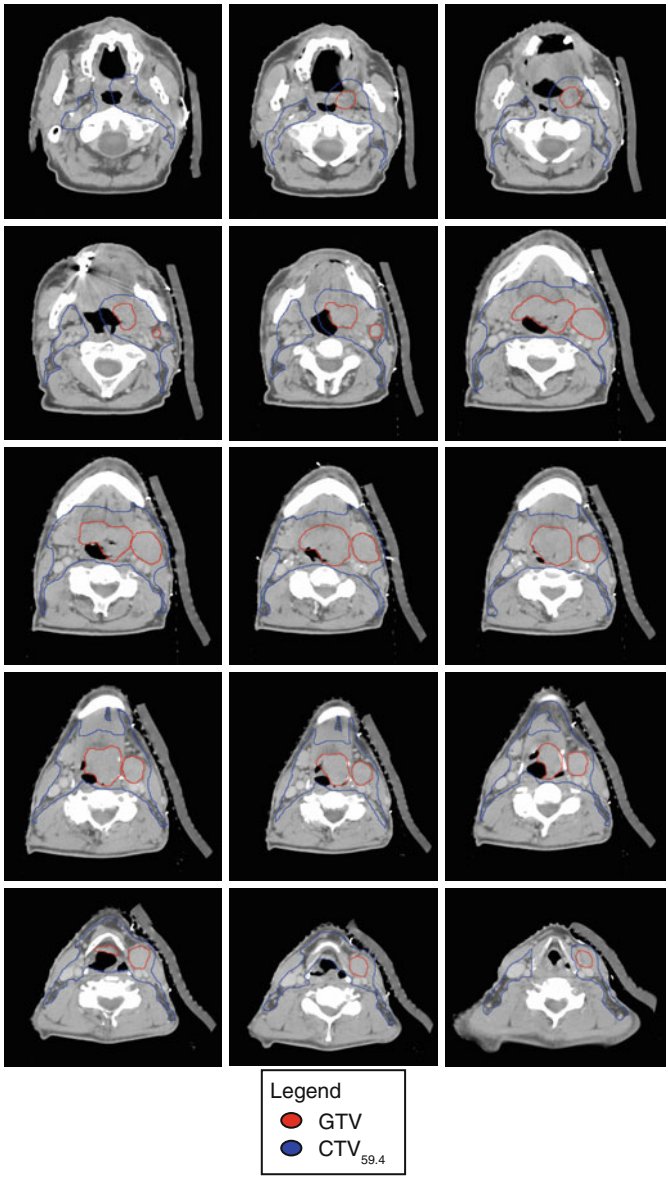

Fig. 2.3 T3N2 base of tongue SCC

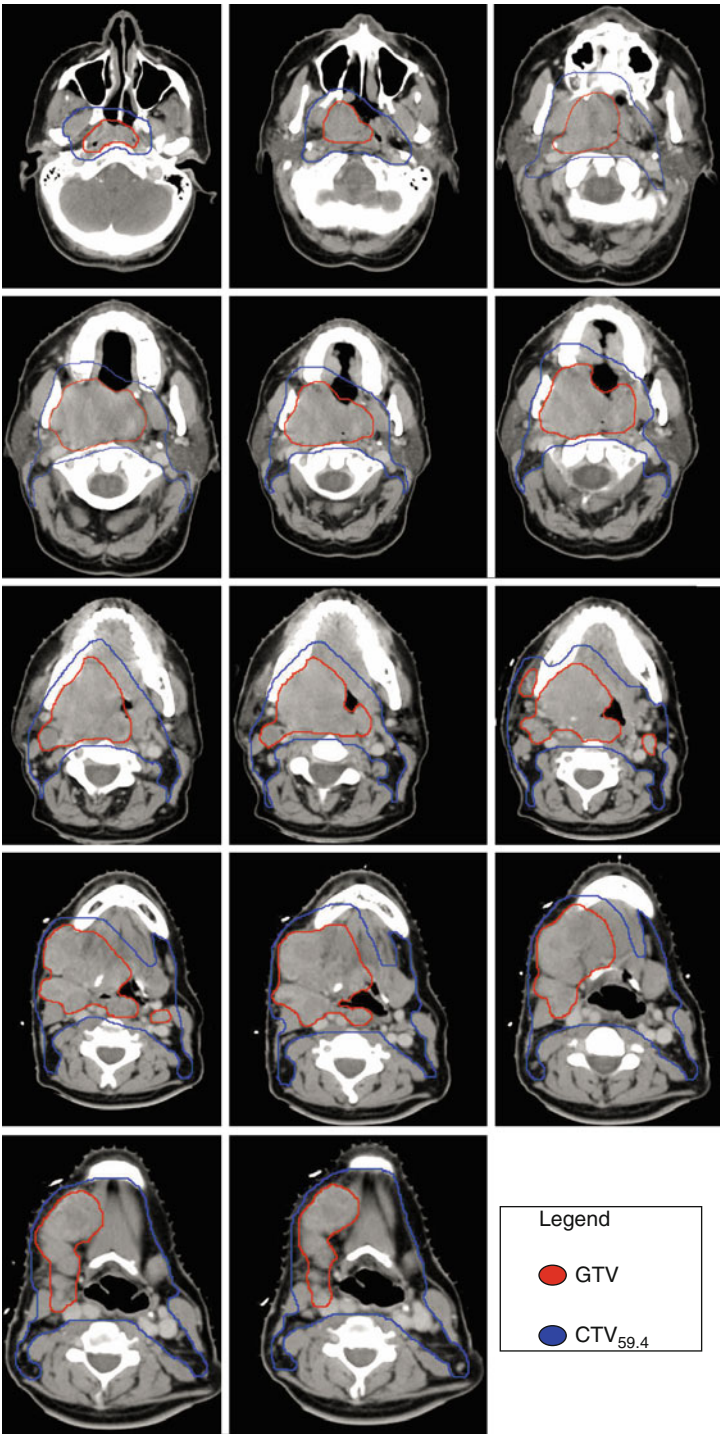

Fig. 2.4 HPV positive T4N3 tonsil SCC, treated with definitive chemoradiation; NED at 42 months

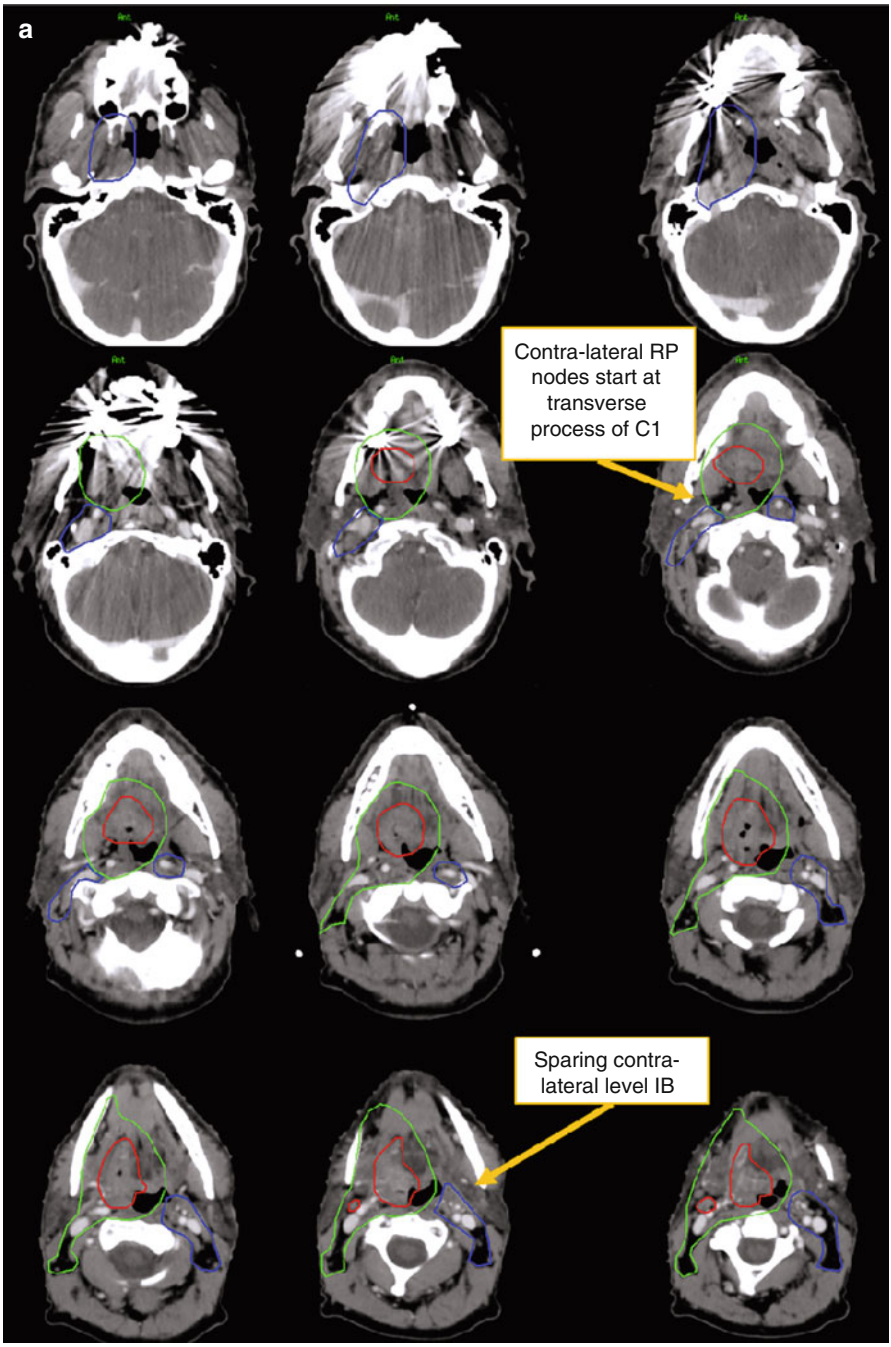

Fig. 2.5 A 65-year-old male with a right-sided T3N2b SCC of the right base of tongue. He was treated with definitive chemoradiotherapy. The CTV_{70} is in *red*, the $CTV_{59.4}$ is in *green*, and the CTV_{54} is in *blue*. Please note that these are representative slices and not all slices are included. The low neck was treated with a LAN field. Coverage of the contralateral RP nodal region starts at C1 for the contralateral node-negative neck

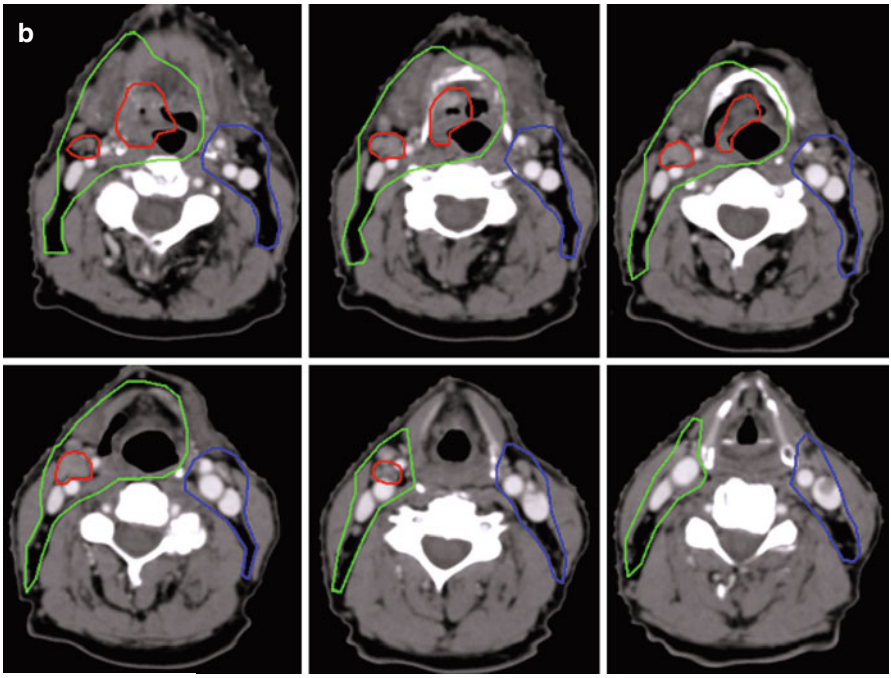

Fig. 2.5 (continued)

Further Reading

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Larynx Cancer

3

Oren Cahlon, Nadeem Riaz, and Nancy Y. Lee

General Principles of Planning and Target Delineation

For early-stage glottic carcinoma, carotid-sparing IMRT should be considered. ACT-based opposed lateral technique is also acceptable. For all supraglottic tumors, and locally advanced glottic tumors, where neck irradiation is required, IMRT is preferred to maximize target coverage and normal tissue sparing.

When the cervical lymph nodes are at risk, the bilateral neck nodes are always required because the larynx is a centrally located structure with bilateral lymph node drainage; unilateral neck irradiation is not advised.

Because the target volume includes the larynx, a comprehensive all IMRT plan is preferred to a split-field technique.

In addition to thorough physical exam, high-quality imaging is essential to accurate staging and treatment of larynx cancer. Exam anesthesia by experienced ENT is helpful to evaluate the mucosal extent of disease, especially for subglottic extension, which can be difficult to appreciate on imaging and office laryngoscopy. High-resolution CT scan is most useful for determining extralaryngeal spread of disease including thyroid cartilage invasion. Because of motion artifact from swallowing, CT scan is often preferable to MRI. PET scan is also useful in detecting small volume nodal disease and metastatic disease.

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Table 3.1 Suggested target volumes at the gross disease region

Target volumes	Definition and description
GTV_{70} (the subscript 70 denotes the radiation dose delivered)	Primary: all gross disease on physical examination and imaging Neck nodes: all nodes ≥1 cm or PET positive should be included as GTV – include borderline lymph nodes in doubt as GTV to avoid undertreatment. For borderline lymph nodes, the dose can be reduced to 6300 cGy
CTV_{70}	Usually same as GTV_{70} (typically no need to add margin unless there is uncertainty of the gross disease). Depending on quality of imaging, add 0–0.5-cm margin to GTV_{70} to create CTV_{70}
PTV_{70*}	CTV_{70} + 3–8 mm, depending on comfort level of daily patient positioning

For larynx tumors which require treatment of the primary and the neck, suggested dose to gross disease is 69.96 Gy in 2.12 Gy/fraction (33 fractions)
For T1N0 glottic tumors, a dose of 63 Gy in 2.25 Gy/fraction is typically used
For T2 N0 glottic tumors, a dose of 65.25 Gy in 2.25 Gy/fraction is typically used
For T2 N0 glottic tumors, a dose of 79.2 Gy in 1.2 Gy/fraction bid is also used

Table 3.2 Suggested target volumes for high-risk subclinical regions

Target volumes	Definition and description
$CTV_{59.4*}$	Three components $CTV_{59.4}$ should encompass the entire GTV (PTV-GTV) Includes the entire larynx, from the top of the thyroid notch to the bottom of the thyroid cartilage High-risk nodal regions, levels II–IV on the involved N+ neck. IB optional – typically included if level II positive. No need to include level V. No need to include RP nodes unless bulky adenopathy. No typical drainage from larynx to RP nodes, but can get retrograde lymphatic flow to RP nodes with bulky adenopathy. Include level VI if subglottic extension
$PTV_{59.4*}$	$CTV_{59.40}$ +3–5 mm, depending on immobilization, localization, etc.

*High-risk subclinical dose: 1.8 Gy/fraction to 59.4 Gy

CT simulation (preferably with contrast) should be used for all patients. Even patients with early-stage glottic cancer being treated with opposed lateral portals benefit from 3-D planning.

A customized aquaplast mask should be used for all patients to immobilize the head, neck, and shoulders. A bite block can be helpful for some patients to displace the higher dose regions for the hard palate. For patients with a large amount of metal fillings, a custom mouthguard can be helpful to absorb electron scatter from the metal and reduce mucosal dose.

GTV should be delineated using all information from laryngoscopy, CT, and PET. PET fusion can be helpful. On every slice, the physician should delineate GTV, CTV 59.4, and CTV 54 (as applicable). A small margin is then added to create the respective PTVs. Margin size ranges from 0.3 to 0.8 cm, depending on level of confidence of immobilization, localization, and motion.

Suggested target volumes for select larynx cancer cases are detailed in Tables 3.1, 3.2, and 3.3 (Figs. 3.1, 3.2, and 3.3).

Table 3.3 Suggested target volumes for low-risk subclinical regions

Target volumes	Definition and description
CTV_{54*}	Levels II–IV of the uninvolved neck. No need for IB coverage on the uninvolved side. Level VI included if subglottic extension
PTV_{54*}	$CTV_{59.40}$ + 3–5 mm, depending on immobilization, localization, etc.

*High-risk subclinical dose: 1.64 Gy/fraction to 54 Gy

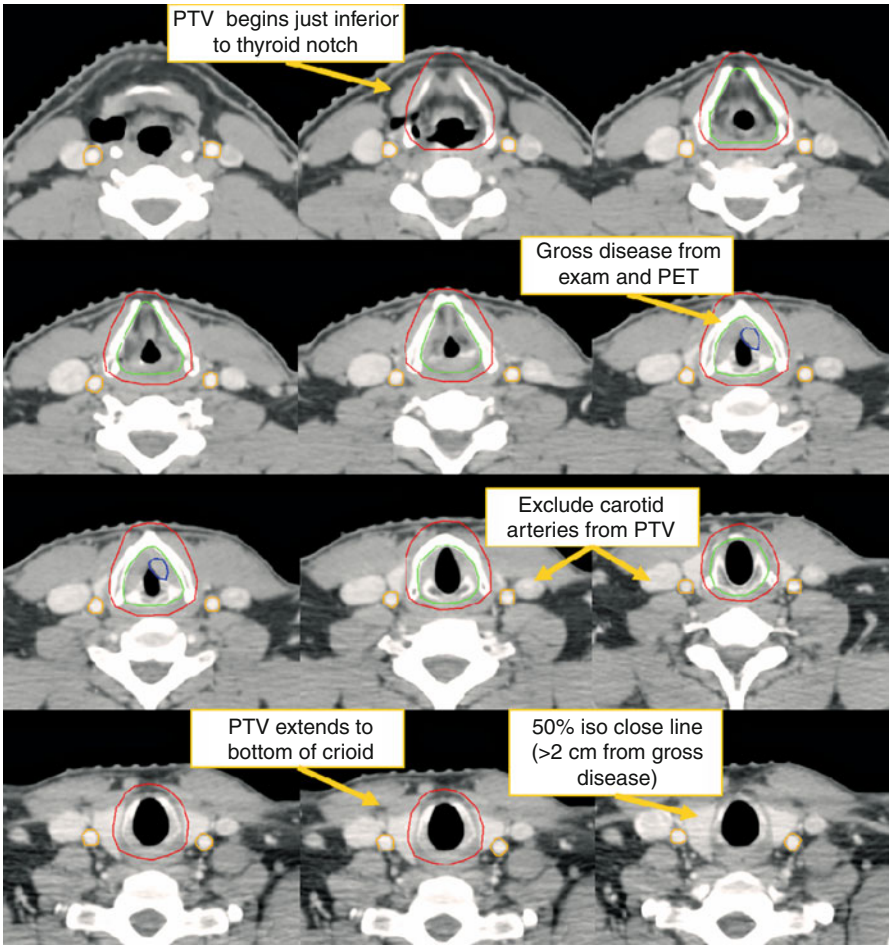

Fig. 3.1 A patient with T1N0 squamous cell carcinoma of the left vocal cord. Because of the low rate (<5%) of nodal metastases for early-stage glottic cancer, there is no elective nodal irradiation. Please note that these are representative slices and not all slices are included. *Blue* GTV, *Green* CTV, *Red* PTV. GTV is delineated by laryngoscopy findings only. For T1 larynx tumors, there are typically no CT abnormalities. The entire larynx is delineated as CTV to include both false and true vocal cords, anterior and posterior commissures, arytenoids and aryepiglottic folds, as well as the subglottic region. The PTV extends from thyroid notch to the bottom of the cricoid cartilage. A 5-mm margin added in all directions except posterolaterally was limited to 3 mm respect the ICA. The *orange circle* is the carotid artery

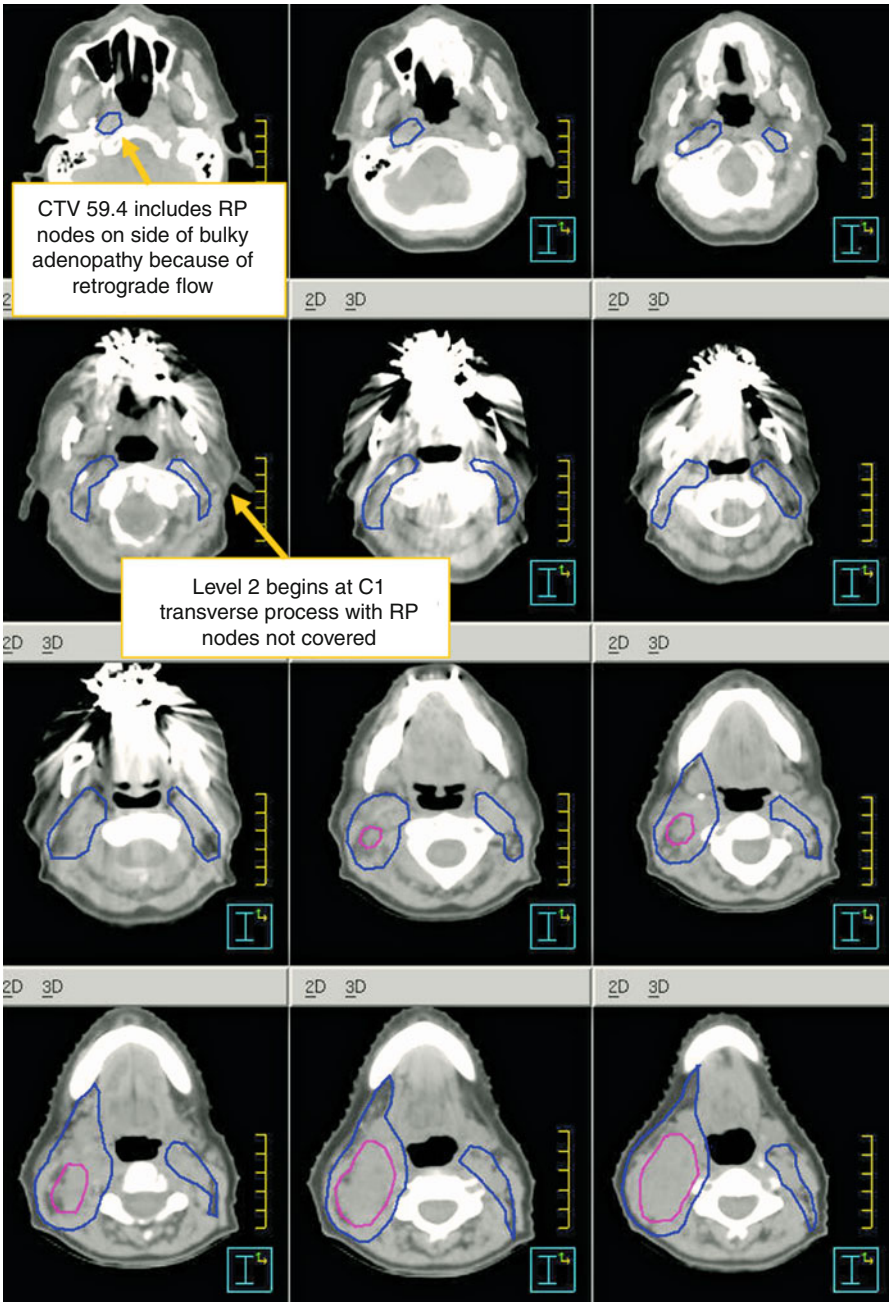

Fig. 3.2 A patient with T2 N2c M0 squamous cell carcinoma of the epiglottis involving right AE fold and bilateral cervical lymph nodes. Please note that these are representative slices and not all slices are included. *Magenta* GTV LN, *Purple* GTV primary, *Blue* CTV 59.4, *Orange* CTV 54

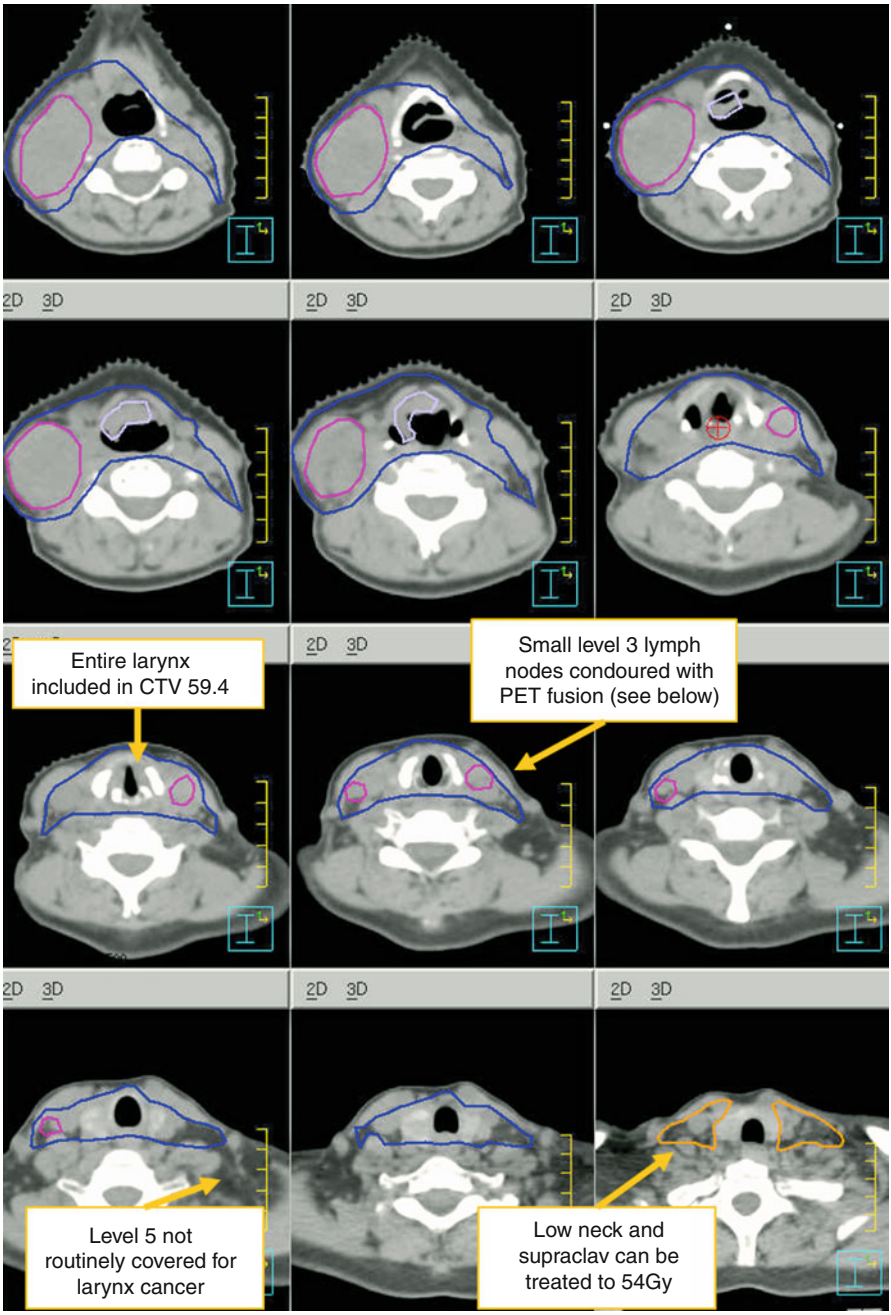

Fig. 3.2 (continued)

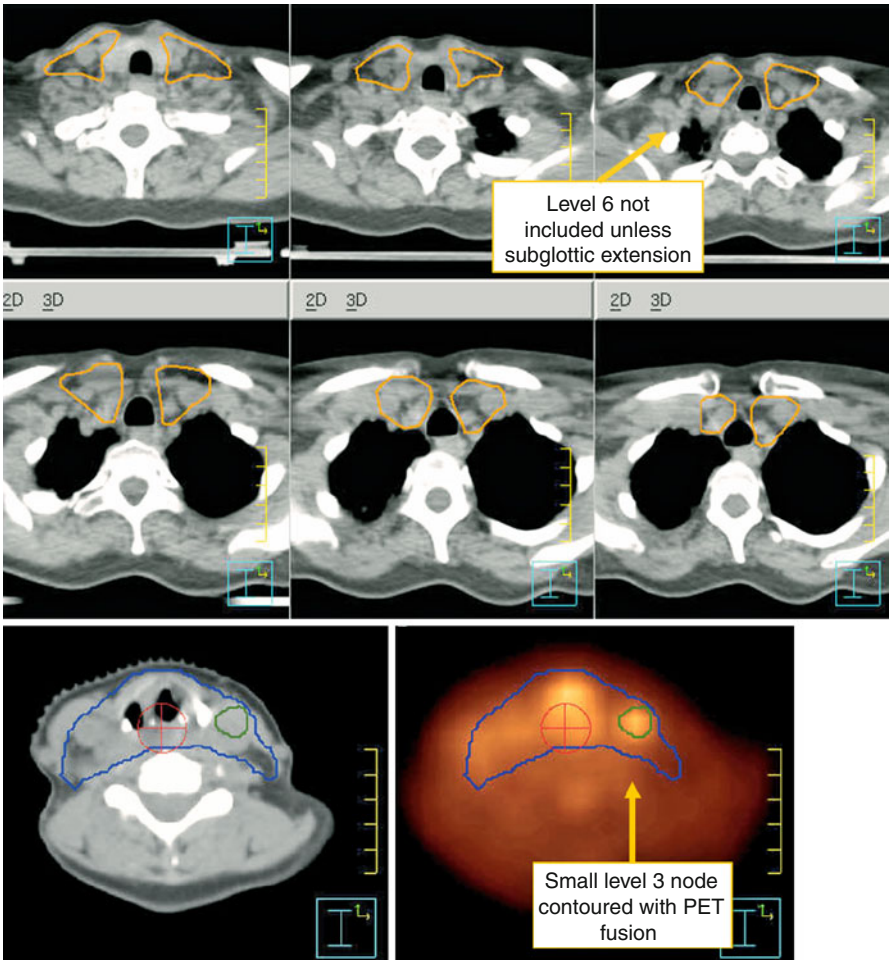

Fig. 3.2 (continued)

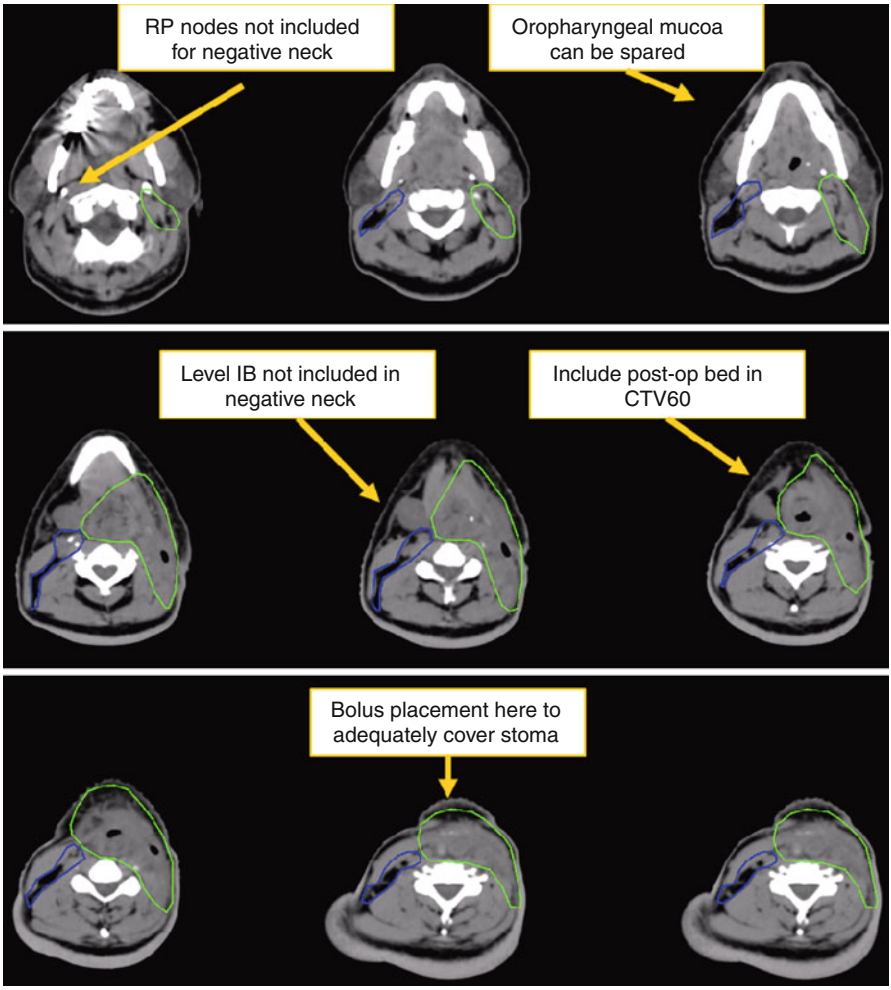

Fig. 3.3 A patient with pT4 N0 M0 squamous cell carcinoma of the left glottis status total laryngectomy and left neck dissection. In the postoperative setting, the high-risk CTV (operative bed) receives 60 Gy in 2 Gy/fraction and the low-risk CTV receives 54 Gy in 2 Gy/fraction. *Blue* CTV 54, *Green* CTV 60

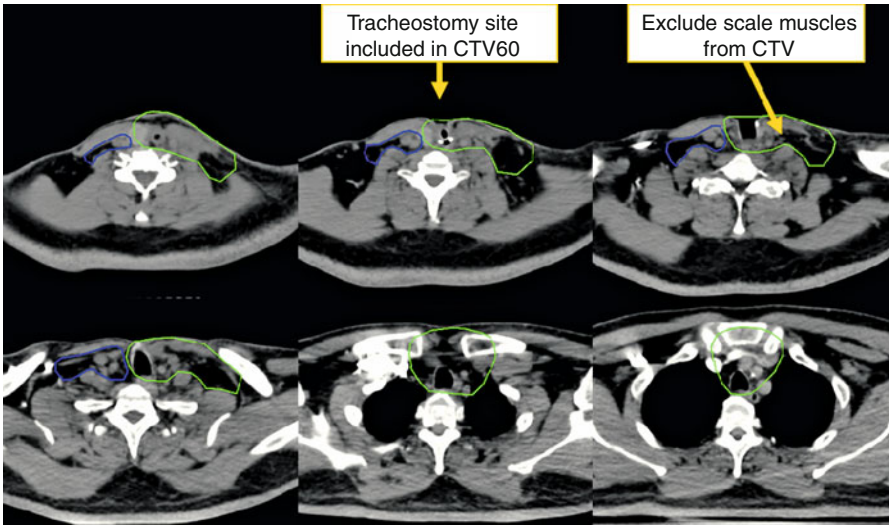

Fig. 3.3 (continued)

Hypopharyngeal Carcinoma

4

Gaorav P. Gupta and Nancy Y. Lee

General Principles of Planning and Target Delineation

- The hypopharynx consists of the pyriform sinuses, posterior pharyngeal wall, and postcricoid region. It has extensive lymphatic drainage to level 2–4 jugulodigastric nodes, retropharyngeal nodes (including the nodes of Rouviere), and for inferior tumors involving the postcricoid region additional drainage to the paratracheal lymph nodes. Level 5 and level 1b LNs are infrequently involved but may be at elevated risk when adjacent lymph node stations have been infiltrated.
- Clinical examination with a thorough laryngoscopic evaluation is critical in defining the mucosal extent of hypopharyngeal cancers, particularly for those arising in the pyriform sinus.
- CT simulation with IV contrast is used (unless medically contraindicated) to delineate the primary tumor, gross lymphadenopathy, and additional regions at risk. The simulation scan should extend from the top of the skull to the carina. MRI may better delineate primary tumor borders, inform regarding potential cartilage or esophageal invasion, and may also facilitate identification of abnormally enhancing lymph nodes [1–4]. FDG-PET provides metabolic information and may identify hypermetabolic cancer cells within morphologically normal-appearing lymph nodes [5, 6], which should be included within the high-dose PTV.
- The patient should be immobilized with a 5-point thermoplastic head and neck mask or with a 3-point thermoplastic head and neck mask and a shoulder pull board. The neck should be maximally hyperextended to pull as much of the oral

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cavity and mandible out of the field as possible, and the shoulders should be pulled inferiorly to minimize the risk of beam interference.

- Due to concerns regarding treatment-related late toxicities, hypofractionation and/or simultaneous integrated boost with IMRT are not recommended for this disease site. We utilize dose-painting IMRT [7] and prescribe to 70 Gy in 2 Gy fractions to sites of gross disease, 59.5 Gy in 1.7 Gy fractions to high-risk subclinical regions, and 56 Gy in 1.6 Gy fractions to lower-risk subclinical regions. Additional fractionation regimens as well as cone-down IMRT approaches are also appropriate. We routinely use all-in-one IMRT for hypopharynx cancers, as a match line to a low anterior neck field would frequently fall in the region of the primary tumor or involved lymph nodes.
- Suggested treatment target volumes for gross disease (Table 4.1), high-risk subclinical (Table 4.2), and lower-risk subclinical regions (Table 4.3), are described in the following tables. The principles of target delineation are similar for early and advanced stages (Figs. 4.1 and 4.2).

Table 4.1 Suggested target volumes at the gross disease region

Target volumes	Definition and description
GTV_{70*} (the subscript denotes the total radiation dose prescribed, in Gy)	Primary: all gross disease on physical examination and imaging
	Neck nodes: all nodes ≥1 cm in short axis; grossly abnormal as well as suspicious lymph nodes should be contoured as GTV
CTV_{70*}	Usually the same as GTV_{70} (no need to add margin); if a margin is needed due to uncertainty of macroscopic disease, add 5 mm so that $GTV_{70}+5\ mm=CTV_{70}$
	For suspicious nodes that are small (i.e., ≤1 cm), a lower dose of 66 Gy may be considered
PTV_{70*}	$CTV_{70}+10$ mm for the primary tumor, depending on comfort level of daily patient positioning. Hypopharynx structures are highly mobile, so we do not recommend smaller PTV margins. An exception might be posterior pharyngeal wall disease, where posterior expansion margins are minimized due to decreased motion in that direction, and to maintain adequate separation from the spinal cord
	$CTV_{70}+3$–5 mm for lymph nodes, depending on precision of daily positioning

*Suggested dose to gross disease is 2 Gy/fraction to 70 Gy

Table 4.2 Suggested target volumes at the high-risk subclinical region: primary tumor expansion and N+ neck

Target volumes	Definition and description
$CTV_{59.5*}$	Primary: the $CTV_{59.5}$ should encompass the entire CTV_{70} with at least 1-cm margin, and should include the entire subsite of the involved hypopharynx as well as adjacent superior and inferior structures. Potential directions of microscopic mucosal and submucosal spread should be considered and targeted. The larynx (from hyoid to cricoid) is at high risk for subclinical disease and should be included in the $CTV_{59.5}$. Adjacent fat spaces, such as the pre-epiglottic fat and prevertebral fascia, should be included in this high-risk region Neck nodes: CTV59.5 should encompass at least 3-mm margin on CTV_{70} lymph node regions. Include ipsilateral cervical LN levels Ib–IV as well as the lateral retropharyngeal lymph nodes. If there is gross adenopathy in levels II–IV, coverage of ipsilateral level V should be considered. For postcricoid and posterior pharyngeal wall tumors that are close to midline, the same RT dose may be prescribed to both sides of the neck. For an N+ neck, retropharyngeal lymph node coverage should extend superiorly to the entrance of the carotid canal at the skull base. Similarly, upper level II lymph nodes in the retrostyloid space should also be included in the target volume, superior to the level where the posterior belly of the digastric muscle crosses over the internal jugular vein. Inferior hypopharyngeal cancers that involve the postcricoid region mandate coverage of the paratracheal lymph nodes in the superior mediastinum as well Any tissue that lies between the primary tumor and level III–IV lymphadenopathy should be contoured in the $CTV_{59.5}$, as it is at high risk for submucosal microscopic invasion
$PTV_{59.5*}$	$CTV_{59.5}$ + 3–5 mm, depending on comfort level of daily patient positioning

*Example high-risk subclinical dose: 1.7 Gy/fraction to 59.5 Gy

Table 4.3 Suggested target volumes at the lower-risk subclinical region

Target volumes	Definition and description
CTV_{56*}	The CTV_{56} should include lymph node levels II–IV and retropharyngeal LNs in the N0 neck. The only exception is for midline tumors, where an N0 neck might also be considered high risk if there is contralateral nodal disease. For the contralateral N0 neck considered lower risk, the superior extent of level II coverage need not extend beyond where the posterior belly of the digastric muscle crosses over the internal jugular vein. Similarly, coverage of the superior retropharyngeal nodes in the contralateral N0 neck can terminate at the level of the C1 vertebral body
PTV_{56*}	CTV_{56} + 3–5 mm, depending on comfort level of daily patient positioning

*Example lower-risk subclinical dose: 1.6 Gy/fraction to 56 Gy

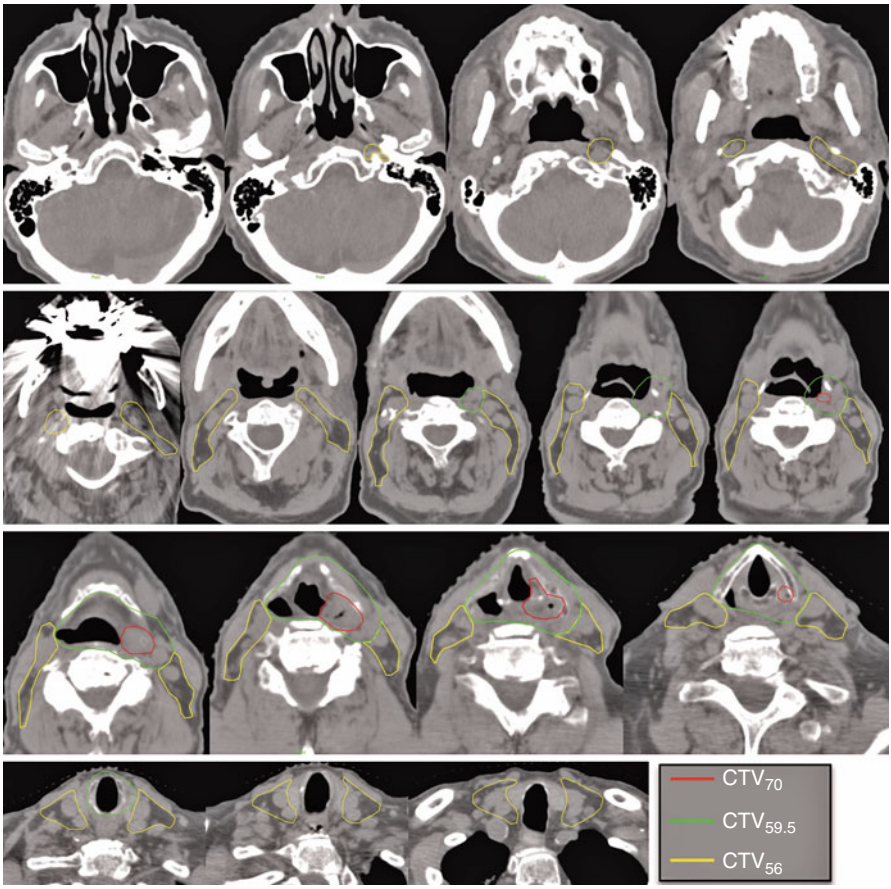

Fig. 4.1 Early-stage T2N0 left pyriform sinus HNSCC. The principles of targeting early-stage hypopharyngeal cancers are shared among all subsites. It is critical to perform multiple imaging studies including CT with IV contrast, MRI, and/or PET to confirm with highest certainty that there is no detectable nodal disease. For high confidence cN0 disease, the bilateral neck may receive the lower-risk RT dose, e.g., 56 Gy

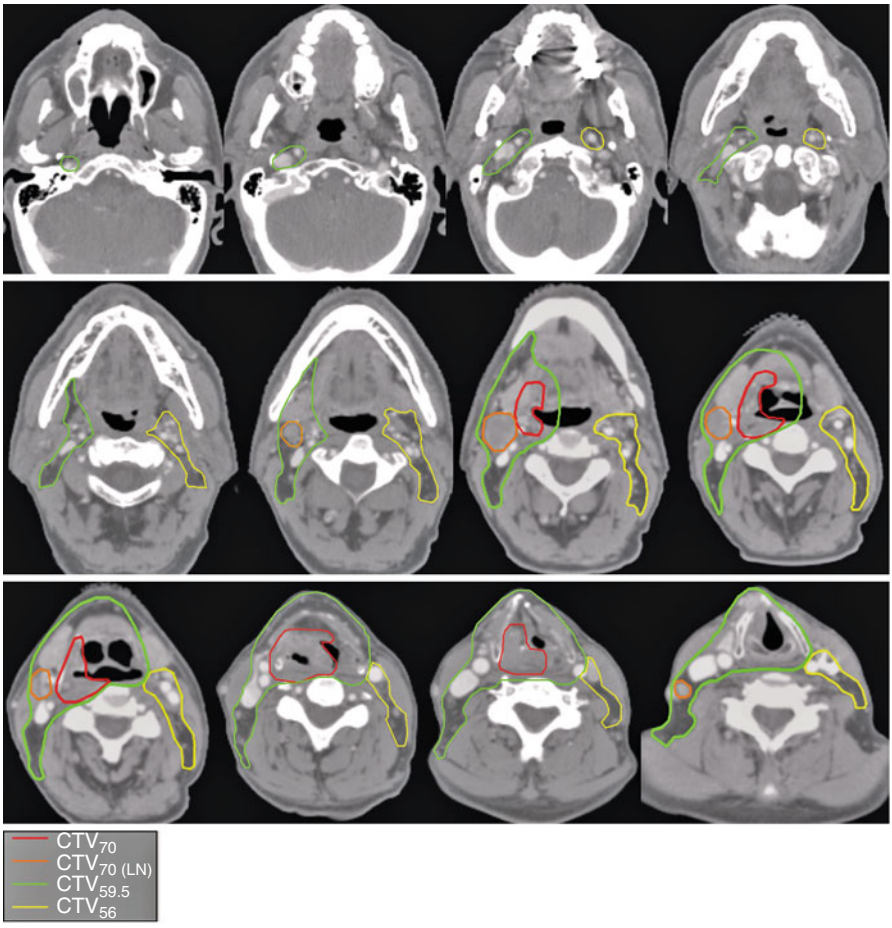

Fig. 4.2 Advanced stage T2N2b pyriform sinus HNSCC. Similar principles are used to delineate IMRT targeting for all subsites of advanced stage hypopharyngeal cancer. Inferior tumors involving the postcricoid region must include the paratracheal LNs of the superior mediastinum as well as consideration of the central compartment of the neck in the high-risk subclinical treatment volume. It is important that targeting of the N+ neck extends superiorly to the base of skull

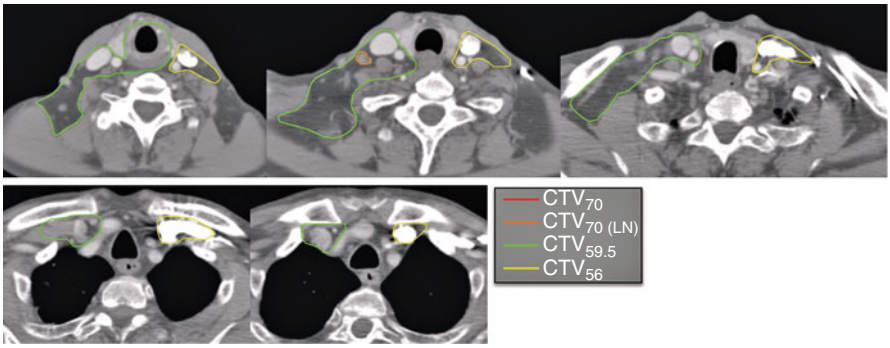

Fig. 4.2 (continued)

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Oral Cavity Cancers

5

Keith Unger, Nadeem Riaz, Allen Chen,
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General Principles of Planning and Target Delineation

- Patients should undergo a comprehensive oral examination, biopsy, and imaging studies for staging and treatment planning. Computed tomography (CT) scan is commonly used to evaluate the local extent of the tumor and regional spread to cervical lymph nodes. CT is particularly valuable for detecting invasion into the mandible, maxilla, and pterygopalatine fossa. MRI is superior to CT in evaluating soft tissue and perineural spread. Positron emission tomography (PET) scan is useful for detecting regional lymph nodes involvement and distant disease.
- CT simulation with IV contrast should be performed. A bite block can be placed during simulation and throughout radiation to depress the tongue and protrude the lower lip, as well as to elevate the hard palate. In the case of extranodal extension or when the scar is at risk, tissue-equivalent skin bolus can be used. A wire should be placed on any surgical scars and drain sites. The patient should be immobilized in the supine position with the neck extended using a thermoplastic mask.
- In the definitive treatment setting, the clinical target volumes include the gross tumor volume which is also known as CTV_{70}; the high-risk CTV ($CTV_{59.4}$); and

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Table 5.1 Suggested target volumes for definitive treatment of oral cavity cancers

Target volumes[a]	Definition and description
GTV_{70}	Primary: all gross disease on physical examination and imaging Neck nodes: all gross disease on physical examination and imaging
CTV_{70}	GTV_{70} + 5–10 mm margin, excluding bone CTV_{70} alternatively known as GTV_{70}
$CTV_{59.4}$	Primary: encompass the entire CTV_{70} with an additional margin of 5–10 mm Neck nodes: nodal levels with pathologic involvement and adjacent ipsilateral or contralateral nodal regions at high risk for subclinical disease (site-specific recommendations given in Table 5.3)
CTV_{54}	Ipsilateral and/or contralateral uninvolved nodal levels at low risk for subclinical disease (site-specific recommendations given in Table 5.3)

[a]Subscript numbers represent suggested prescribed doses. PTV_{70} is 69.96 Gy in 2.12 Gy/fraction, $PTV_{59.4}$ is 59.4 Gy in 1.8 Gy/fraction, and PTV_{54} is 54 Gy in 1.64 Gy/fraction

Table 5.2 Suggested target volumes for postoperative treatment of oral cavity cancers

Target volumes[a,b]	Definition and description
CTV_{66}	Primary: regions of soft tissue/bone invasion or microscopically positive margins if present Neck nodes: regions of extracapsular extension if present
CTV_{60}	Primary: preoperative gross disease and the entire tumor bed Neck nodes: preoperative gross disease; entire operative bed; and ipsilateral or contralateral nodal regions (site-specific recommendations given in Table 5.3)
CTV_{54}	Ipsilateral and/or contralateral uninvolved nodal levels at low risk for subclinical disease (site-specific recommendations given in Table 5.3)

[a]Subscript numbers represent suggested prescribed doses. PTV_{66} is 66 Gy in 2.2–2.0 Gy/fraction, PTV_{60} is 60 Gy in 2 Gy/fraction, and PTV_{54} is 54 Gy in 1.8 Gy/fraction
[b]If gross residual disease is present, then a GTV should be delineated

the low-risk CTV (CTV_{54}) as detailed in Table 5.1. In the postoperative setting, the clinical target volumes include the gross disease CTV (CTV_{70}) if gross residual disease is present; the high-risk CTV (CTV_{66}) if positive margins or extranodal extension is present; intermediate risk CTV (CTV_{60}) without positive margins or extracapsular extension; and low-risk CTV (CTV_{54}) as detailed in Table 5.2.

- Suggested target volumes for specific subsites within the oral cavity are detailed in Table 5.3 (Figs. 5.1, 5.2, 5.3, and 5.4).

Table 5.3 Site-specific guidelines for clinical target delineation of oral cavity cancers

Tumor site	Stage	High-risk clinical target volume ($CTV_{59.4}$ or CTV_{60})[a]	Low-risk clinical target volume (CTV_{54})
Oral tongue, floor of mouth	T1-T4N0	Tumor bed and bilateral levels I–IV at physician's discretion[b]	Bilateral levels I–IV at physician's discretion[b]
Oral tongue, floor of mouth	T1-T4N1-3	Tumor bed and ipsilateral levels I–V or bilateral levels I–V if involved contralateral nodes[c]	Contralateral levels I–V if uninvolved
Buccal mucosa, retromolar trigone, hard palate, gingiva	T1-T2N0	Tumor bed and ipsilateral levels I–IV at physician's discretion[b]	Ipsilateral lymph nodes levels I–IV at physician's discretion[b]
Buccal mucosa, retromolar trigone, hard palate, gingiva	T3-T4N0	Tumor bed and ipsilateral levels I–IV	Contralateral lymph nodes levels II–IV[c]
Buccal mucosa, retromolar trigone, hard palate, gingiva	T1-T4N1-3	Tumor bed and ipsilateral levels I–V or bilateral levels I–V if contralateral involved nodes[c]	Contralateral lymph nodes levels II–IV[c] if uninvolved

[a]66 Gy for microscopically positive margins or extracapsular extension; 70 Gy if gross residual disease
[b]Decision to include in low- or high-risk region based on other tumor features, and at physician's discretion
[c]Nodal levels I–V and retropharyngeal nodes can be treated at physician's discretion
Note: for buccal mucosa cancer, treatment of the contralateral neck can be omitted at the discretion of the treating physician

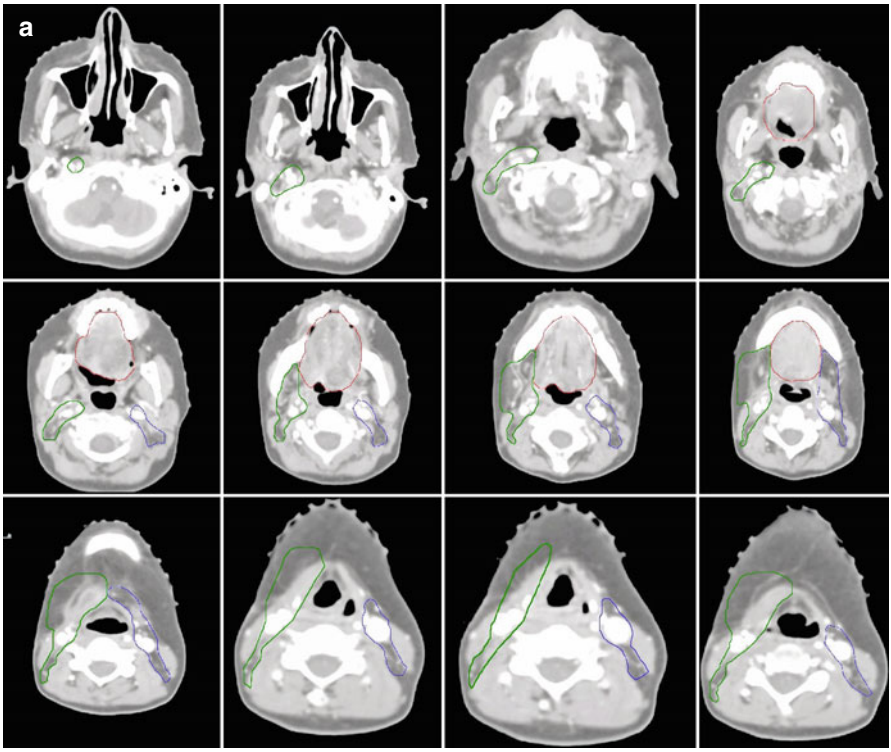

Fig. 5.1 A patient with pathologic stage T3N2b squamous cell carcinoma of the oral tongue, status post-partial glossectomy with microscopically positive surgical margins. (**a**) The high-risk clinical target volume (CTV_{66}) is shown in *red* and receives 66 Gy due to the presence of positive margins. The high-risk CTV (CTV_{60}) is shown in *green*, and the low-risk CTV (CTV_{54}) is shown in *blue*. The low necks can be treated with an anterior field. Neck nodal levels I to V are included on the ipsilateral side and levels I to IV are included on the contralateral uninvolved side. Coverage of level V is recommended for oral tongue primaries, especially after surgical manipulation of the neck and ipsilateral nodal disease. (**b**) Level IA should be covered for oral tongue primaries. (**c**) The ipsilateral retrostyloid space is at risk for nodal metastasis, especially with level II nodal involvement. Of note, if clinically indicated, can include all anterior fat space. The use of bolus and flash is recommended when there are concerns of soft tissue involvement

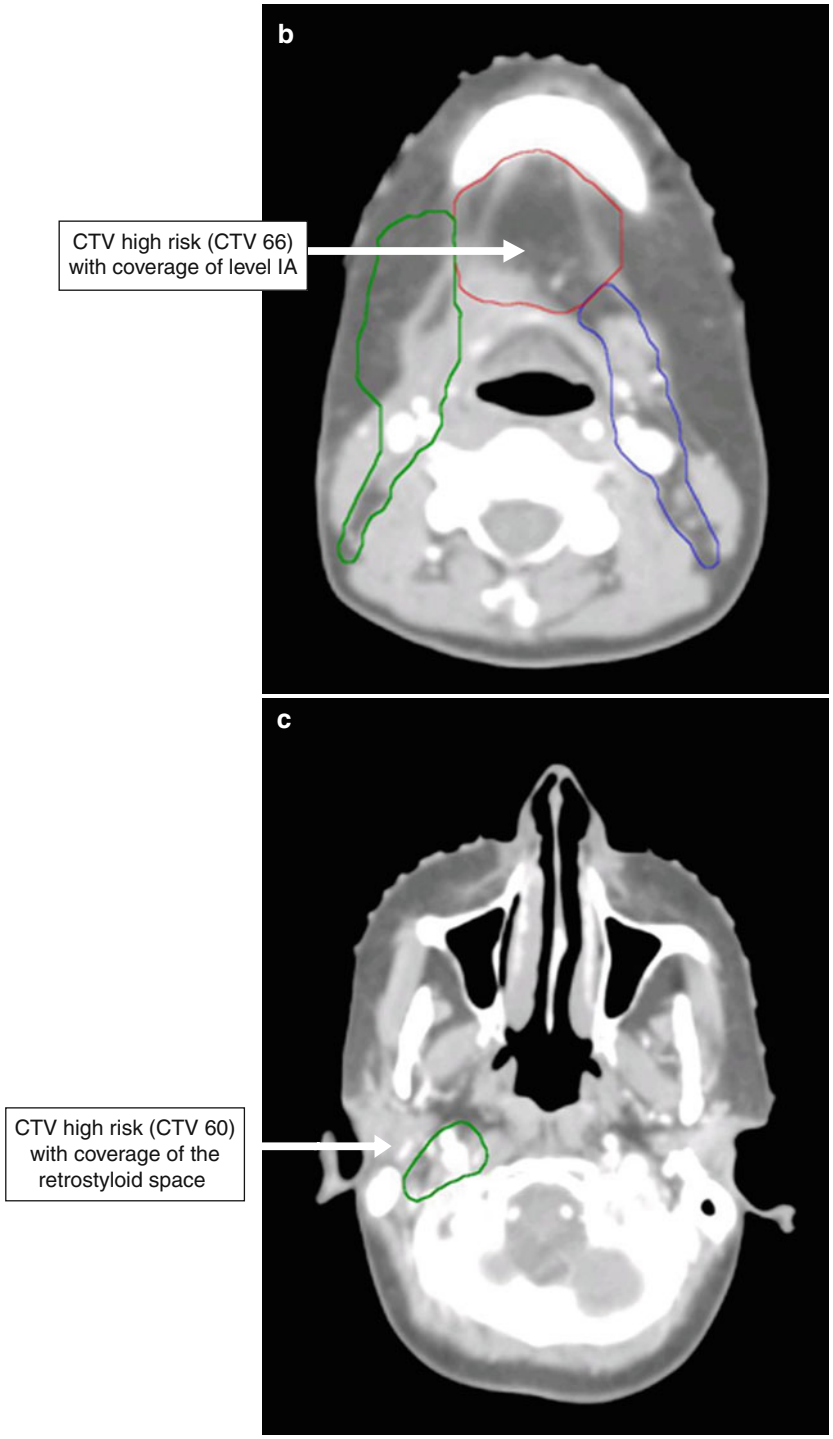

Fig. 5.1 (continued)

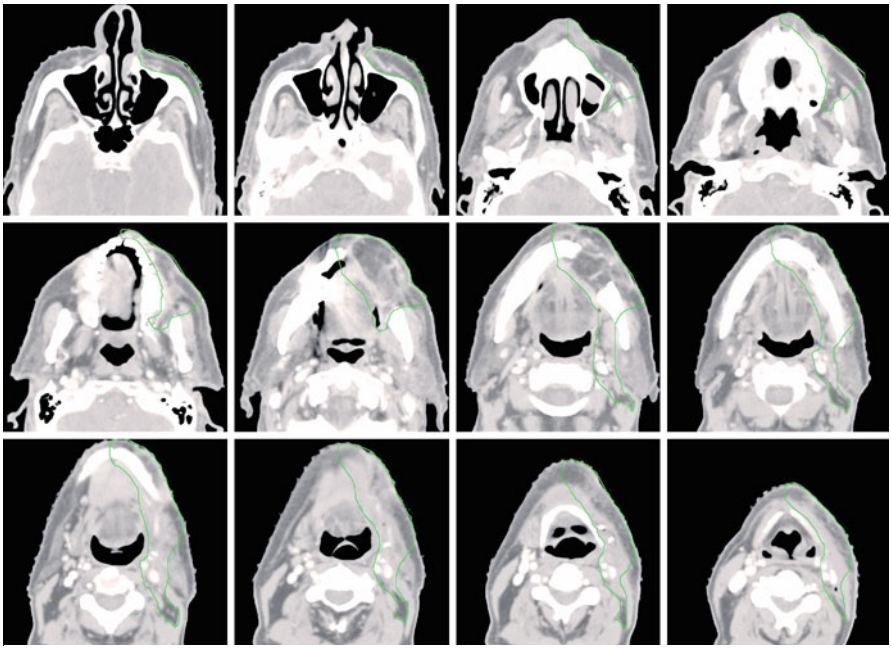

Fig. 5.2 A patient with squamous cell carcinoma of the buccal mucosa, pathologic stage T4aN0 with minimal cortical bone invasion status post-tumor resection, marginal mandibulectomy, and left neck dissection. The surgical margins were widely clear. The high-risk CTV (CTV_{60}) is shown in *green*. Neck nodal levels I to IV are included on the ipsilateral side. The CTV extends cranially to the buccal-gingival sulcus and infratemporal fossa, caudally to the buccal-gingival sulcus and submandibular gland, anteriorly at least to the lip commissure, and posteriorly to the retromolar trigone. Bolus is placed on the skin to provide adequate coverage of the high-risk CTV. Can include ipsilateral parotid if clinically concerned

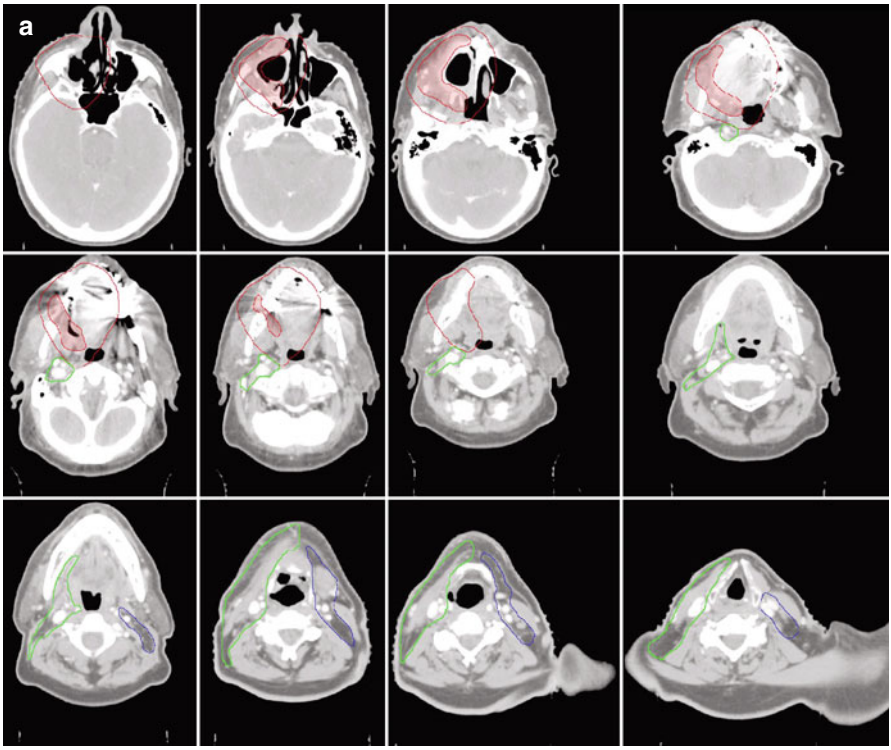

Fig. 5.3 A patient with squamous cell carcinoma of the retromolar trigone, pathologic stage T4aN2b with medial pterygoid involvement, status post-resection with gross residual disease and right neck dissection. (**a**) The gross disease CTV (CTV70) is shown in shaded red and is delineated based on operative findings as well as pre- and postoperative imaging. The high-risk CTVs (CTV59.4) are shown in *green* and *red*, and the low-risk CTV (CTV54) is shown in *blue*. (**b**) The pterygopalantine fossa is a gateway for tumor spread to the middle cranial fossa and should be adequately covered, especially with tumor invading the pterygoid muscle. (**c**) Postoperative tumor volumes should include coverage of the entire operative bed based on visualization of tissue inflammation and edema on the planning CT

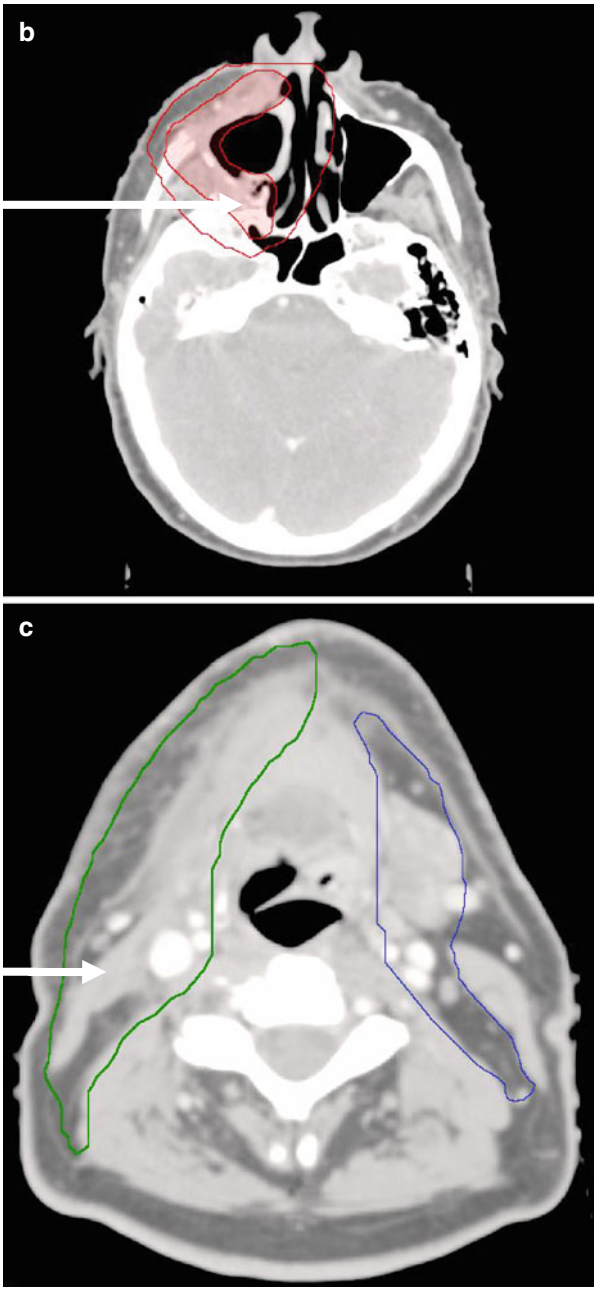

Fig. 5.3 (continued)

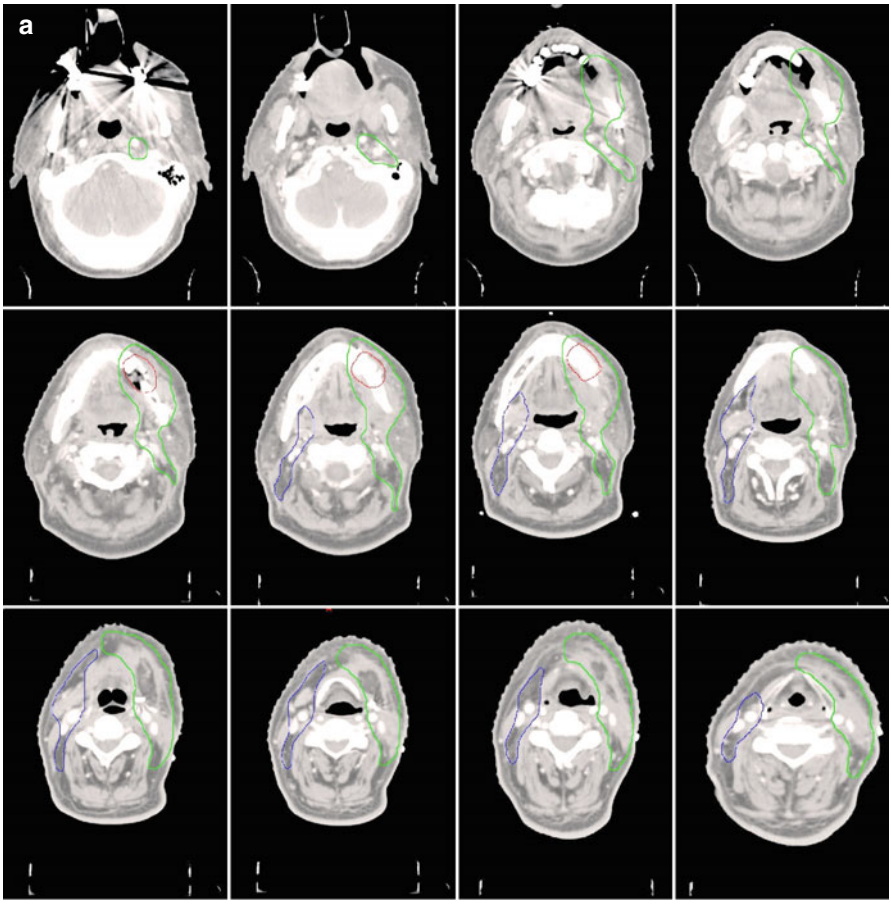

Fig. 5.4 (**a**) A patient with T4aN1 gingiva with bone invasion, status post-tumor resection, marginal mandibulectomy, and left neck dissection. The high-risk CTV (CTV66) is shown in *red*, the high-risk CTV (CTV60) is shown in *green*, and the low-risk CTV (CTV 54) is shown in *blue*. The surgical margins were clear, but due to the extent of bone invasion, 66 Gy was employed in this region. Neck nodal levels I to IV were included on the ipsilateral neck and levels I to III were included on the contralateral neck. (**b**) Following surgery, the contralateral neck is at elevated risk for nodal metastasis with involved ipsilateral neck nodes

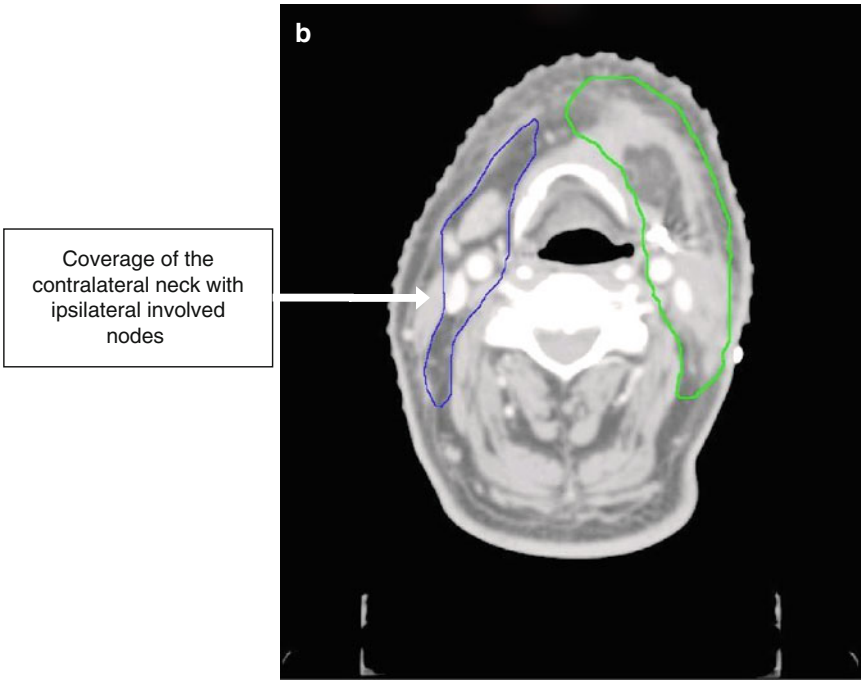

Fig. 5.4 (continued)

The Paranasal Sinuses

6

Daniel Spratt, Ruben Cabanillas, and Nancy Y. Lee

General Principles of Target Delineation

- The surgical approach (midfacial degloving, lateral rhinotomy, craniofacial, or endoscopic), can complicate the radiation field. If a craniofacial resection has been performed, the frontal graft should be included in the target volume. Fiducial markers implanted during surgery can help to delineate the tumor bed.
- Preoperative CT and MRI should be evaluated to ensure that the initial tumor volume is covered in the high-risk CTV. Detailed description of the surgical procedure and pathology report is mandatory to properly define the CTV that should encompass all initial sites of disease and the subclinical tumor spread. MRI should be used in all cases to help delineation of the tumor unless medically contraindicated.
- Adenoid cystic carcinomas are highly neurotrophic so radiotherapy volumes must encompass the afferent and efferent local nerves to the skull base. Esthesioneuroblastomas arise in the superior nasal cavity and in their early stages tend to invade the cribriform plate and anterior cranial fossa, and therefore, these regions should be encompassed in the target volume.
- Lymph node metastases are unusual, so elective treatment of the neck is not mandatory but can be done at the discretion of the treating physician. However, elective neck irradiation should be considered for esthesioneuroblastoma; high-grade, high-stage squamous cell carcinoma, especially if originating from the maxillary sinus or there is invasion of the mucosa of the palate or of the nasopharynx; when there is involvement of

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Table 6.1 Suggested target volumes for gross disease

Target volumes	Definition and description
GTV_{70}	All gross disease on physical examination and imaging (CT and MRI). PET can help further define the tumor extent
CTV_{70}	Usually same as GTV_{70}. If a margin is needed due to uncertainness during gross disease delineation, add 3–5 mm so that $GTV_{70} + 3–5\ mm = CTV_{70}$
PTV_{70}	$CTV_{70} + 3–5$ mm depending on comfort level and can be as small as 1 mm when near critical normal structures

Table 6.2 Suggested target volumes at the high- and low-risk subclinical regions

	Definition and description	
Target volumes	Ethmoid	Maxillary
CTV_{66}	Tumor implantation area or microscopically affected margins	
CTV_{60}	The CTV_{60} should encompass the areas at high risk of microscopic tumor spread from initial macroscopic tumor. Although the CTV_{60} has to be defined in a case-by-case evaluation, the general proposed limits are:	
	Superior: if the cribriform plate has not been resected, it should be included for ethmoid sinus tumors; if it has been resected, the CTV_{60} should encompass the dura or the dural graft, extending at least 10 mm superior to the cribriform plate or encompass the initial gross tumor volume	
	Inferior: the inferior turbinate; if the inferior border of the tumor allows a 10-mm margin around the original disease, then the entire hard palate does not need to be included	*Inferior*: the inferior border of the maxilla and the hard palate but should encompass a 10-mm margin around the initial gross disease
	Lateral: the nasal cavity, ethmoid sinuses, and the ipsilateral maxillary sinus and when indicated the volume should extend to the rectus muscle	*Lateral*: medial aspect should be the nasal septum, unless violation of midline structures occurs
	Posterior: include the sphenoid sinus. The retropharyngeal lymph nodes should be encompassed if the tumor extended close to the nasopharynx or if there are metastatic neck nodes from an ethmoidal carcinoma	*Posterior*: the pterygopalatine and the infratemporal fossa should be included, paying special attention to encompass the masticator space and the infraorbital fissure
PTV_{66*}	CTV66 + 3–5 mm, depending on comfort level of daily patient positioning. Image guidance is recommended to reduce random and systematic setup errors. The PTV can be further modified to produce expansions as small as 1 mm in areas adjacent to critical normal structures	
PTV_{60*}	CTV60 + 3–5 mm, depending on comfort level of patient positioning but can be as small as 1 mm in areas adjacent to critical normal tissues	

*High-risk subclinical dose: postoperatively 2 Gy/fraction to 60 Gy or 66 Gy (any region that has been surgically violated should be kept at least to 2 Gy per fraction); for the nonsurgically violated neck or prophylactic cranial nerves coverage, consider 1.8 Gy/fraction to 54 Gy (PTV_{54}). In the radical setting when a simultaneous integrated boost is used with chemotherapy, the suggested doses are 1.8 Gy/fraction to 59.4 Gy, and 1.64 Gy/fraction to 54 Gy. PTV_{70} can be treated either in 2 Gy or 2.12 Gy per fraction

the skin of the cheek or of the anterior nose; and invasion of the maxillary gingiva or the alveolus. Depending on the clinical situation (if tumor is well lateralized or if it crosses the midline), the lymph node levels Ib-IV can be covered (either unilaterally or bilaterally based on the clinical scenario).

- Suggested target volumes at the gross disease and high- and low-risk regions are detailed in Tables 6.1 and 6.2 (Figs. 6.1 and 6.2).

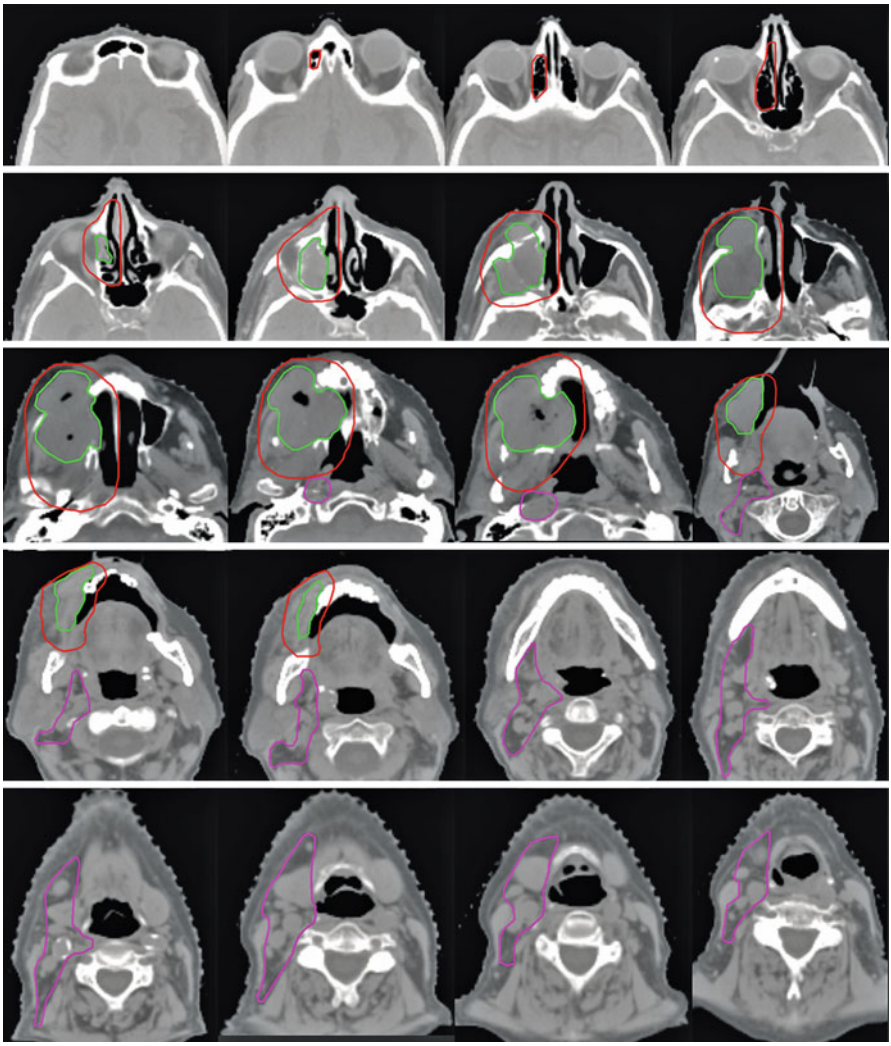

Fig. 6.1 An example of a 91-year-old patient with a cT4aN0 squamous cell carcinoma of the maxillary sinus. Patient refused surgery and was treated with definitive chemoradiation. The GTV is noted in the *green color* while the high-risk subclinical CTV is noted in the *red color*. Only the ipsilateral neck was included in the pink color given the lateralized right maxillary sinus location as well as the patient's advanced age

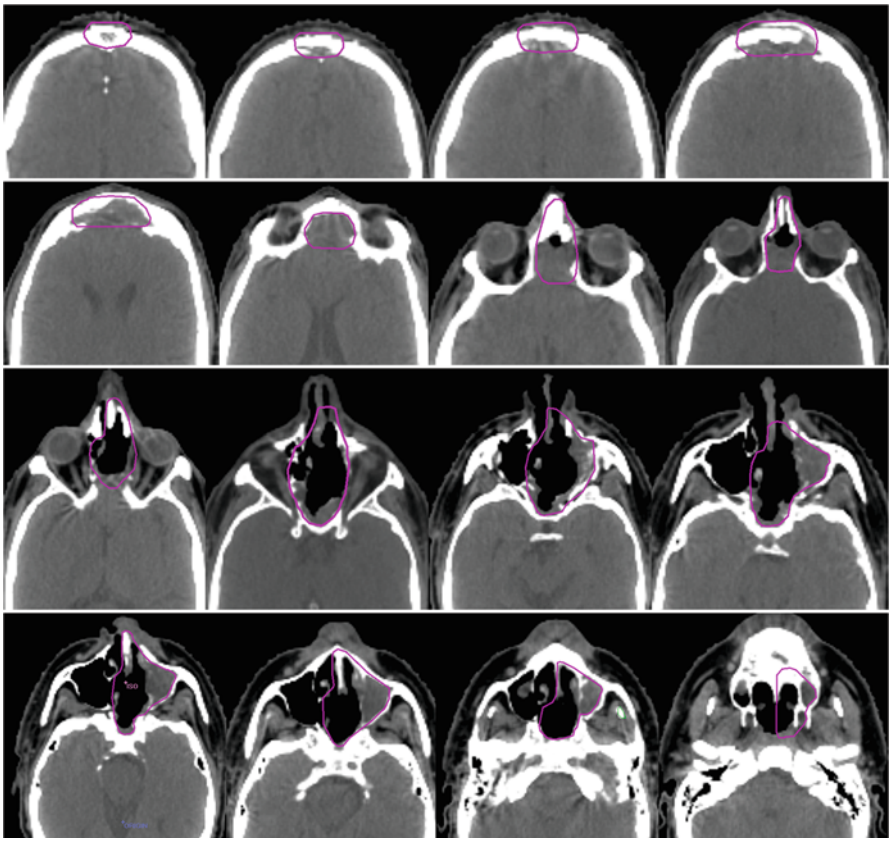

Fig. 6.2 An example of a 43-year-old patient with a pT4aN0 squamous cell carcinoma of the ethmoid sinus. Patient is s/p ethmoidectomy, sphenoidectomy, nasal exenteration, and anterior craniotomy. Patient then received adjuvant chemoradiation. The CTV is noted in the *pink color*. As this was a low-grade tumor with no neck involvement, no LN regions were treated

Further Reading

Bristol IJ, Ahamad A, Garden AS et al (2007) Postoperative radiotherapy for maxillary sinus cancer: long-term outcomes and toxicities of treatment. Int J Radiat Oncol Biol Phys 68:719–730

Chen AM, Daly ME, Bucci MK et al (2007) Carcinomas of the paranasal sinuses and nasal cavity treated with radiotherapy at a single institution over five decades: are we making improvement? Int J Radiat Oncol Biol Phys 69:141–147

Le QT, Fu KK, Kaplan MJ et al (2000) Lymph node metastasis in maxillary sinus carcinoma. Int J Radiat Oncol Biol Phys 46:541–549

Major Salivary Glands

7

Ivan W.K. Tham and Nancy Y. Lee

General Principles of Planning and Target Delineation

- Contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) of the head and neck region, from the base of skull to the clavicles, should be performed for salivary gland cancer.
- Neoplastic lesions are better visualized and delineated with MRI, given the superior soft tissue contrast in the gland. The T1-weighted images can give an excellent assessment of the margin of the tumor, its deep extent, and its pattern of infiltration. With the addition of fat-saturated, contrast-enhanced T1-weighted imaging, perineural spread, bone invasion, or meningeal infiltration can be better visualized.
- CT simulation with intravenous contrast can be performed where the primary tumor is in situ to help guide gross target volume (GTV) delineation. Fusion with diagnostic MRI when available is recommended.
- Suggested target volumes at the gross disease and high-risk regions are detailed in Tables 7.1 and 7.2 (Figs. 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, and 7.8).

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Table 7.1 Suggested target volumes at the gross disease region

Target volumes	Definition and description
GTV_{70*} (the subscript 70 denotes radiation dose delivered)	Parotid or submandibular primary: all gross disease on physical examination and imaging Neck nodes: all nodes ≥1 cm in short axis diameter or nodes with necrotic center
CTV_{70}	Add 5 mm so that $GTV_{70}+5\ mm=CTV_{70}$ For nodes that are small but suspicious for disease (i.e., <1 cm), consider a lower dose of 63–66 Gy
PTV_{70}	Margin specific to treatment center and less if image guidance available Typically $CTV_{70}+3–5\ mm=PTV_{70}$

*Suggested dose to gross disease is 2 Gy/fraction to 70 Gy

Table 7.2 Suggested target volumes at the high-risk subclinical region

Target volumes	Definition and description
CTV_{60}	Parotid or submandibular CTV_{60} should encompass the entire GTV or the surgical bed for postoperative patients *Landmarks for the parotid surgical bed* Anterior: masseter muscle Lateral: soft tissue of neck Medial: styloid process at depth Posterior: mastoid bone *Landmarks for the submandibular surgical bed* Include the entire surgical bed, all postoperative changes, and use the contralateral submandibular gland as a guide Highly consider a boost of 6–10 Gy to residual disease or positive margins. The surgeon should be encouraged to leave clips where possible for localization
CTV_{50}	*Clinically node positive tumors* Electively irradiate rest of the ipsilateral neck (levels Ib–V) to 50 Gy *Clinically node negative tumors* *Ipsilateral neck:* Include at least levels Ib–III for high-grade or large (T3–4) tumors. Adenoid cystic or acinic cell cancers typically do not require elective nodal irradiation because of the low risk of lymphatic spread *Contralateral neck:* *Parotid tumors*: Consider treating when clinically concerned, e.g., multiple nodes <1 cm *Submandibular tumors*: Treat contralateral levels I–III for tumors close to midline
PTV_{60}	Margin specific to treatment center and less if image guidance available Typically $CTV_{60}+3–5\ mm=PTV_{60}$

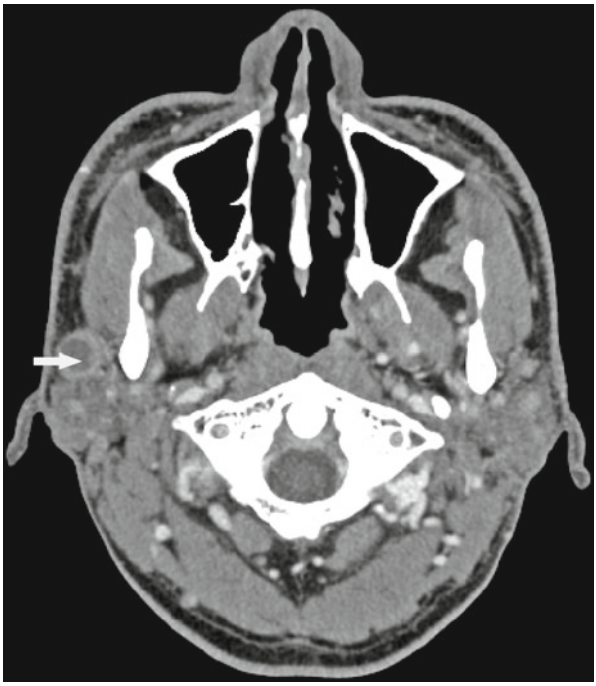


Fig. 7.1 Axial contrast-enhanced CT image of a patient with a history of excision of a cutaneous squamous cell carcinoma (SCC) in the right temporal region, who now presents with an ipsilateral parotid mass, (*arrowed*) confirmed on biopsy to be metastatic SCC

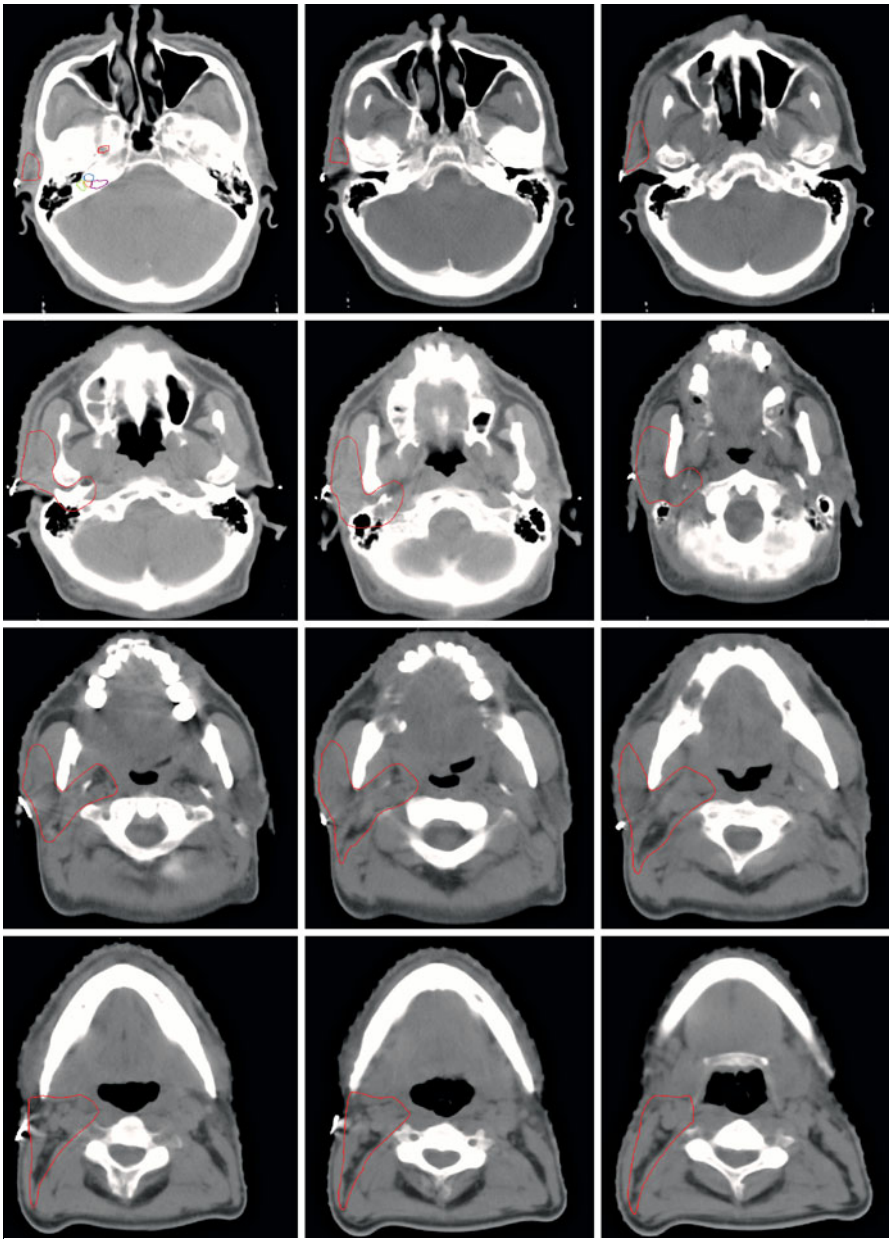


Fig. 7.2 CT simulation with 3-mm slices in a head shell was performed in the same patient following superficial parotidectomy with clear margins. These are representative slices and not all slices are included. Of note, the temporal region where the skin cancer originated should also be included using either electrons matching to IMRT or 3D CRT, or an all inclusive IMRT or 3D CRT plan, especially if the primary site treatment was less than a year prior. The structures at the base of skull in the first figure are labelled in Fig. 7.3. The orange contour denotes the CTV_{60}

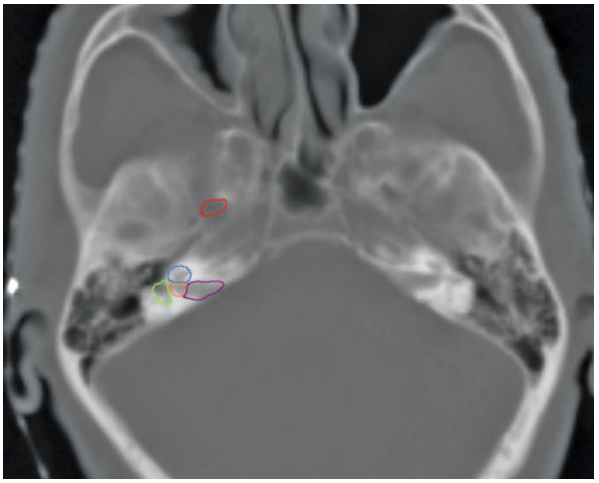


Fig. 7.3 BASE OF SKULL Delineation of structures should be done using bone windows. Structures as follows: *red* foramen ovale, *blue* cochlea, *orange* vestibule, *violet* internal auditory canal, *green* semicircular canals

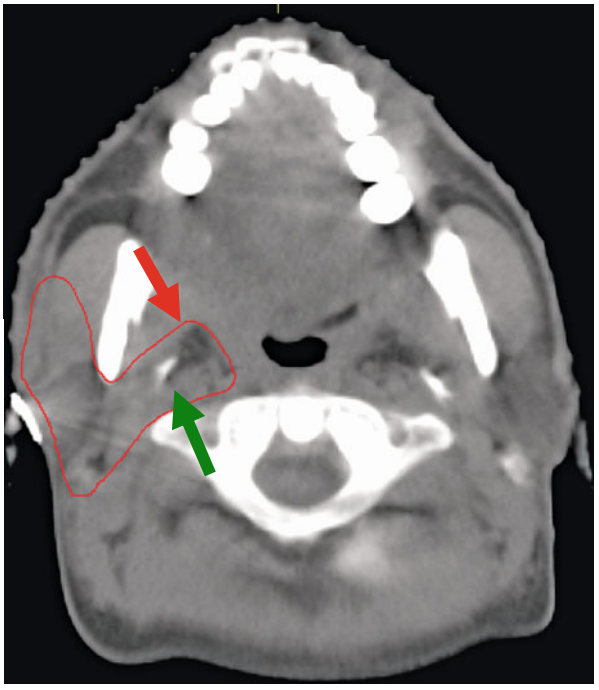
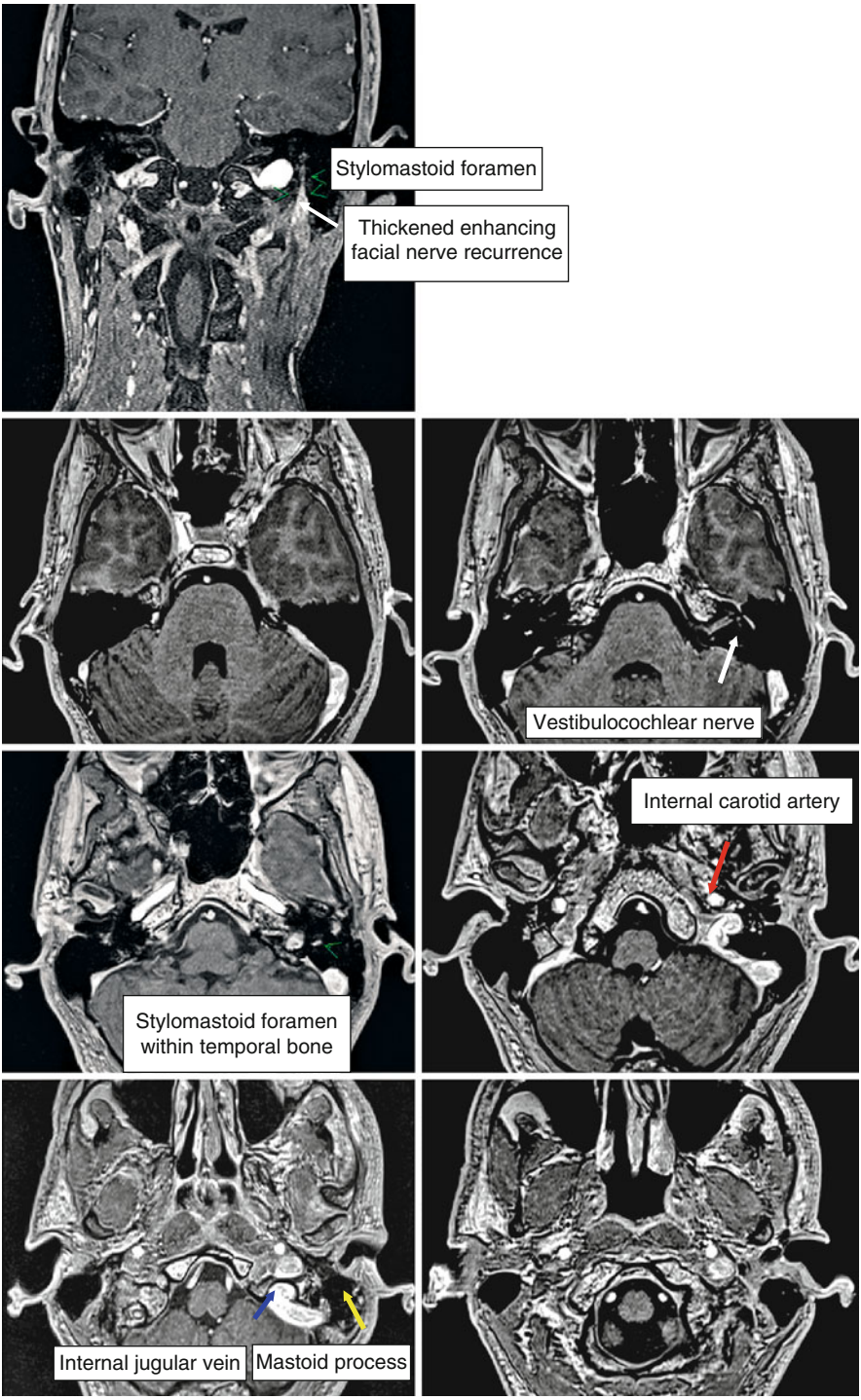


Fig. 7.4 THE PARAPHARYNGEAL SPACE (*red arrow*) is a predominantly fat-filled space extending from the base of skull to the hyoid and should be included for large or deep parotid tumors. The RETROSTYLOID SPACE (*green arrow*) is posterolateral to the styloid process, may contain lymph nodes, and should be included in the CTV_{60}


Stylomastoid foramen
Thickened enhancing facial nerve recurrence
Vestibulocochlear nerve
Internal carotid artery
Stylomastoid foramen within temporal bone
Internal jugular vein
Mastoid process

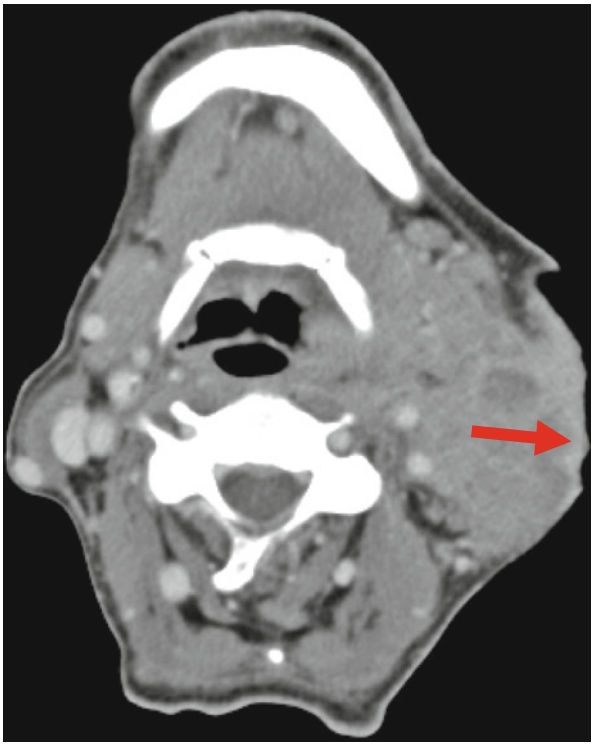


Fig. 7.6 SKIN. Include involved skin as a target structure by utilizing a bolus if there is clinical or radiological (*red arrow*) evidence of dermal infiltration. Include the scar in cases with perioperative tumor spillage

Fig. 7.5 STYLOMASTOID FORAMEN. Note pattern of perineural recurrence in these T1-weighted contrast-enhanced MRI images, which show recurrent mucoepidermoid carcinoma of the left parotid gland infiltrating the left facial nerve through the stylomastoid foramen (*green arrow heads*). For parotid tumors, include facial nerve when involved or if histology is adenoid cystic carcinoma. Include intra-temporal course of the nerve, via the facial canal, which extends from the internal auditory canal to the stylomastoid foramen

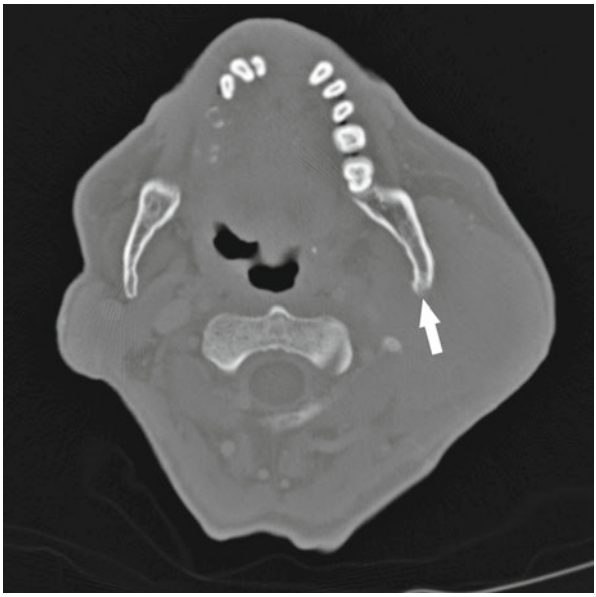
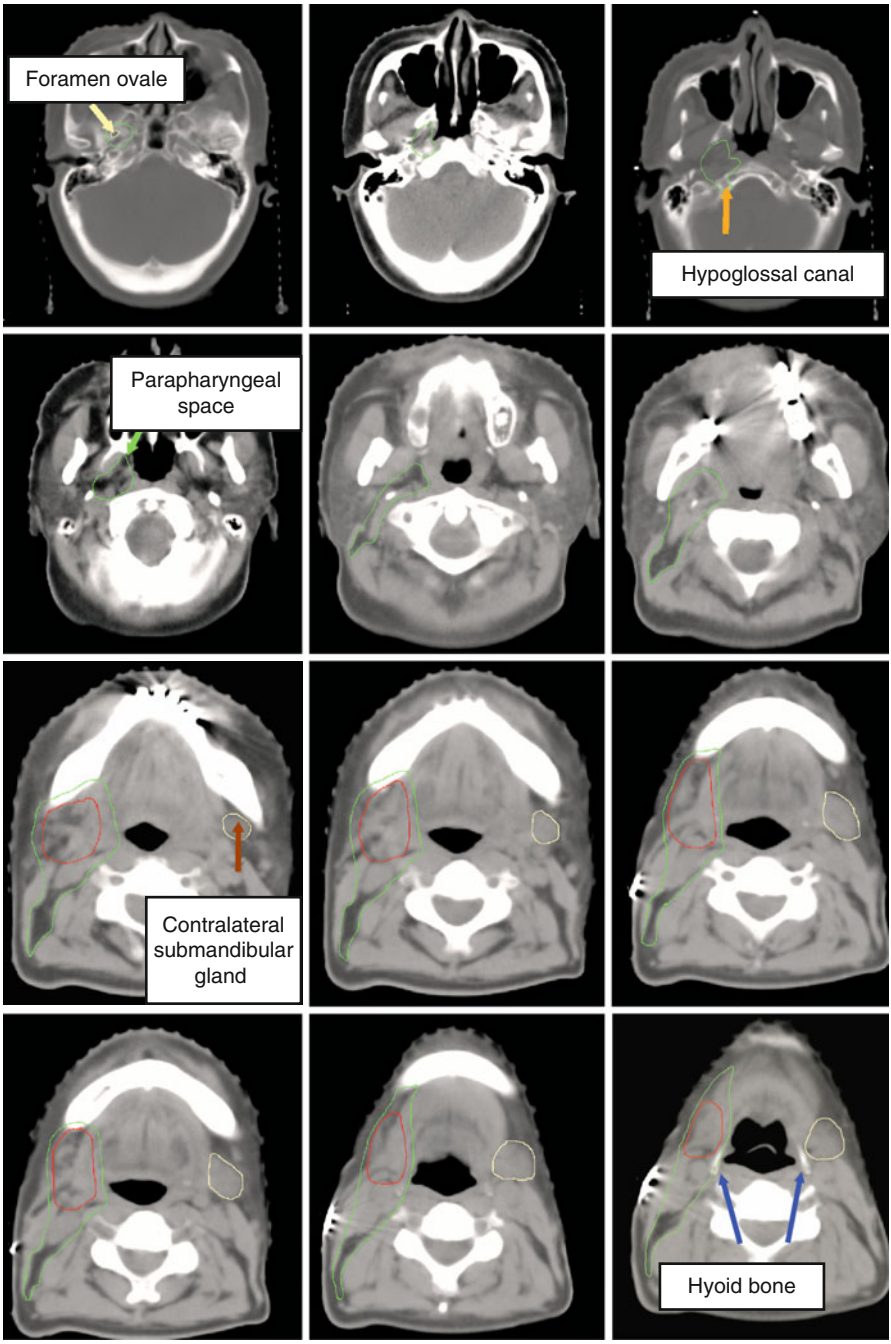


Fig. 7.7 BONE. Assess bone involvement with bone windows on CT scans and include in CTV if required. *White arrow* indicates periosteal reaction at posterior aspect of left ramus of mandible, suggesting involvement

Fig. 7.8 Submandibular gland. Selected CT simulation images of a patient who underwent complete excision of a cT1N1M0 high-grade mucoepidermoid carcinoma of the right submandibular gland with clear margins. Structures as follows: *red* $CTV_{60–66}$ (surgical bed), *green* $CTV_{50–54}$ (ipsilateral nodal stations and parapharyngeal space to base of skull). Lingual or hypoglossal nerves should be treated to base of skull especially when these named nerves are involved. The lingual nerve originates from the mandibular (V3) branch of the trigeminal nerve at the foramen ovale and courses deep to the lateral pterygoid muscle, then between the medial pterygoid muscle and the ramus of the mandible towards the medial aspect of the submandibular gland before terminating in the tongue


Foramen ovale
Hypoglossal canal
Parapharyngeal space
Contralateral submandibular gland
Hyoid bone

Thyroid Cancer

8

Shyam S.D. Rao, Nadeem Riaz, Nancy Y. Lee,
and Robert L. Foote

General Principles of Planning and Target Delineation

- Intensity-modulated radiation therapy (IMRT) is the recommended technique for definitive or postoperative radiation therapy for thyroid cancer.
- In addition to thorough physical examination, adequate imaging studies should be obtained for diagnosis, staging, and planning. The use of iodinated contrast with CT imaging should be avoided if the patient will subsequently require radioactive iodine administration as it can interefere uptake for up to 6 months. MRI and ultrasound may be valuable in detecting lymphadenopathy or extrathyroidal extension. Unlike most well-differentiated thyroid carcinomas, poorly differentiated or anaplastic thytoid cancer may be FDG-avid.
- CT simulation should be performed to help guide the gross target volume (GTV) delineation, particularly for the lymph nodes. As above, the use of iodinated contrast should be clearly justified as neccesary before administered.
- A thermoplastic mask to immobilize the head, neck, and shoulders is preferable to immobilzing only the head and neck region. The head should be slightly extended to lower the dose to the oral cavity.
- Gross disease or tumor bed with positive margins should be treated to 66–70 Gy. At-risk regions should be treated to 54–63 Gy. Patients may be treated in 30–35 fractions with an all-in-one dose-painting IMRT plan or alternatively an initial IMRT course followed by a boost. We recommend clinical target volume (CTVs) be treated with daily fractions sizes between 1.8 and 2.2 Gy.

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- Target volumes include GTV and CTV which should be delineated on every slice of the planning CT. Accurate selection and delineation of CTV for gross disease (i.e., $CTV_{66–70}$) and at-risk subclinical region ($CTV_{54–63}$) is critical for the treatment of thyroid cancer using IMRT.

Suggested target volumes for gross disease and at-risk regions are detailed in Tables 8.1 and 8.2 (Figs. 8.1 and 8.2).

Table 8.1 Suggested target volumes for gross disease

Target volumes	Definition and description
$GTV_{66–70*}$ (the subscript 66–70 denotes the radiation dose delivered)	Primary: all gross disease on physical examination and imaging. Neck nodes: all nodes ≥1 cm or with necrotic center.
$CTV_{66–70*}$	Usually same as $GTV_{66–70}$. If a margin is needed due to uncertainty of the gross disease, add 3–5 mm so that $GTV_{66–70} + 3–5\ mm = CTV_{66–70}$. If the GTV is adjacent to the spinal cord, a 1-mm margin is acceptable, as protection of the spinal cord is required. For suspicious nodes that are small (i.e., ~1 cm), a lower dose of 66 Gy (CTV_{66}) can be considered.
$PTV_{66–70*}$	$CTV_{66–70}$ + 3–5 mm, depending on variability in daily patient positioning. If the CTV is adjacent to the spinal cord, a 1-mm margin is acceptable.

*Suggested dose for gross disease is 70 Gy. In cases where there is concern for brachial plexus, laryngeal, spinal cord, lung, or esophageal toxicity, 66 Gy may be considered. In postoperative cases with gross resection but significant concern for residual disease based on positive margin(s), the tumor bed or region of concern can be treated to 66 Gy.

Table 8.2 Suggested target volumes for at-risk subclinical region

Target volumes	Definition and description
$CTV_{54–63*}$	Primary: should include tracheoesophageal groove and >5-mm margin around any $CTV_{66–70}$ In the postoperative setting, should encompass tumor bed and tracheoesophageal groove on the involved side(s). If tracheostomy performed, should also encompass tracheostomy stoma to the skin surface. Optimally, the upper larynx (vocal cords/arytenoid cartilage and above) and posterior esophagus should be excluded, if not adjacent to tumor/tumor bed. (See Table 8.1, regarding positive margins) Neck regions: Include bilateral nodal levels II–VII. Consideration should be given to include the upper mediastinum from the brachiocephalic vein down to the level of the carina for node-positive disease. (The level I and retropharyngeal nodes may be covered if adjacent level II nodes are involved.)
$PTV_{54–63*}$	$CTV_{54–63}$ + 3–5 mm, depending on variability in daily patient positioning. If the CTV is adjacent to the spinal cord, a 1-mm margin is acceptable.

*Suggested at-risk subclinical dose: 60–63 Gy. Uninvolved nodal regions may be deemed as low-risk subclinical regions and treated to 54 Gy at the discretion of the treating physician.

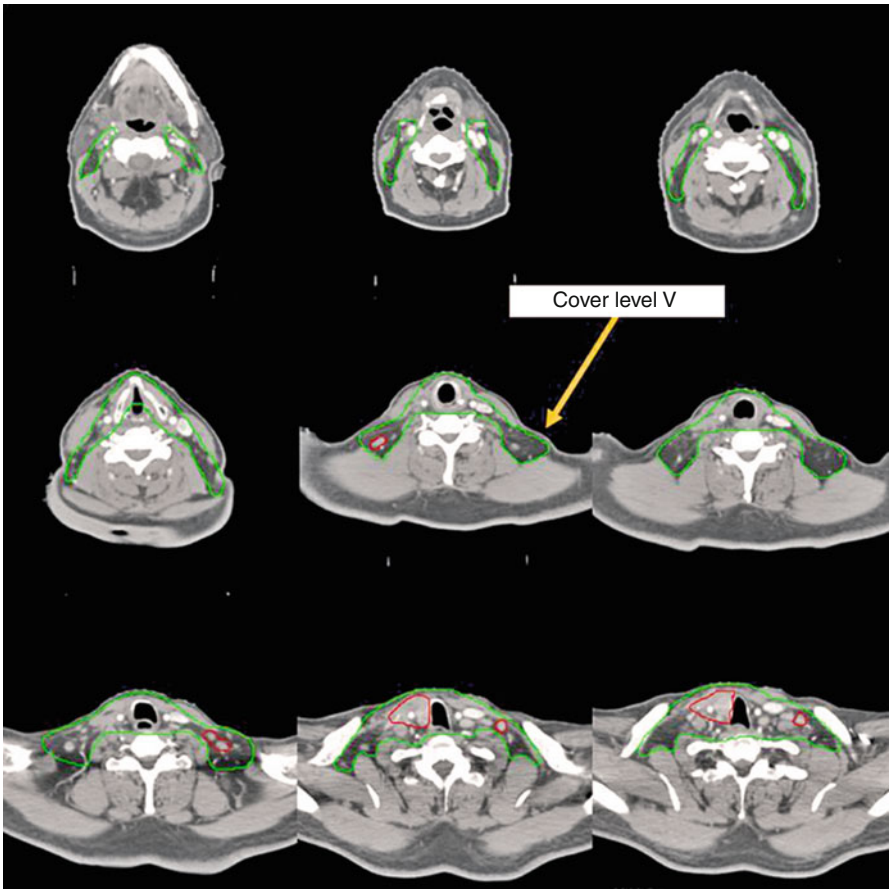

Fig. 8.1 A 58-year-old male with metastatic papillary thyroid carcinoma status post-multiple surgical resections who presented with an unresectable local recurrence and multiple mediastinal lymph nodes. He received definitive chemoradiotherapy to prevent local progression. CTV_{70Gy} is in *red* and CTV_{60Gy} is in *green*. Also, note that these are representative slices and not all slices are included

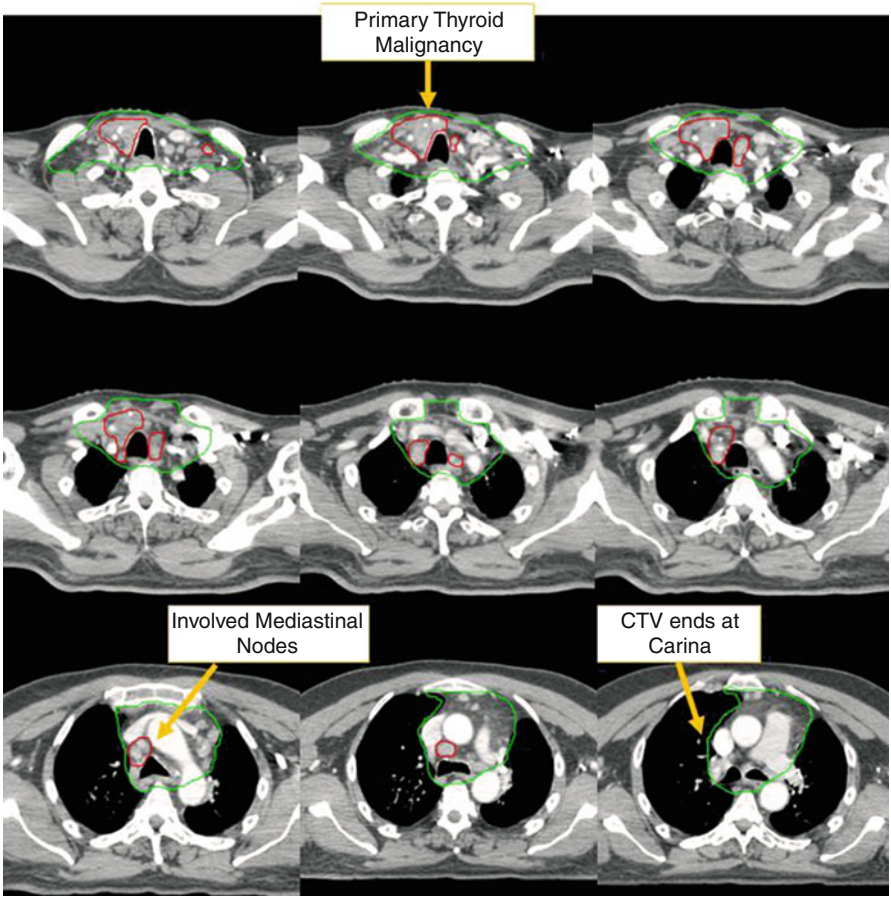

Fig. 8.1 (continued)

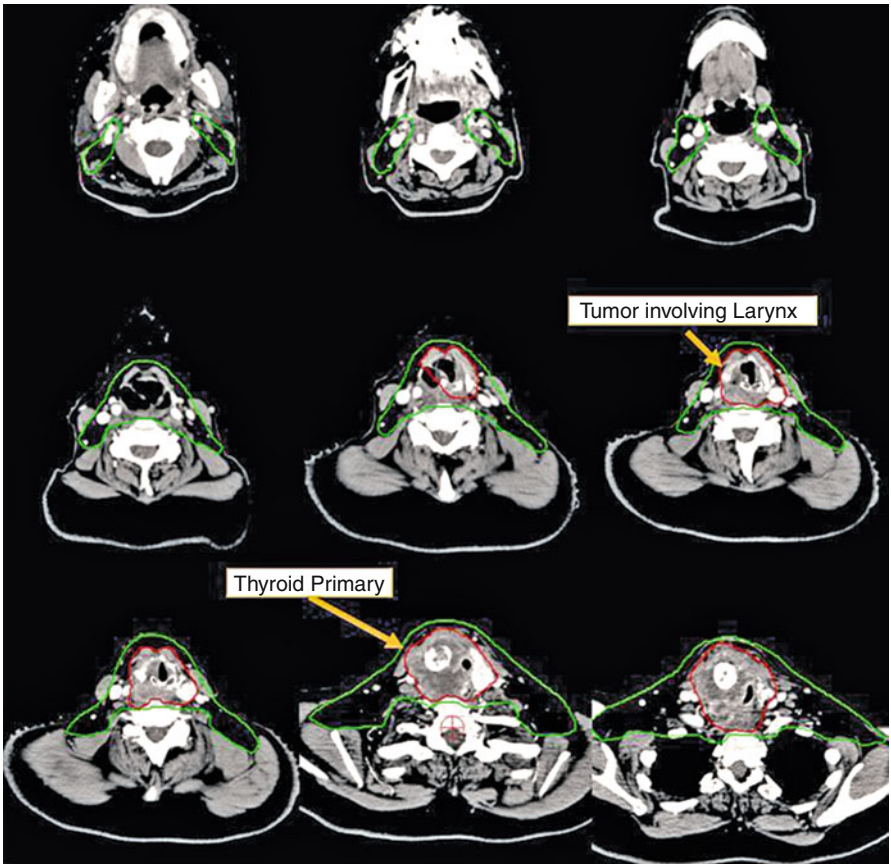

Fig. 8.2 A 73-year-old female with unresectable anaplastic thyroid carcinoma invading the larynx, trachea, and esophagus. She received definitive chemoradiotherapy with concurrent doxorubicin to prevent local progression. CTV_{70Gy} is in *red* and CTV_{60Gy} is in *green*. Although the manubrium is not routinely encompassed in the at-risk volume, it was included for this patient with aggressive bulky anterior neck disease. These are representative slices and not all slices are included

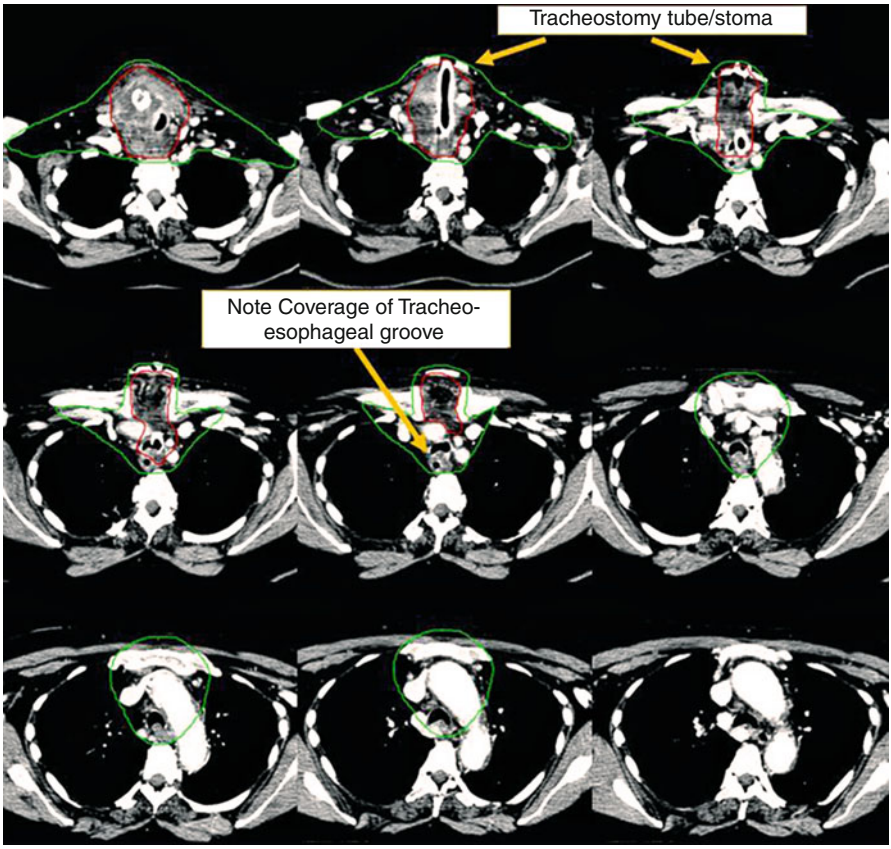

Fig. 8.2 (continued)

Squamous Cell Carcinoma of Unknown Primary in the Head and Neck

9

Nadeem Riaz, Allen Chen, and Nancy Y. Lee

General Principles of Planning and Target Delineation

- A thorough workup is necessary to rule out a site of origin before proceeding with a diagnosis of an unknown primary. At a minimum, this should consist of a careful physical examination including testing of the cranial nerves; fiberoptic examination visualizing the nasopharynx, oropharynx, larynx, and hypopharynx; and cross-sectional imaging with at least a high-resolution CT scan with contrast. Obtaining a careful patient history is also critical to determine risk factors for cancer and to consider possible infraclavicular primary sources (e.g., thoracic, gynecologic, or gastrointestinal). PET/CT can identifiy some additional primaries not detected by other methods but should be performed before biopsy to decrease the incidence of false-positive findings. Panendoscopy may also be useful.
- HPV and EBV testing should be performed to help determine possible primary locations.
- Directed biopsies of all suspicious lesions in the pharyngeal axis are mandatory; blind biopsies of normal appearing mucosa have tradiationally been recommended but are only occasionally helpful in indentiying the primary tumor.
- CT simulation with IV contrast should be performed to help guide delineation of involved lymph nodes.
- If an extended field IMRT plan is used, a thermoplastic mask immobilizing the head, neck, and shoulders is preferable to only immobilize the head and neck region.

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- Treatment to the bilateral neck and areas of pharynx at risk for harboring a primary is typically recommended. Some institutions have treated to the ipsilateral neck alone; however, the neck relapse rate and distant metatsis rate appear to be higher than with comprehensive radiotherapy.
- Traditionally, the entire pharynx has been included in treatment. IMRT allows more specific targeting of the portions of the pharynx most likely to contain the original primary site and can better spare normal structures, thereby minimizing side effects.
- The extent of the pharynx to irradiate must be determined on a case-by-case basis and remains an area of active investigation. For instance, irradiating the oropharynx alone may be sufficient for an HPV+ patient, whereas an EBV+ patient may only need treatment to the nasopharynx. The pattern of lymph node spread can further help guide decisions on how much of the pharynx to treat. Some authors have advocated sparing the larynx when there are no low lymph nodes involved. When in doubt, the entire pharynx should be treated.
- Cervical (levels Ib-V) and retropharyngeal lymph nodes should be included for the node positive neck. For the contralateral neck, nodal levels II–IV and the retropharyngeal nodes should be targetted to a prophylactic dose.
- In the postoperative setting, concurrent chemotherapy should be considered when extracapsular extension is present (ECE). In the definitive setting, advanced nodal disease is a consideration for concurrent chemotherapy.
- Suggested target volumes for gross disease and high-risk regions of the pharynx are detailed in Table 9.1 (Figs. 9.1, 9.2, and 9.3).

Table 9.1 Suggested target volumes

Target volumes	Definition and description
GTV_{70*} (the subscript 70 denotes the radiation dose delivered.)	All lymph nodes ≥1 cm in short axis, significantly FDG avid, or positive on biopsy. Contour any lymph nodes in doubt as GTV
PTV_{70*}	GTV_{70} + 3–5 mm depending on institutional accuracy of daily patient positioning
$CTV_{nasopharynx**}$	Extends from the base of skull superiorly to the soft palate inferiorly. Anteriorly extends from the posterior choana to the posterior pharyngeal wall. Laterally ensures adequate coverage on the fossa of Rosenmüller
$CTV_{oropharynx**}$	Extends superiorly from the surface of the soft palate to the floor of the vallecula inferiorly (or hyoid bone). Anteriorly, the base of tongue should be covered; however, an additional margin covering the oral tongue is not necessary. Laterally, the tonsils should be covered adequately. Posteriorly, the entire pharyngeal wall should be covered
$CTV_{larynx\&hypopharynx**}$	Extends superiorly from the hyoid bone to the bottom of cricoid cartilage
$PTV_{mucosa**}$	A 3–5-mm expansion on the mucosal surface CTVs depending on institutional accuracy of daily patient positioning

Note: If the patient underwent surgery, the postoperative dissected neck should be treated anywhere from 60 to 66 Gy in 2 Gy per fraction

*Suggested dose to gross disease is 69.96Gy with 2.12Gy/fraction

**Suggested dose to mucosal surfaces at risk for harboring a primary is 54–60 Gy in 1.64 and 1.8 Gy fraction sizes, respectively

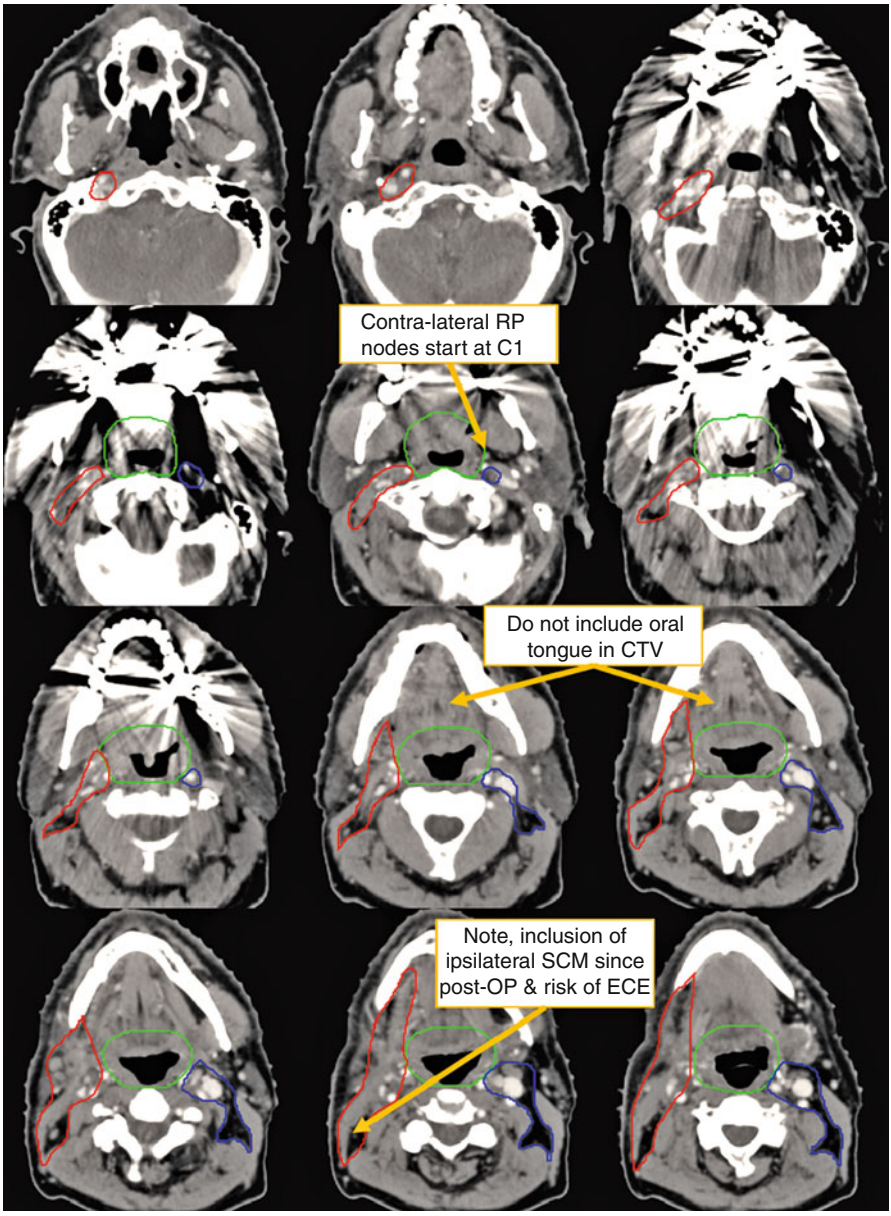

Fig. 9.1 A 62-year-old male with a TxN2a unknown primary referred for postoperative treatment. He underwent bilateral tonsillectomy and a right neck dissection which revealed a single 4.6-cm level II lymph node. Notice the difference in the target delineation in the involved neck versus the contralateral neck. The CTV_{66Gy} is in *red*, the $CTV_{54–60Gy}$ is in *green*, and the CTV_{54Gy} is in *blue*. Please note that these are representative slices and not all slices are included

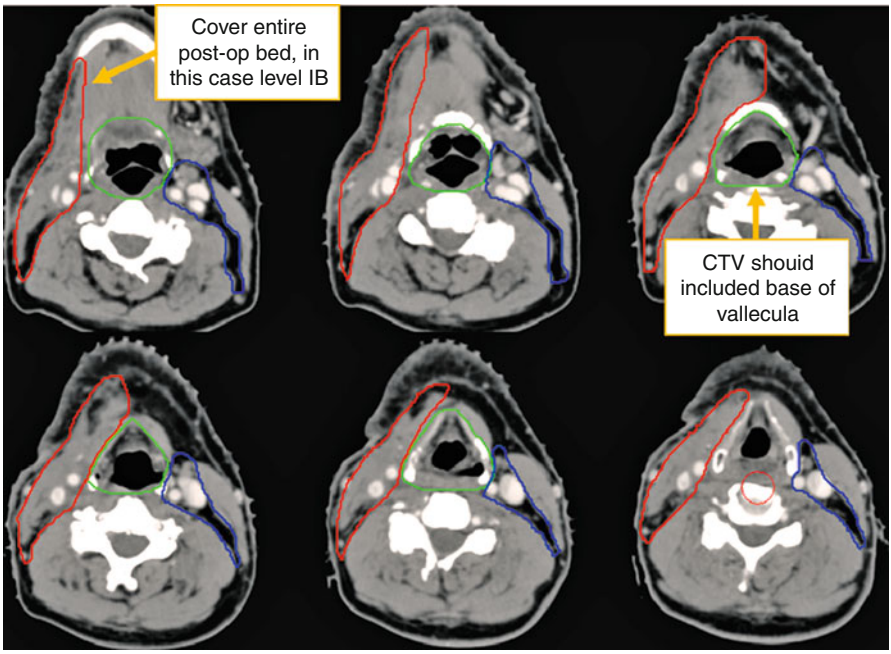

Fig. 9.1 (continued)

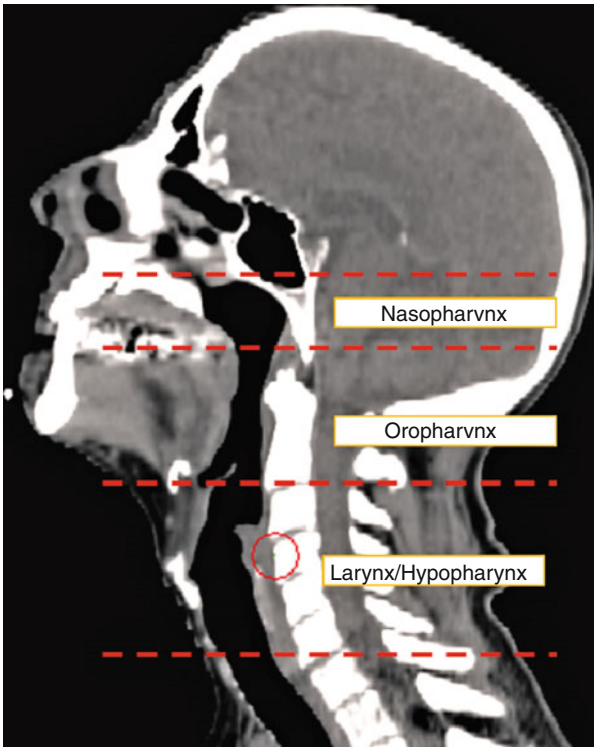

Fig. 9.2 Sagittal image at *midline* demonstrating landmarks deliniating nasopharynx, oropharynx, and larynx/hypopharynx. Viewing contours on the sagittal images can ensure adequate coverage of intended target. *Red circle is radiographic iso-center*

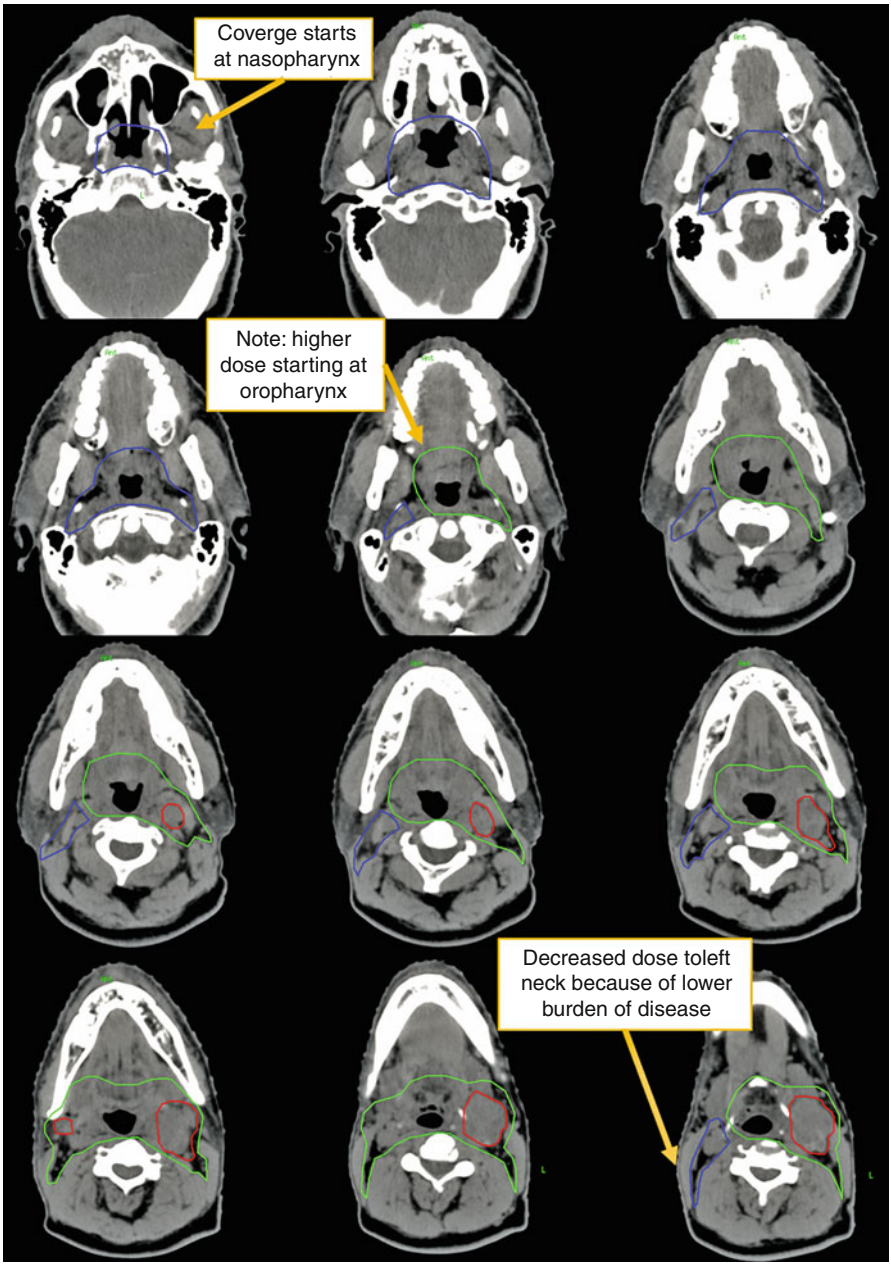

Fig. 9.3 A 50-year-old gentleman with a TxN2c squamous cell carcinoma referred for definitive treatment. An open biopsy of a left-sided lymph node demonstrated extra-nodal extension. HPV ISH and p16 testing were negative. He received definitive chemoradiotherapy. The CTV_{70Gy} is in *red*, the CTV_{60Gy} is in *green*, and the CTV_{54Gy} is in *blue*. Please note that these are representative slices and not all slices are included

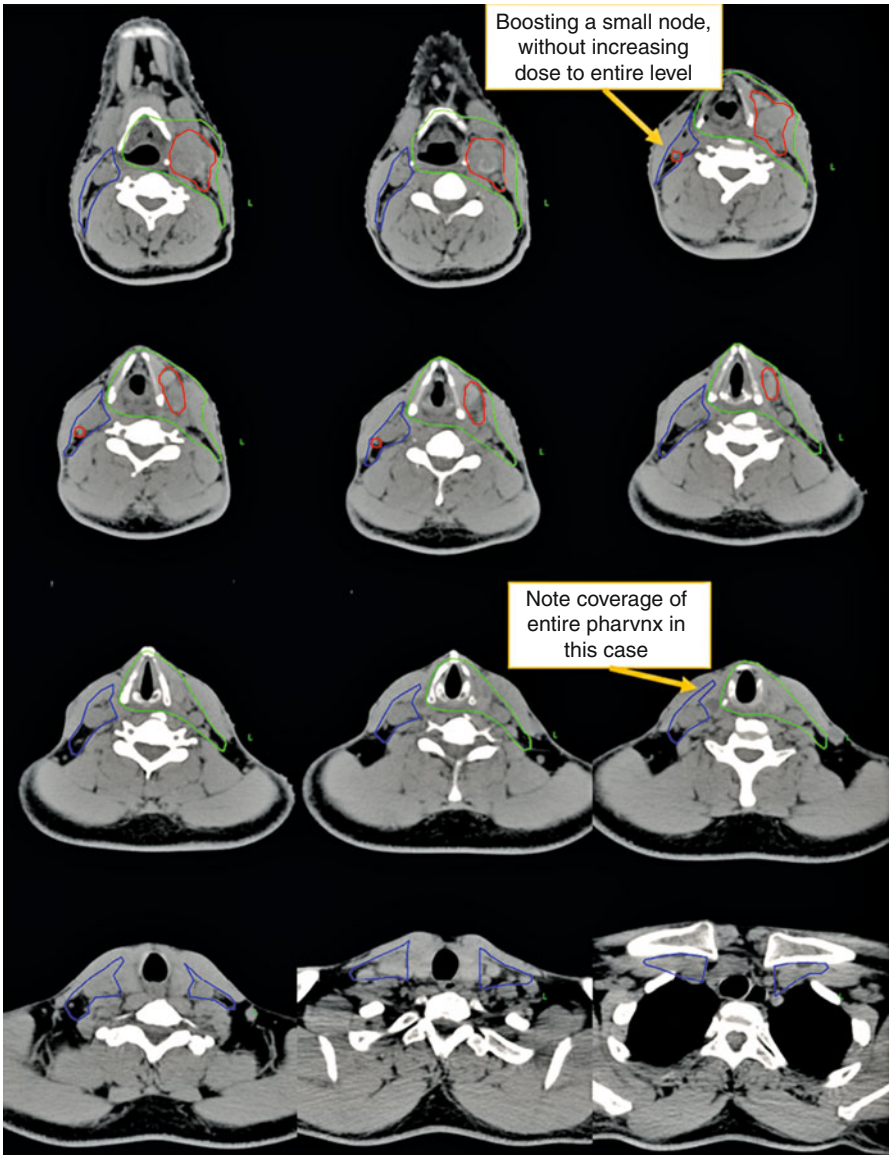

Fig. 9.3 (continued)

Further Reading

Barker CA, Morris CG, Mendenhall WM (2005) Larynx-sparing radiotherapy for squamous cell carcinoma from an unknown head and neck primary site. Am J Clin Oncol 28:445–448

Gillison ML, D'Souza G, Westra W et al (2008) Distinct risk factor profiles for human papillomavirus type 16-positive and human papillomavirus type 16-negative head and neck cancers. J Natl Cancer Inst 100:407–420

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Strojan P, Ferlito A, Medina JE et al (2011a) Contemporary management of lymph node metastases from an unknown primary to the neck: I. A review of diagnostic approaches. Head Neck

Strojan P, Ferlito A, Langendijk JA et al (2011b) Contemporary management of lymph node metastases from an unknown primary to the neck: II. A review of therapeutic options. Head Neck

Early Breast Cancer

10

Shannon M. MacDonald and Brian Napolitano

General Principles of Target Delineation

- Three-dimensional conformal radiation therapy (3D CRT) with appropriate compensation using a field-in-field technique or intensity-modulated radiation therapy (IMRT) to provide homogeneous dose to the breast tissue is the standard technique for definitive radiation therapy for early stage breast cancer. The highest level of evidence supports whole breast irradiation followed by a boost to the lumpectomy cavity as the long-established optimal radiation course. Accelerated partial breast irradiation (APBI), although not yet the standard of care, may be an acceptable alternative for select patients unable to receive several weeks of radiation therapy.
- In addition to thorough physical examination, adequate imaging studies and pathological examination should be obtained for diagnosis, staging, and planning. All patients should undergo mammogram at diagnosis. Imaging also often includes ultrasound and MRI of the breast. These imaging studies should be reviewed prior to radiation planning. Image-guided biopsy generally confirms a diagnosis of cancer. Surgery consisting of segmental excision alone for ductal carcinoma in situ (DCIS) and segmental excision and sentinel lymph node biopsy (SLNB) is recommended for early invasive disease. Pathology should be reviewed to ensure adequate margins and confirm an early stage breast cancer requiring radiation to the breast without inclusion of the regional lymphatics. Surgical clips should be placed at the time of surgery if possible to assist in delineation of the tumor bed and for radiographic localization prior to radiation delivery.

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- For whole breast radiation planning, a CT with ≤3-mm slice thickness should be performed in the supine or prone position. For APBI, a CT slice thickness of 1.5–2 mm through the lumpectomy cavity may enable improved delineation of the lumpectomy cavity.
- For supine positioning, the patient should be positioned on a breast board with arms above the head. Patients with pendulous breasts and/or tumor bed in close proximity to the chest wall and critical structures (heart/lung) may benefit from prone positioning. For prone positioning, patient should be placed prone on a dedicated prone breast board, and care should be taken to ensure that the patient is comfortable as this is very important to facilitate reproducibility. Patients with orthopedic injuries to the back or neck may not be ideal candidates for prone positioning.
- Target volumes include the breast tissue and lumpectomy cavity for whole breast irradiation and lumpectomy cavity, lumpectomy CTV, and lumpectomy PTV for APBI.
- Suggested target volumes are described in Table 10.1 (Figs. 10.1, 10.2, 10.3, 10.4, 10.5, and 10.6).

Table 10.1 Suggested target volumes for 3-Dimensional treatment planning for early stage breast cancer

Target volumes	Definition and description
Breast	Clinical reference is required for breast tissue delineation. Breast tissue may be wired, or borders may be placed clinically at the time of CT. Contour should include all glandular breast tissues. The cranial border should be below the head of the clavicle and at the insertion of the second rib. Caudal border is defined by the loss of breast tissue. Medial border is at the edge of the sternum and should not cross midline. Lateral border is defined by the midaxillary line but is dependent on ptosis of the breast tissue. Anterior border is the skin or a few millimeters from the surface of the skin (for dose reporting), and the posterior border is the pectoralis muscles and muscles of the chest wall. The volume should not include these muscles or the ribs
Lumpectomy cavity	Seroma, surgical clips, and notable differences in the glandular breast tissue should be included. Comparison to the contralateral breast may be useful, particularly when fluid and/or surgical clips are not present. All imaging studies should be reviewed prior to planning to assist in delineating this volume. This volume should not extend outside of the breast tissue
Lumpectomy CTV[a]	Lumpectomy cavity with a 1.0- to 1.5-cm expansion. This volume should not extend outside of the body or into the pectoralis muscles and/or muscles of the chest wall
Lumpectomy PTV[a]	Lumpectomy CTV with a margin based on setup uncertainty and predicted patient motion (generally 0.5–1.0 cm). This volume may extend outside of the patient surface and into the pectoralis muscles and/or muscles of the chest wall. Adjustments to this volume may be necessary for dose-reporting purposes

[a]For APBI only; for whole breast irradiation, the lumpectomy cavity alone is the target for boost

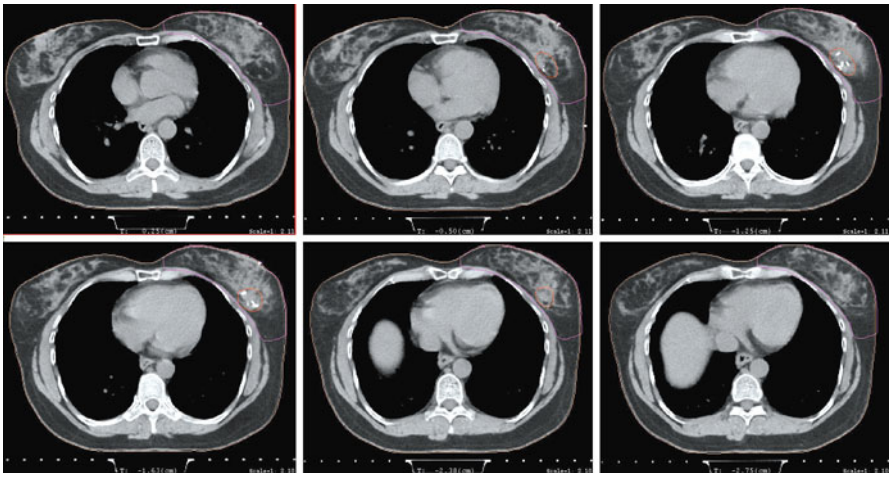

Fig. 10.1 Axial images in the supine position for a woman with left-sided stage I breast cancer

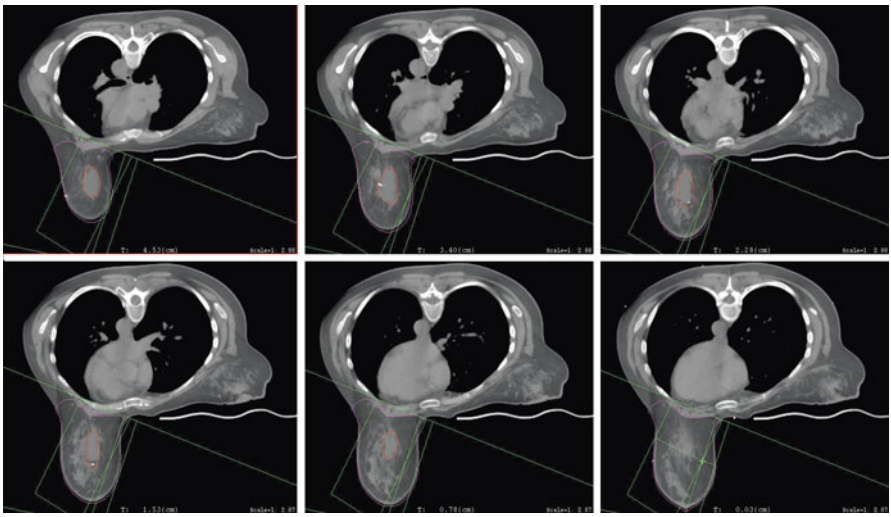

Fig. 10.2 Axial images in the prone position for a woman with left-sided DCIS

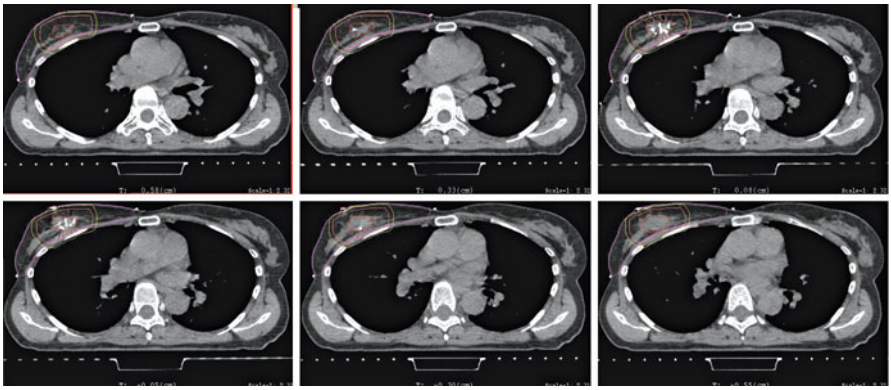

Fig. 10.3 Axial images for APBI. Lumpectomy cavity is based on seroma, clips placed by surgeon, and information from review of mammogram, US, and MRI. CTV is typically a 1.5-cm expansion around the lumpectomy cavity that excludes pectoralis muscle, rib, and chest wall and does not extend outside of the contoured breast tissue. Typically, the CTV does not extend to the skin (restricted to 5 mm from patient surface). PTV is formed by an expansion of approximately 5 mm (depending on institutional setup uncertainty) around the CTV

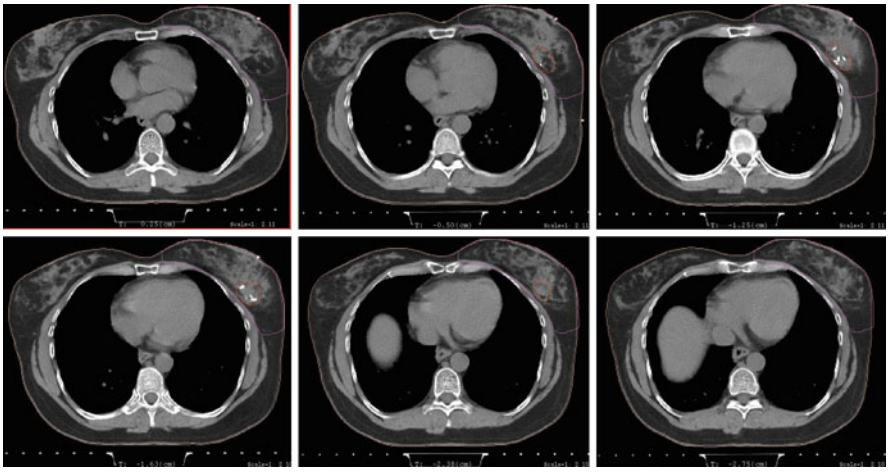

Fig. 10.4 Supine breast plan using tangent fields with a field-in-field technique for homogeneity and a small MLC block for cardiac shielding. Prescribed dose is 50 Gy at 2 Gy per fraction followed by an electron boost to the lumpectomy cavity to 10 Gy at 2 Gy per fraction

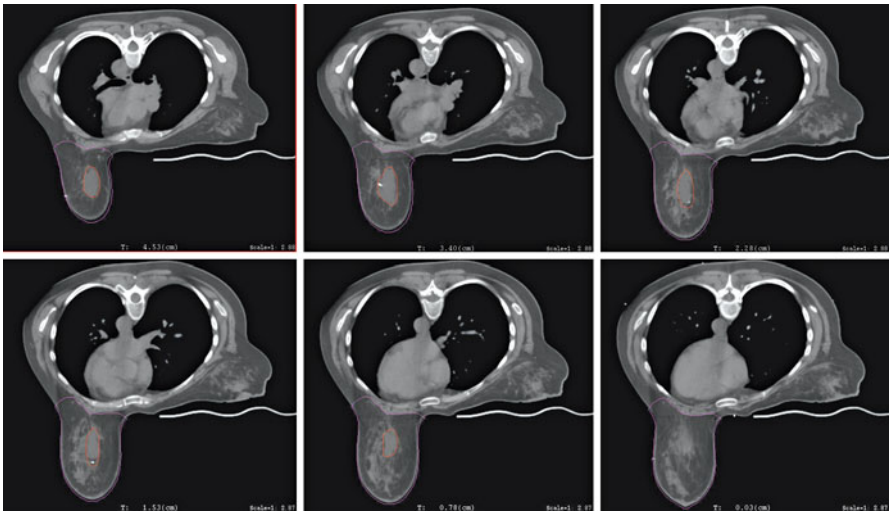

Fig. 10.5 Prone breast plan using tangent fields with a field-in-field technique. Prescribed dose is 50 Gy at 2 Gy per fraction followed by a mini-tangent photon boost to the lumpectomy cavity to 10 Gy at 2 Gy per fraction

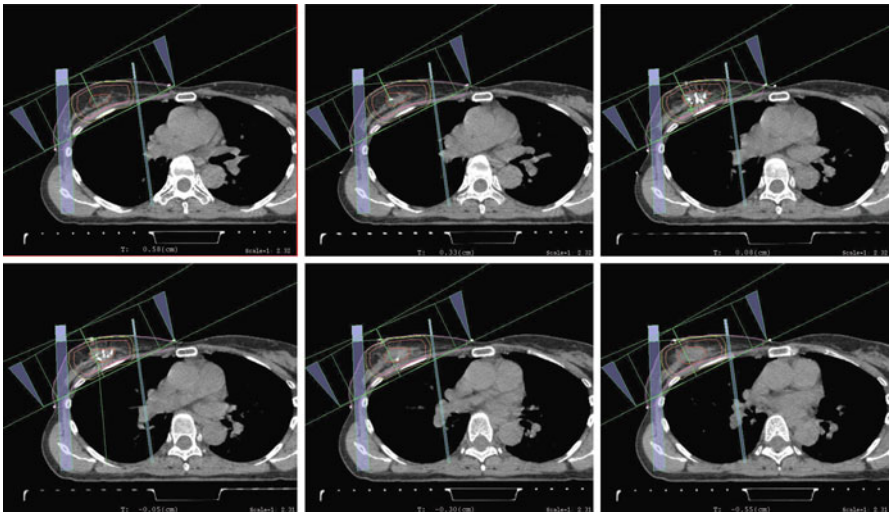

Fig. 10.6 APBI plan using a mini-tangent photon fields in combination with an en face electron field

Locally Advanced Breast Cancer

11

Alice Ho and Simon N. Powell

General Principles of Target Delineation

- Patients undergo CT simulation in the treatment position with both arms extended above their head using an Alpha Cradle or breast board immobilization; IV contrast is not necessary.
- In cases where the patient has an intact breast, the borders of the breast are wired on the patient's skin prior to scanning.
- Patients are scanned from the cricoid through 5 cm below the clinically marked inferior port edge. The entire lung must be included.
- PTV is defined as any breast tissue or chest wall, ipsilateral level I–III axillary lymph nodes, ipsilateral supraclavicular lymph nodes, ipsilateral interpectoral lymph nodes, and ipsilateral internal mammary lymph nodes.
- Bolus of 3–5 mm is used daily over the chest wall or breast (Table 11.1).

Table 11.1 Suggested target volumes at the gross disease region

Target volumes	Definition and description
CTV	Breast tissue or chest wall as defined by RTOG Breast Cancer Atlas[1], ipsilateral regional lymph nodes[2], interconnecting lymphatic drainage routes, and chest wall musculature/skin to be determined at risk for microscopic disease
PTV	A margin of 3–5 mm medially, 5–10 mm laterally, 3–5 mm posteriorly, and 5–10 mm superiorly, inferiorly, and anteriorly (to include the skin surface) will be added to the CTV. The amount of lung can be trimmed per physician discretion

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Target and Nodal Volumes for Unreconstructed Right Chest Wall

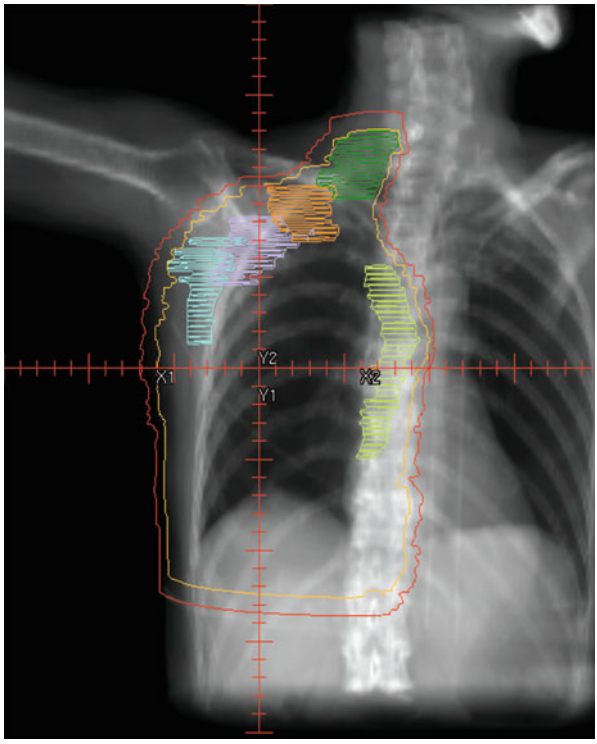

Fig. 11.1 Coronal view. *Red* PTV, *light orange* CTV, *blue* level I lymph nodes, *light purple* level II lymph nodes, *dark orange* level III lymph nodes, *green* supraclavicular lymph nodes, *yellow green* internal mammary nodes (IMN)

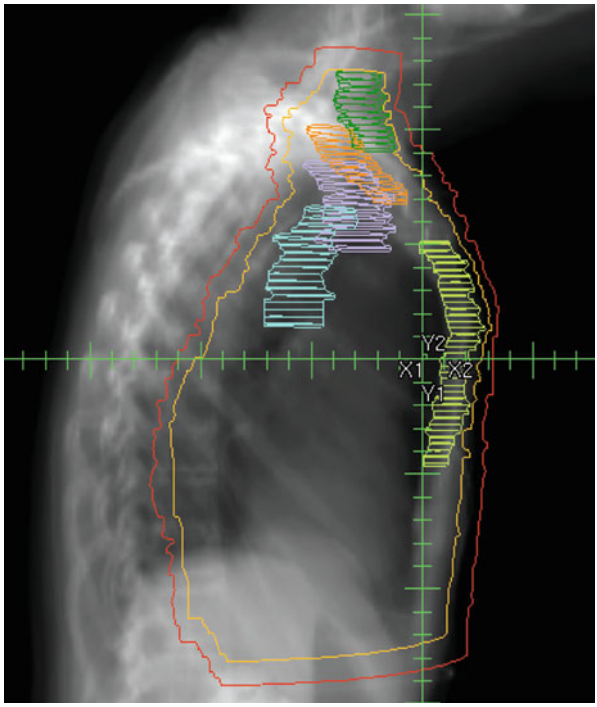

Fig. 11.2 Sagittal view. *Red* PTV, *light orange* CTV, *blue* level I lymph nodes, *light purple* level II lymph nodes, *dark orange* level III lymph nodes, *green* supraclavicular lymph nodes, *yellow green* internal mammary nodes (IMN)

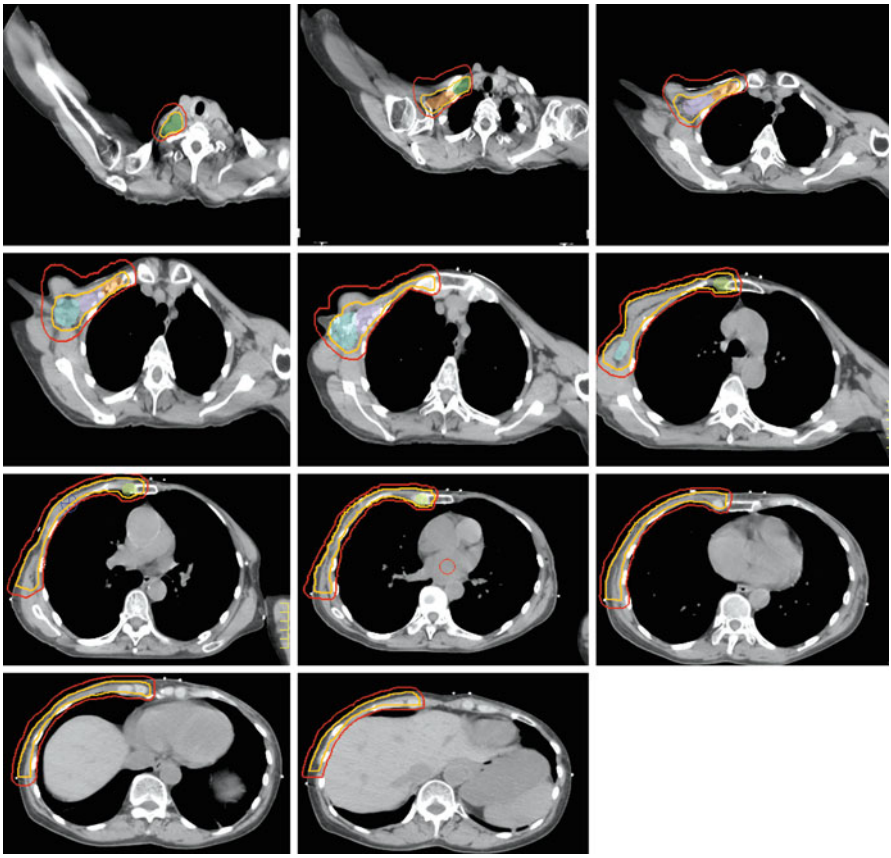

Fig. 11.3 Axial slices in the cranial to caudal direction

Target and Nodal Volumes for Reconstructed (Tissue Expander) LeftChest Wall

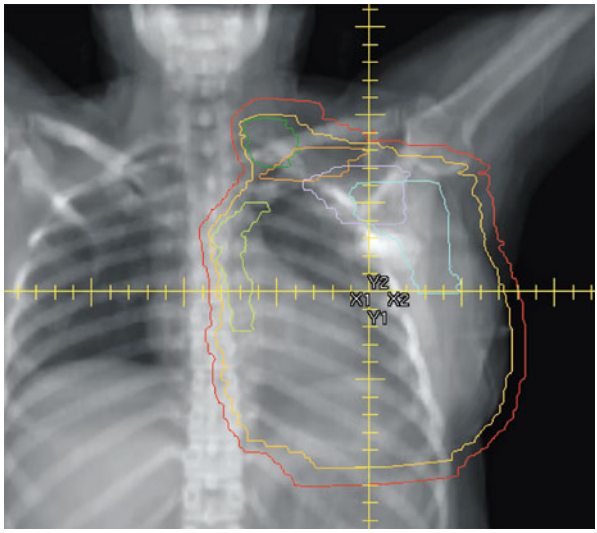

Fig. 11.4 Coronal view: *red* PTV, *light orange* CTV, *blue* level I lymph nodes, *light purple* level II lymph nodes, *dark orange* level III lymph nodes, *green* supraclavicular lymph nodes, *yellow green* internal mammary nodes (IMN), *yellow* heart, *dark purple* contralateral breast

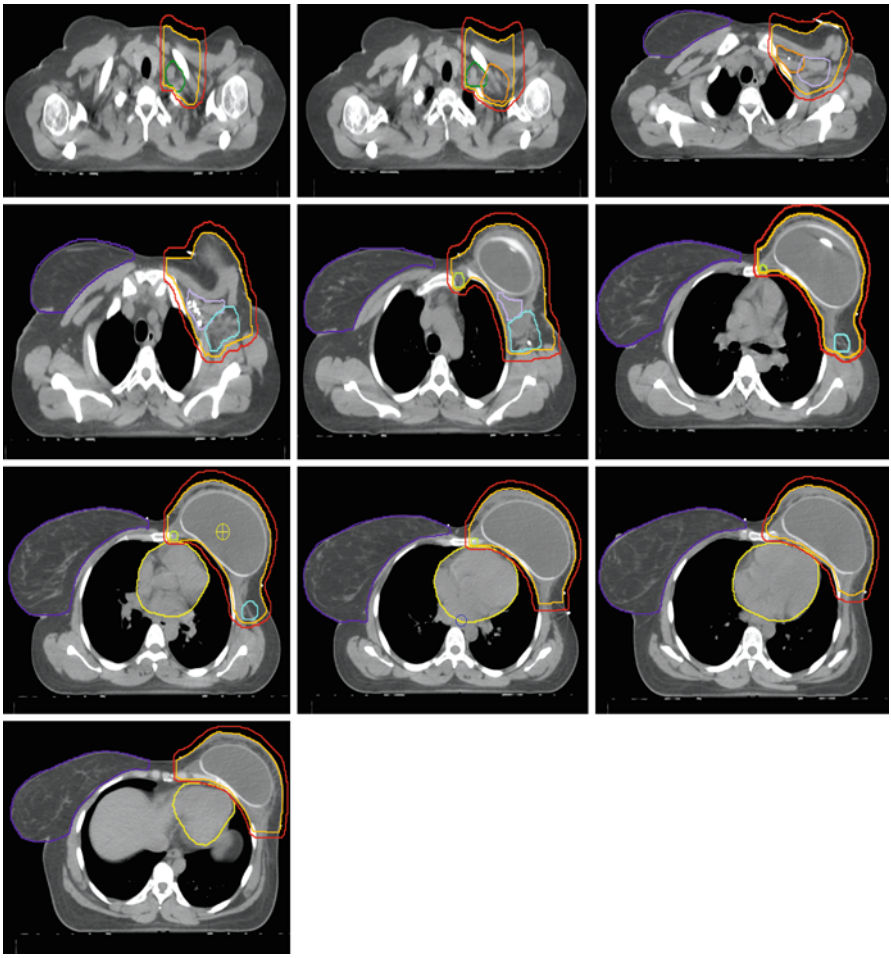

Fig. 11.5 Axial slices in the cranial to caudal direction

Conventional 3D Conformal Planning

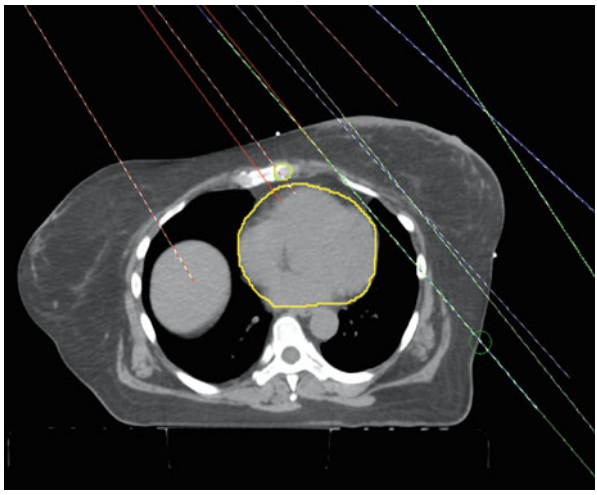

Fig. 11.6 Axial view of three beams: a medial en face electron beam (*red*) matched to two lateral opposing tangent fields (*blue* and *green*)

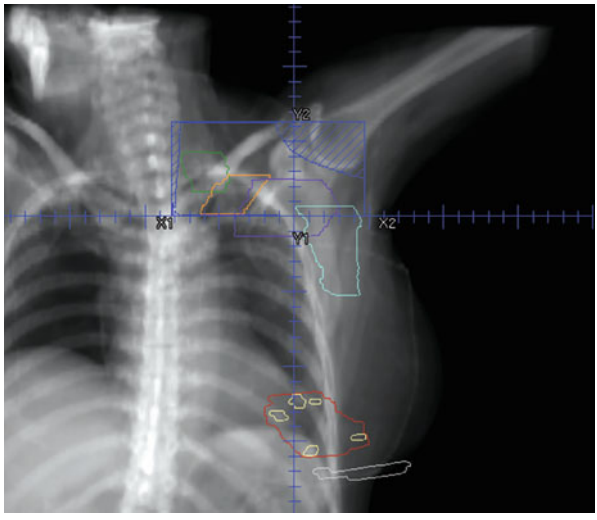

Fig. 11.7 Coronal view of supraclavicular field and lymph node targets

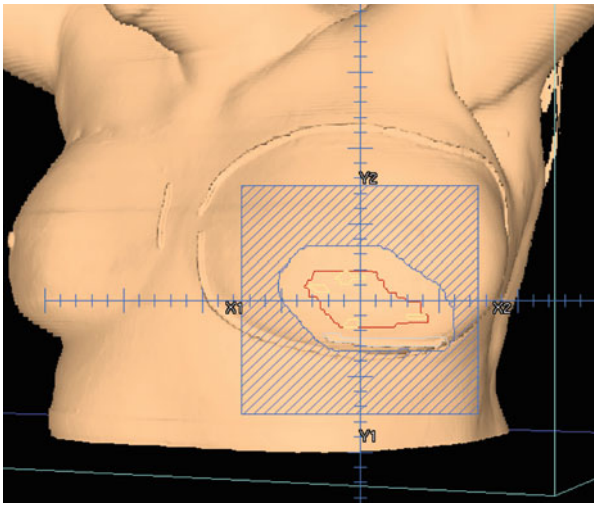

Fig. 11.8 3D view of a boost to the tumor bed: An en face electron field with a custom cutout (*blue*) encompasses the tumor bed (*maroon*), clips (*light green*), and lumpectomy scar (*gray*)

Further Reading

Dijkema IM, Hofman P, Raaijmakers CP et al (2004) Loco-regional conformal radiotherapy of the breast: delineation of the regional lymph node clinical target volumes in treatment position. Radiother Oncol 71:287–295

White J, Tai A, Arthur D et al (2011) Breast cancer atlas for radiation therapy planning: consensus definitions. Radiat Ther Oncol Group. http://www.rtog.org/CoreLab/ContouringAtlases/BreastCancerAtlas.aspx

Non-small Cell Lung Cancer (NSCLC) and Small Cell Lung Cancer (SCLC)

12

Daniel R. Gomez and Zhongxing Liao

General Principles of Planning and Target Delineation

- Computed tomography (CT)-based planning utilizing conformal techniques is the standard of care for NSCLC and SCLC. Three-dimensional conformal radiation therapy (3D-CRT) and intensity-modulated radiation therapy (IMRT) both involve the utilization of a number of beam angles and the generation of a dose-volume histogram. It is essential in this setting to accurately delineate both critical normal structures and target volumes. In addition, it is necessary to have an understanding of the nodal levels of the mediastinum, as has been previously published in consensus atlases such as a recent study by the University of Michigan [1].
- Assessment of respiratory motion and appropriate radiation simulation is vital to the planning process. Patients should ideally be simulated with their arms above their head to maximize the number of beam arrangements that can be used. A four-dimensional (4D) simulation should be performed to assess for internal motion. If a 4D study is not available, then the following measures can be taken to estimate internal motion of intrathoracic structures: (1) simulation with a slow helical CT scan or (2) acquisition of CT images at maximal inspiration and expiration, with the difference being the total extent of motion of the target and critical structures.
- In addition to the target volume, the following normal structures should be contoured: heart, lungs, spinal cord, esophagus, and the brachial plexus for superiorly located tumors or high paratracheal/supraclavicular lymph node involvement.

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The liver should be contoured for right lower lobe tumor located close to diaphragm. Recent publications have outlined consensus delineation of the brachial plexus [2] and should be referenced for accurate contouring.

- The following target structure should be delineated: gross tumor volume (GTV), when applicable; clinical target volume (CTV); internal target volume (ITV); and planning target volume (PTV).
- For both NSCLC and SCLC in the setting of gross disease, an involved field approach is widely accepted based on prior publications demonstrating a low rate of failure in elective nodal regions [3, 4] and a randomized trial showing improved outcomes with an involved field vs. elective nodal approach [5]. Therefore, elective nodal regions should not routinely be covered if the treating physician is confident in the understanding of the sites of active disease.
- Treating physicians should utilize the following information to delineate active disease: physical examination, CT scan with contrast, positron emission tomography (particularly in NSCLC), and evaluation of the mediastinum with either a mediastinoscopy or endobronchial ultrasound (EBUS).
- There are two potential approaches for expanding the GTV. The first involves an expansion of the GTV to the CTV, followed by a further expansion to the ITV to account internal motion, followed by a PTV expansion for daily variations in patient position and movement. The second technique, often utilized at our institution, is performed by delineating the GTV and then assessing for internal motion. We then define a structure called the iGTV, which is then expanded to create the iCTV (which is very similar to the ITV) and further expanded to yield the PTV.
- Standard treatment margins from the GTV (or iGTV) to CTV are 0.6–0.8 cm, as have been defined on prior pathologic studies [6]. Clinical target volume (or ITV) to PTV margins are: 1.0–1.5 cm if no assessment of management for internal motion or daily image-guided radiation therapy (IGRT), such as kV imaging or cone-beam CT scan; 0.5–1.0 cm for either 4D CT planning or CBCT, but not both; 0.5 cm for 4D CT planning and daily kV imaging; 0.3 cm for 4D CT planning and CBCT guidance. At our institution, we utilize daily CBCT scan for patients treated with stereotactic body radiation therapy (SBRT) or hypofractionated radiation therapy for a 0.3-cm CTV to PTV margin. For conventional fractionated radiation therapy with or without chemotherapy, daily kV imaging (often with weekly CBCT scans) is preferred for a 0.5-cm CTV to PTV margin.
- In the postoperative scenario for NSCLC, there is no clear consensus as to target delineation. With the development of CT planning, some institutions utilize a more limited approach, such as treating the involved lymph node regions, ipsilateral hilum, and one lymph node level above and below the involved region. In the scenario of a comprehensive mediastinal lymph node dissection, our institution opts for this latter approach, similar to that used in the Lung ART trial [7].

Table 12.1 Appropriate radiation treatment regimens for lung cancer.

Lung malignancy	Accepted treatment doses
NSCLC, stage I stereotactic body radiation therapy (SBRT)	50–70 Gy in 5–20-Gy fractions
NSCLC, stage II–III standard fractionated	60–74 Gy in 1.8–2.0-Gy fractions daily
Pancoast tumor	60–74 Gy in 1.8–2.0-Gy fractions daily Or Twice-daily regimen to minimize late neurologic effects, i.e., 1.2 Gy × 58 BID = 69.6 Gy
SCLC, limited or extensive stage	45 Gy in 1.5-Gy fractions BID Or 61.2-Gy concomitant boost: 1.8 Gy daily per fraction × 16 fractions, then 1.8 Gy BID × 18 fractions (9 days) Or 70 Gy in 2.0-Gy fractions daily

Historically, large fields have been utilized, covering the involved lymph node levels at surgery, the bilateral mediastinum, ipsilateral hilum, and inclusion of the supraclavicular lymph nodes for superiorly located tumors. This approach is rarely used.

- For SCLC, a "standard" GTV to CTV margin has not been well defined. Margins of 0.5–1.0 cm are considered acceptable, often to include the ipsilateral hilum, as recommended in the ongoing cooperative trial of the Cancer and Leukemia Group B (CALGB) 30610/Radiation Therapy Oncology Group (RTOG) 0538. The CTV to PTV margin follows similar guidelines as that for NSCLC as noted above. At our institution, image guidance is standard, and thus, we utilize CTV to PTV margins of 0.3–0.5 cm.
- Recommended target delineation and prescription doses do not differ significantly between limited and extensive stage SCLC. An involved field technique is utilized in both scenarios, with standard doses as depicted below. While one randomized trial in extensive stage SCLC utilized doses of 54 Gy in 1.5-Gy fractions twice daily (BID) to the mediastinum [8], 45 Gy in 1.5-Gy fractions BID is also acceptable and frequently utilized at our institution.
- Standard treatment doses for NSCLC and SCLC are depicted in the table below. Dose constraints are dependent on the total dose and the number of fractions delivered and are summarized in the recent *Quantitative Analyses of Normal Tissue Effects in the Clinic* publications [9]. The stages cited are as per the 7th Edition Staging by the American Joint Committee on Cancer [10] (Table 12.1, Figs. 12.1, 12.2, 12.3, 12.4, 12.5, and 12.6).

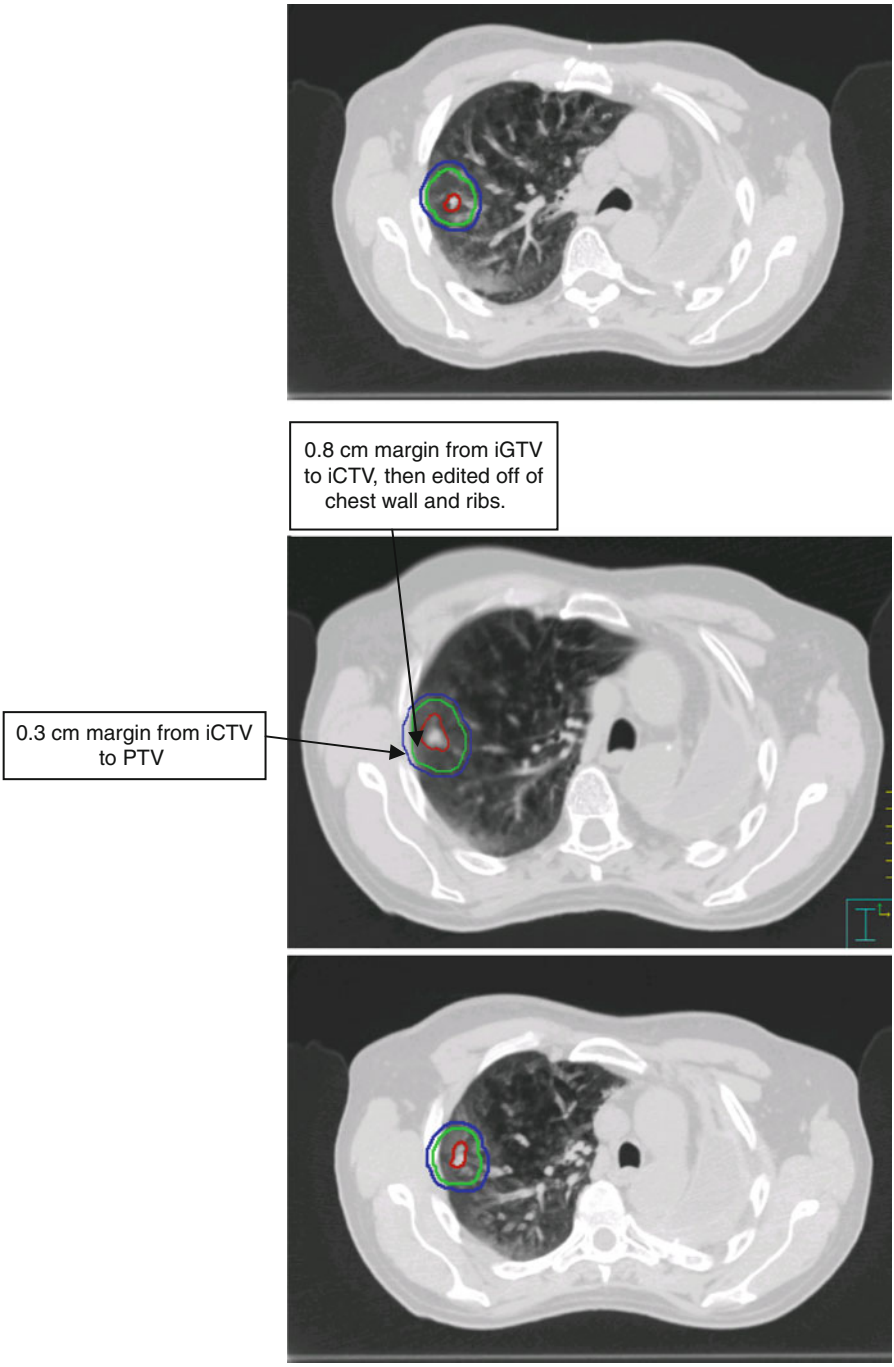


Fig. 12.1 Stage T1N0 NSCLC (adenocarcinoma). The patient had a right upper lobe tumor and had significant chronic obstructive pulmonary disease, and was thus not a candidate for surgical resection. The prescription dose was 12.5 Gy × 4 fractions = 50 Gy. *Red* iGTV, *green* iCTV, *blue* PTV

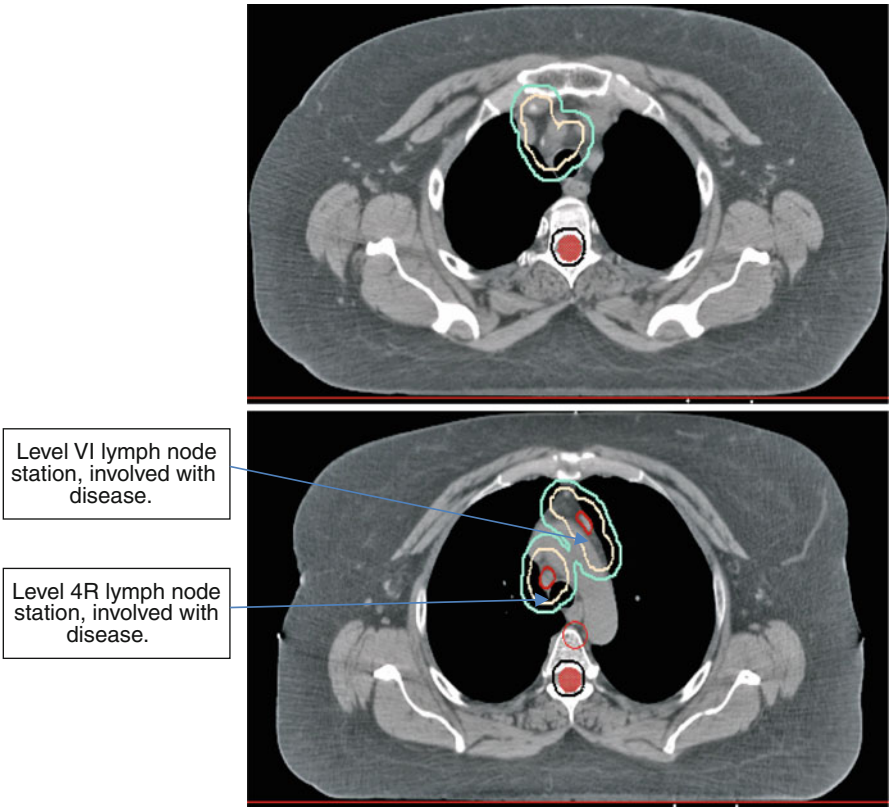
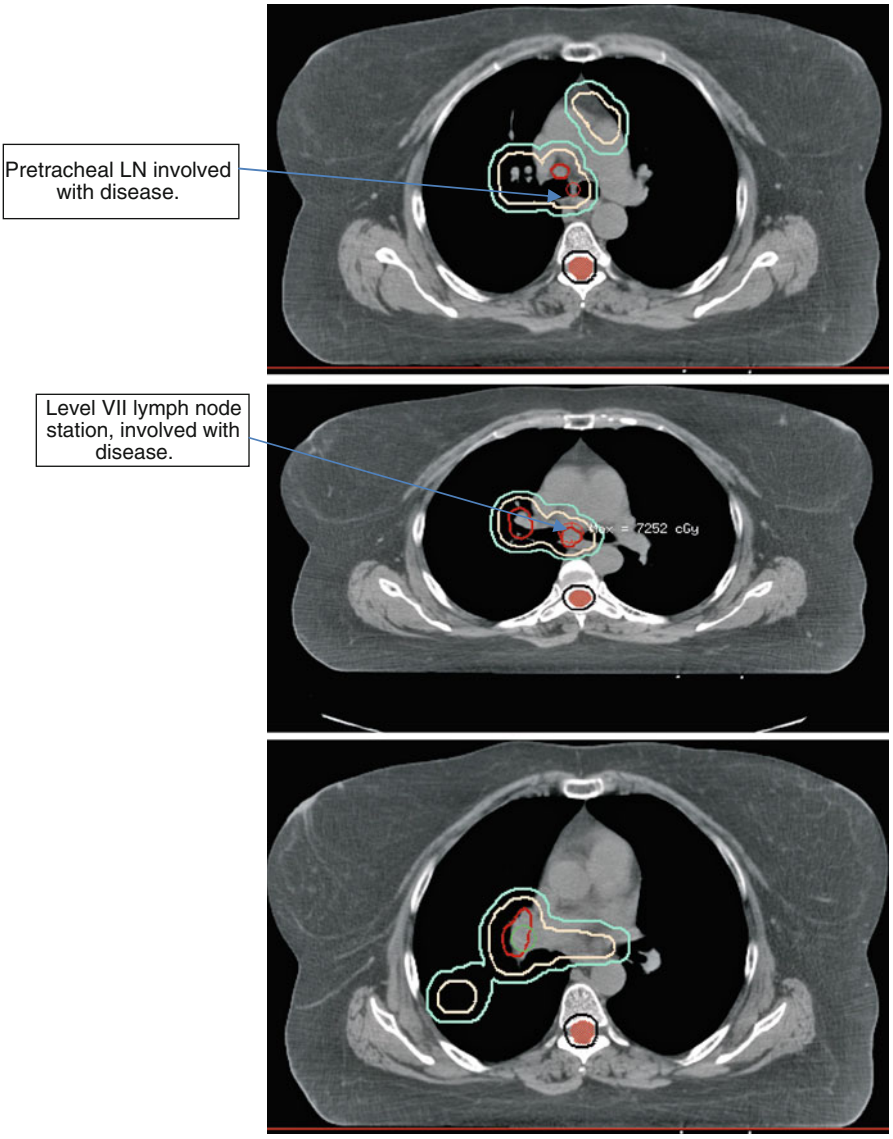


Fig. 12.2 Stage IIIB NSCLC. The patient had a 4-cm right upper lobe tumor with right hilar and subcarinal lymphadenopathy. Lung windows on CT scan are utilized to delineate the primary tumor and hilar region, and abdominal windows can best elucidate the mediastinal nodal stations. *Red* GTV, *gold* CTV, *turquoise* PTV



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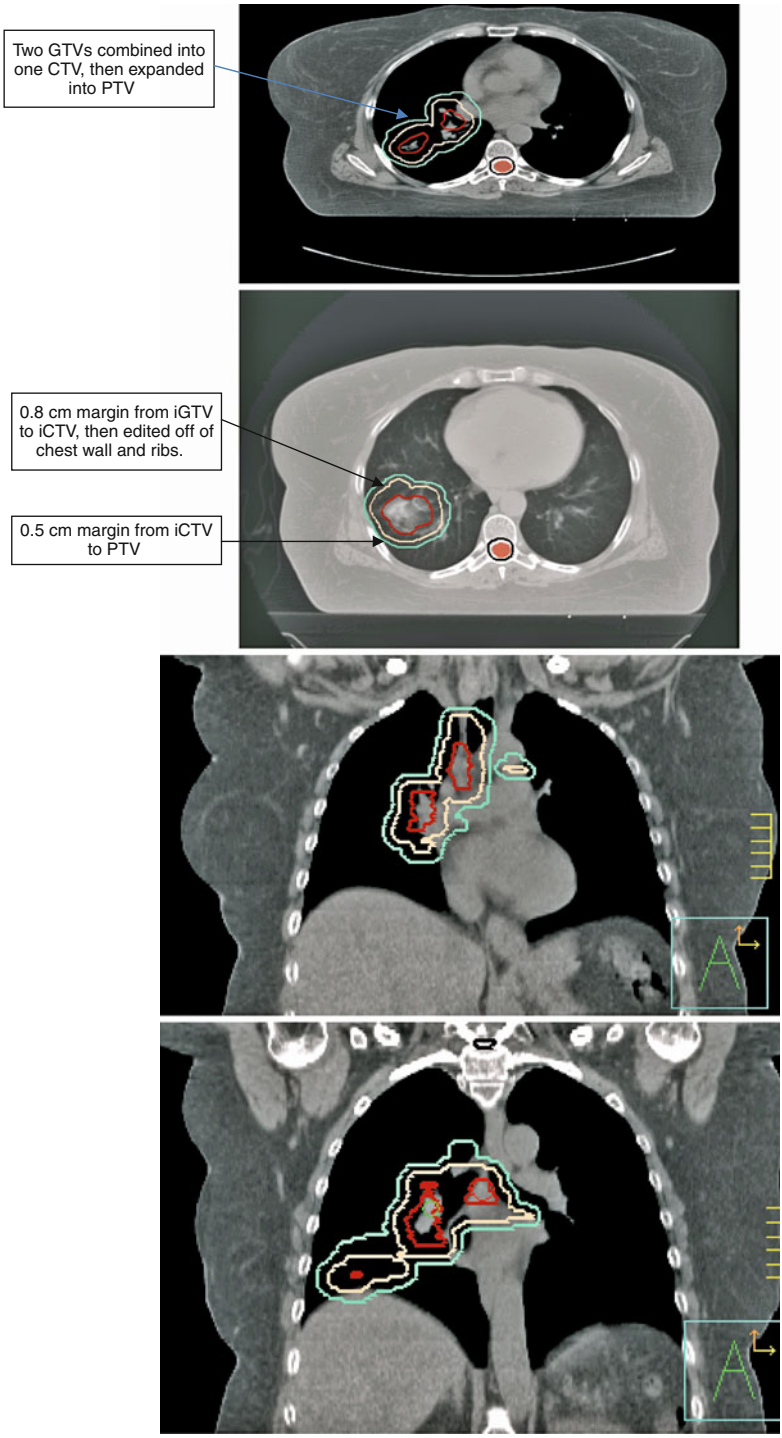

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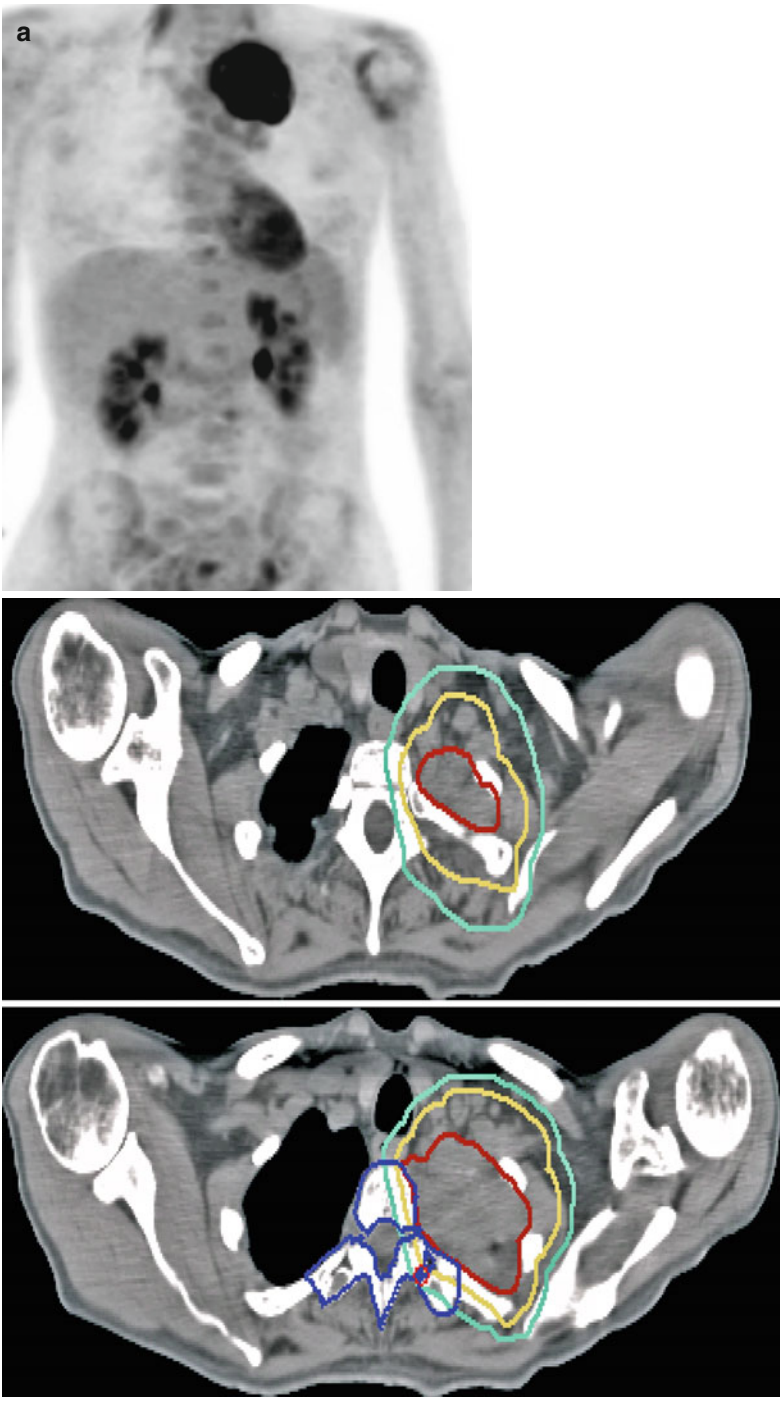
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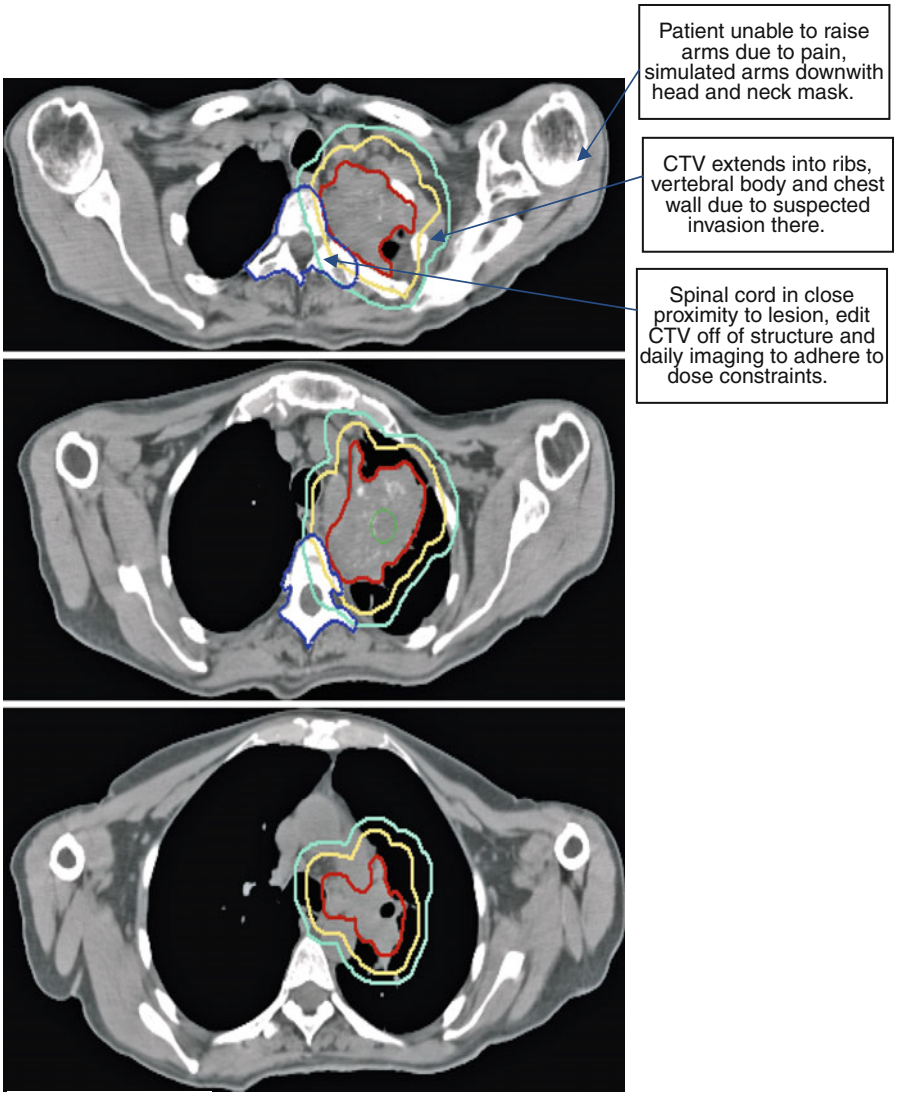


Fig. 12.3 (continued)

Fig. 12.3 Superior sulcus tumor. Stage T4NX SCC of the LUL, with suspected invasion into vertebral body and chest wall and contiguous with conglomerate lymphadenopathy. The patient received 1.2 Gy × 58 fractions twice daily (BID) = 69.6 Gy to the involved regions with concurrent chemotherapy. *Red* GTV, *Yellow* CTV, *Green* PTV

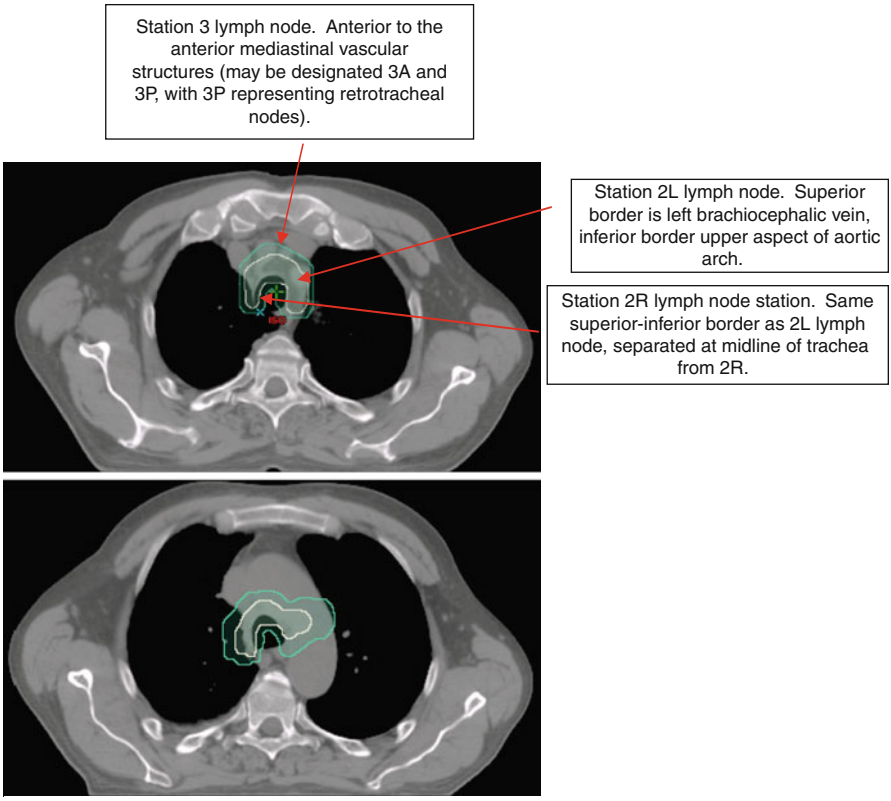
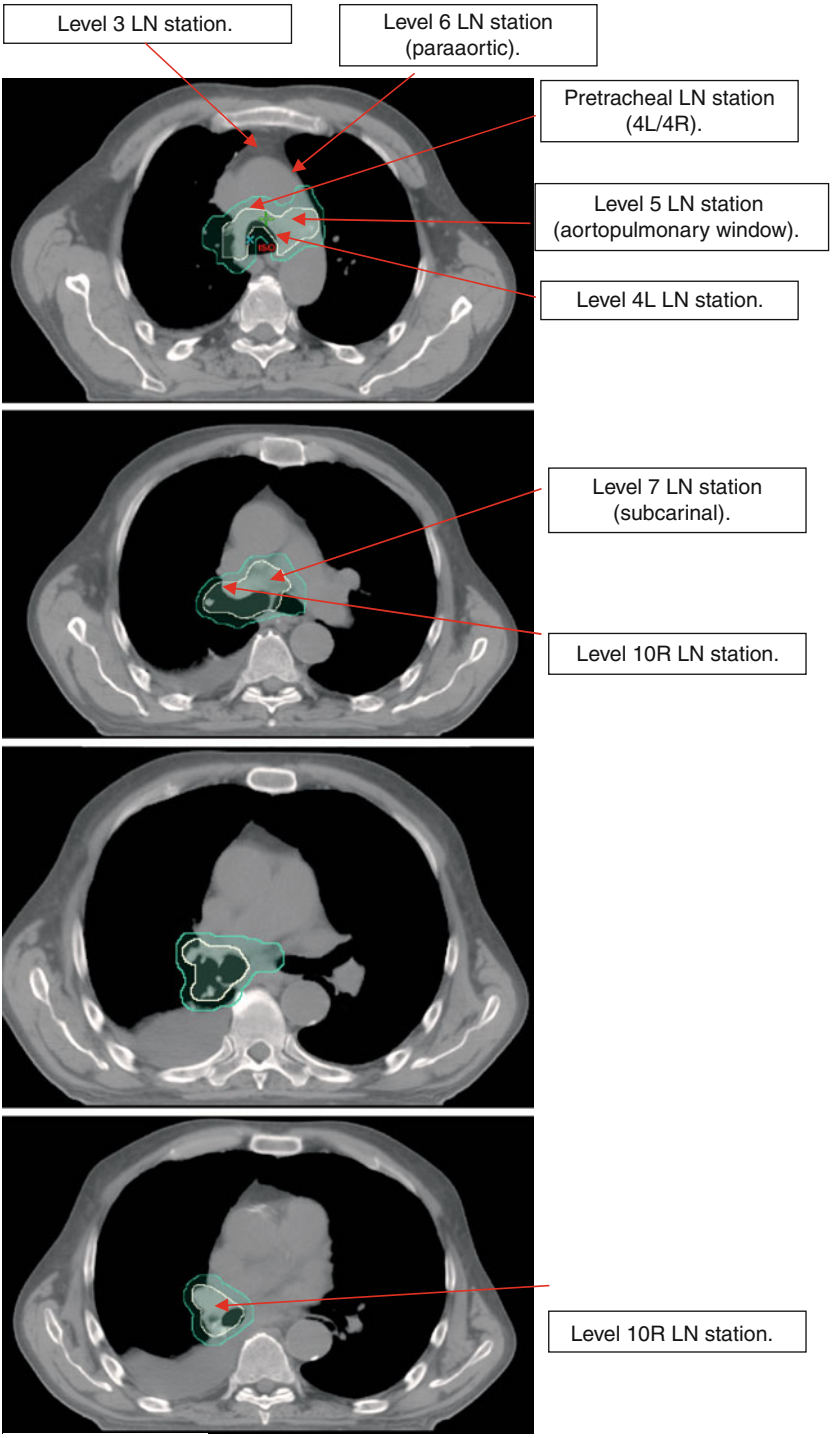


Fig. 12.4 Postoperative radiation for NSCLC, case #1. The patient had a 3-cm RUL tumor and received neoadjuvant chemotherapy. Pathologic findings from surgery included negative margins, but levels 10R, 4R, and 4L were positive for malignancy. The case below represents an extensive postoperative field in which the bilateral mediastinum and ipsilateral hilum are covered. This includes levels 2R, 2L, 4R, 4L, 5, 7, and the right hilum. The prescription dose was 2 Gy × 25 fractions = 50 Gy. *Gold* CTV, *turquoise* PTV



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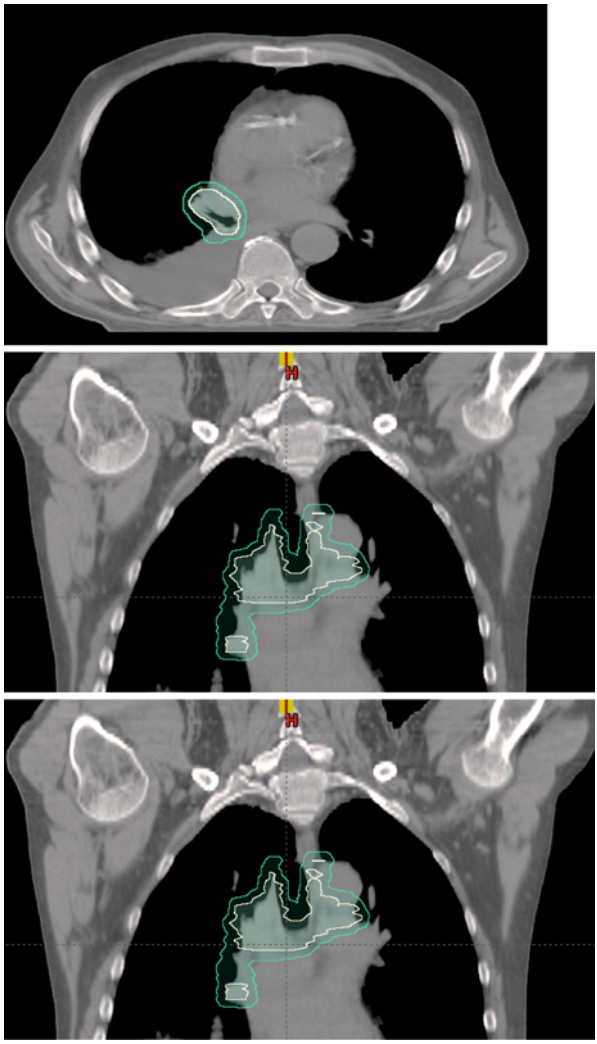
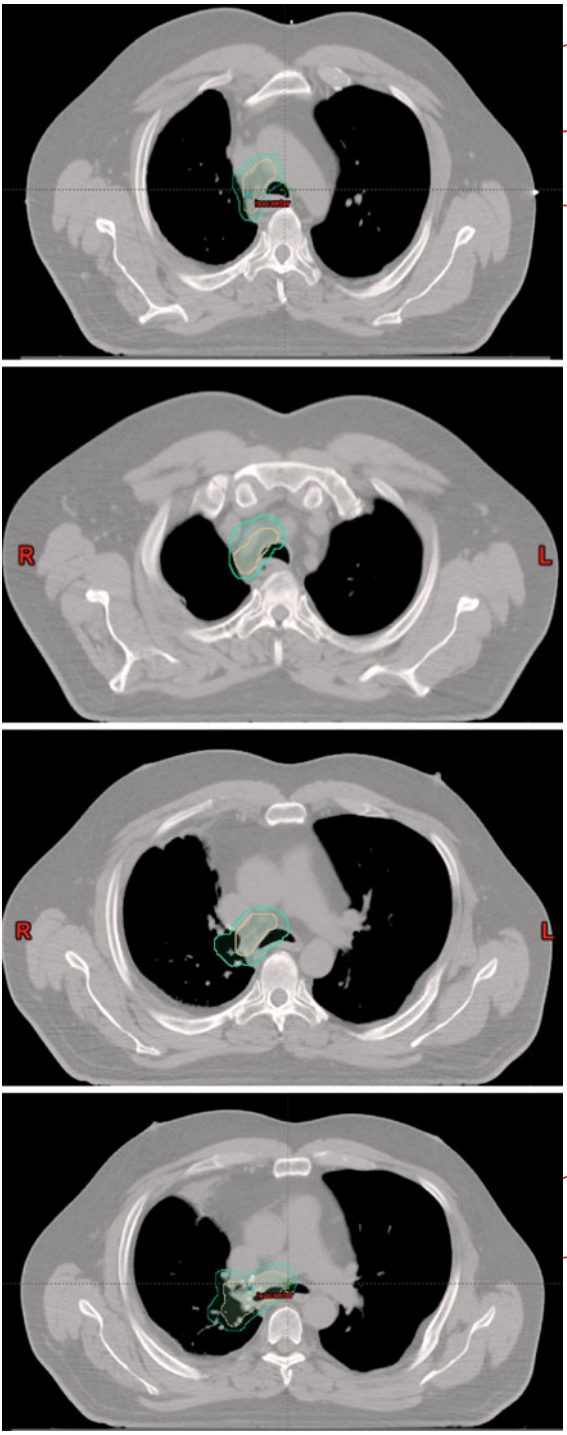


Fig. 12.5 Postoperative radiation for NSCLC, case #2. The patient had a 2.5-cm RUL tumor with levels 4R and 10R positive for malignancy on resection. The patient was treated with a limited postoperative field, covering 2R, 4R, 10R, and 11R. The prescription dose was 2 Gy × 25 fractions = 25 Gy. Please note the small right-sided pleural effusion, which was postoperative (benign)



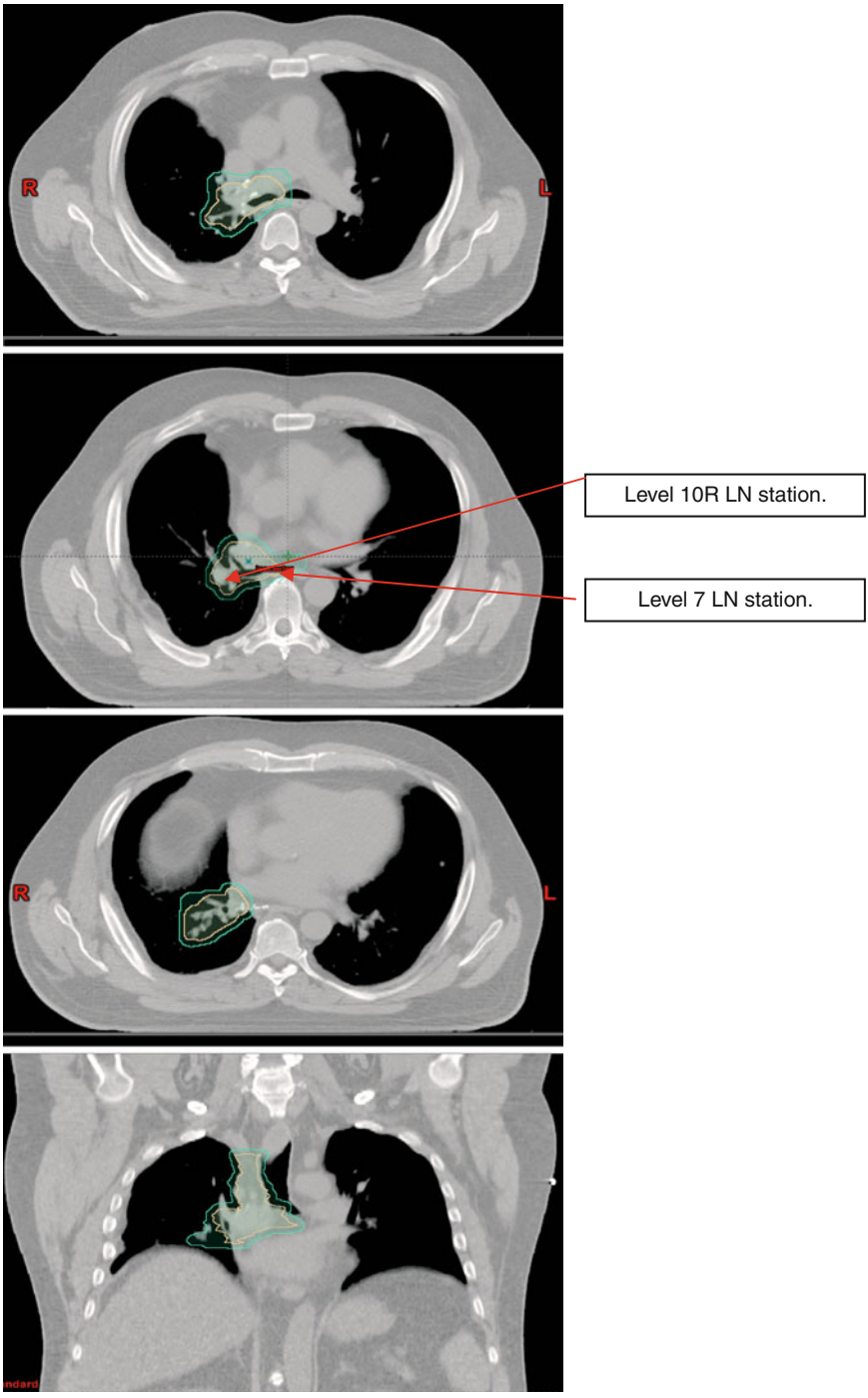
Level 3A LN station.

Level 6 LN station.

Level 4R LN station.

Level 10R LN station.

Level 7 LN station.



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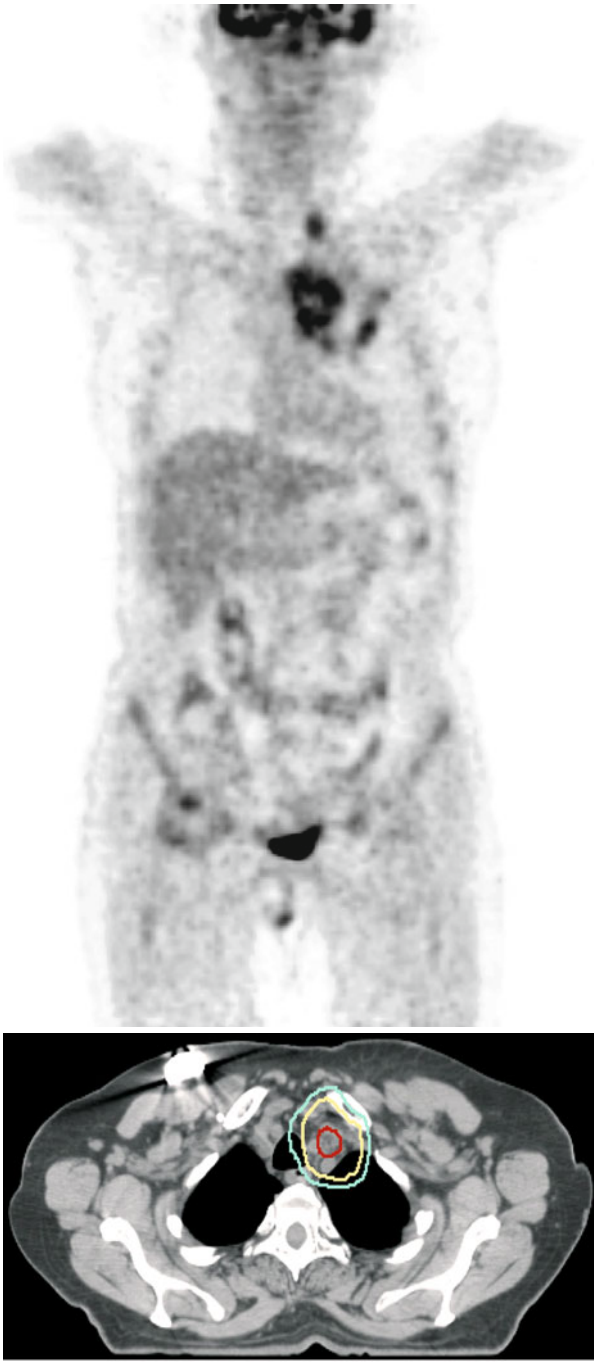
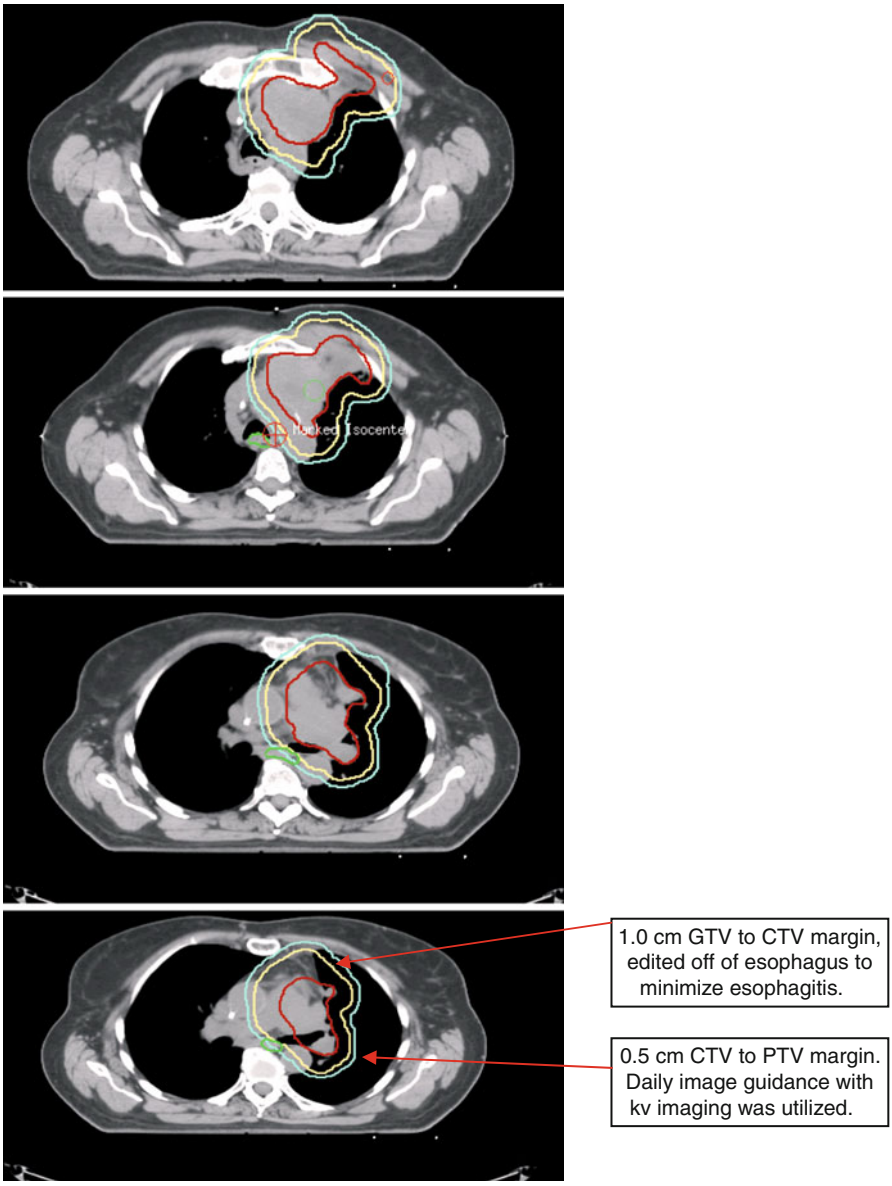


Fig. 12.6 Small cell lung cancer. The patient was found to have limited stage SCLC, with involvement of the anterior mediastinum and contiguous involvement of the left hilum and para-aortic lymph node stations. As is the case with NSCLC, an involved nodal treatment field was used, with coverage of the appropriate mediastinal and hilar regions. The prescription dose was 1.5 Gy × 30 fractions BID = 45 Gy. *Red* GTV, *yellow* CTV, *turquoise* PTV, *green* esophagus



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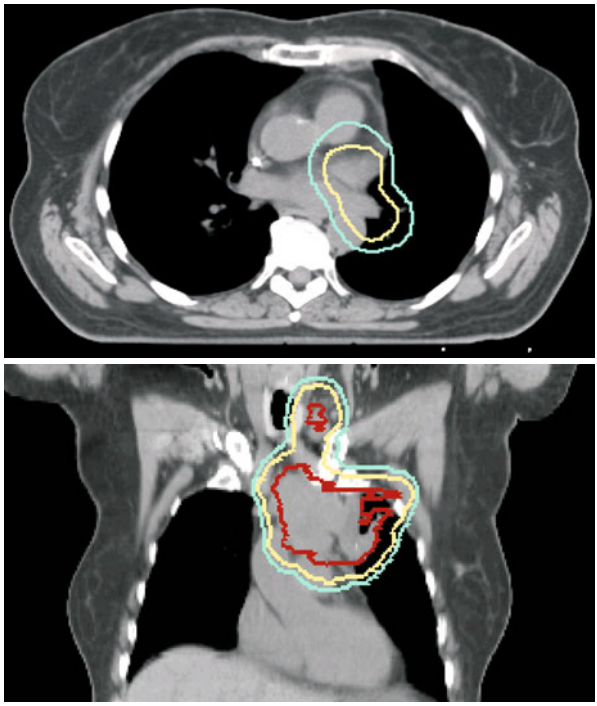

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Esophagus Cancer

13

Daniel R. Gomez, Steven H. Lin, Stephen Bilton, and Zhongxing Liao

General Principles of Planning and Target Delineation

- Computed tomography (CT)-based planning utilizing conformal techniques is the standard of care for esophagus cancer. Three-dimensional conformal radiation therapy (3D-CRT) and intensity-modulated radiation therapy (IMRT) both involve the utilization of a number of beam angles and the generation of a dose-volume histogram. It is essential in this setting to accurately delineate both critical normal structures and target volumes. In addition, it is necessary to have an understanding of mediastinal anatomy, including of the lungs, heart, spinal cord, brachial plexus, normal esophagus, and heart. These have been delineated and can be referenced in various atlases [1].
- *Simulation*. Patients should ideally be simulated with their arms above their head to maximize the number of beam arrangements that can be used. Four dimensional (4D) scanning can be considered at simulation. If a 4D study is not available, then the following measures can be taken to estimate internal motion of intrathoracic structures: (1) simulation with a slow helical CT scan, or (2) acquisition of CT images at maximal inspiration and expiration, with the difference being the total extent of motion of the target and critical structures. Patients with tumors involving the distal esophagus should be advised to be nil per os (NPO) for at least 3–4 h prior to simulation and with each treatment so as to limit variations in gastric bowel gas that may affect dose distribution on a day-to-day basis. If IMRT is being utilized, intravenous contrast can be considered at the time of simulation to better delineate nodal fields.

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- For the purposes of contouring, esophageal malignancies can be divided anatomically into two regions: upper esophagus tumors (including malignancies of the cervical esophagus) or lower esophagus tumors (including tumors of the gastroesophageal [GE] junction). Tumors that originate in the lower esophagus and extend to the upper esophagus can follow the contouring guidelines of both subsets.
- In all esophageal malignancies, we recommend contouring of the entire esophagus and lung for proper DVH analysis. In upper esophagus tumors, we recommend contouring of the brachial plexus and larynx. In lower esophagus tumors, the heart, liver, and kidneys should be delineated.
- The following target structure should be delineated: gross tumor volume (GTV), clinical target volume (CTV), internal target volume (ITV), and planning target volume (PTV).
- Treating physicians should utilize the following information to delineate active disease: physical examination, CT scan with contrast, positron emission tomography (PET), and evaluation of esophageal invasion and lymph nodes with an upper endoscopy and endoscopic ultrasound. The endoscopic ultrasound can be used to better classify small intrathoracic lymph nodes that are difficult to classify with CT or PET scan.
- Standard GTV to CTV expansions are 3–5 cm in the superior-inferior direction and 1 cm laterally and anteroposteriorly. Note that larger margins are utilized in the superior-inferior direction to account for submucosal spread, which can be significant, as well as the possible presence of skip lesions. For involved lymph nodes, a GTV to CTV margin of 0.5–1.0 cm can be utilized. These margins can be adjusted based on the use of motion assessment and the treating physician's confidence in knowing the extent of disease.
- For patients with a significant proportion of tumor involving the gastric cardia or the stomach, many institutions would consider these tumors of gastric origin rather than of esophageal origin. Based on contouring guidelines of gastric cancers (please see gastric cancer chapter for details), consideration should be made for diagnostic laparoscopy and J-tube placement, and preoperative chemoradiation [2] or postoperative chemoradiation [3] can be considered. The volume for coverage should be nodal risk regions, such as periesophageal, perigastric, splenic hilum, left gastric, porta hepatis, celiac, and SMA nodal regions. Patients should obtain a renal perfusion scan to assess for safe treatment delivery (Table 13.1, Figs. 13.1 and 13.2).

Table 13.1 Summary of recommendations for contouring esophagus tumors

Tumor location	Definition	GTV to CTV margin	CTV to PTV margin[a]	Elective nodal coverage	Dose[b]
Upper esophagus	Above carina	3–5 cm longitudinally, 1 cm axially	No IGRT or motion assessment – 1.0–1.5 cm IGRT or motion assessment – 0.5–1.0 cm IGRT and motion assessment – 0.5 cm	Periesophageal, supraclavicular	50.4–70 Gy in 1.8–2.0 Gy per fraction
Lower esophagus	Below carina	Same as upper esophagus	Same as upper esophagus	Periesophageal, celiac Based on extension into stomach, consider perigastric, splenic hilum, left gastric, porta hepatis, SMA nodal regions	41.4–50.4 Gy in 28 fractions[a]

[a]Clinical target volume (or ITV) to PTV margins are as follows: 1.0–1.5 cm if there is no assessment of management for internal motion or daily image-guided radiation therapy (IGRT), such as kV imaging; 0.5–1.0 cm for either 4D CT planning or IGRT, but not both; and 0.5 cm for 4D CT planning and daily kV imaging

[b]Based on the dose escalation trial INT0123 that did not demonstrate an advantage with a dose of 65 Gy [4]

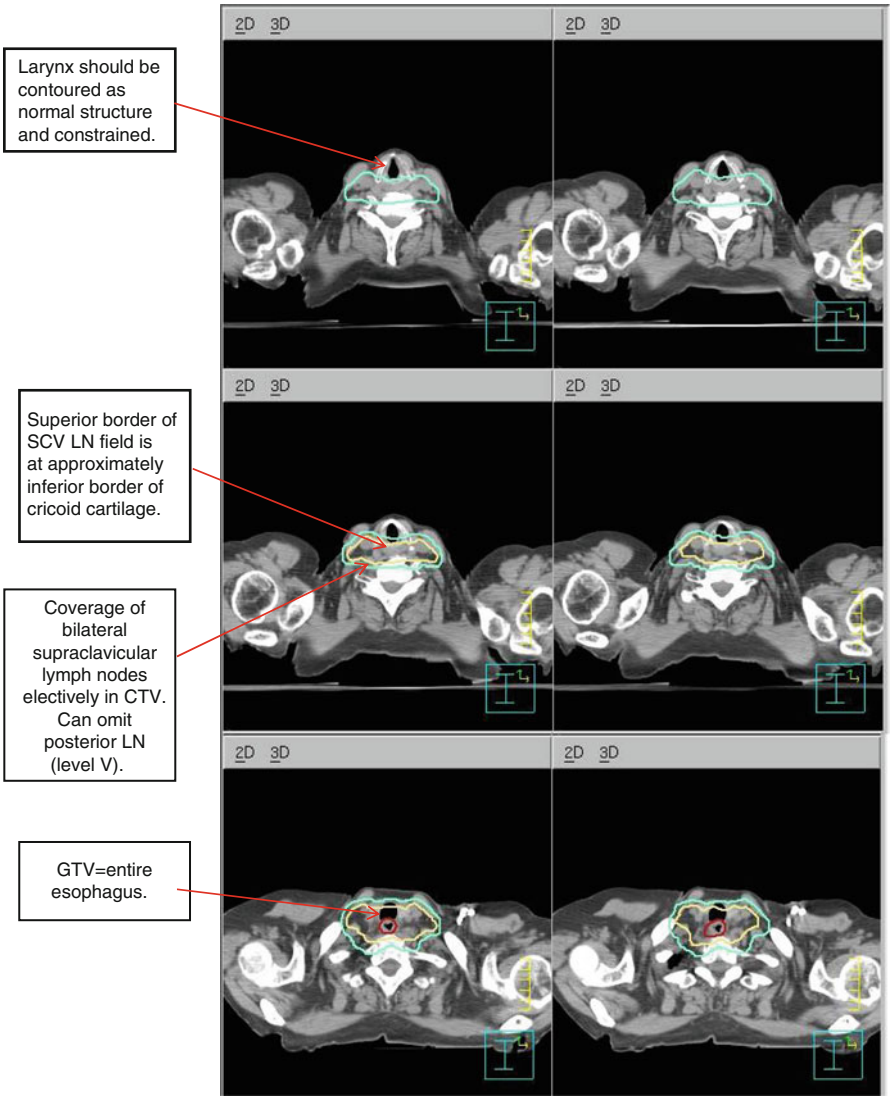

Fig. 13.1 History of stage uT3N0 squamous cell carcinoma of the proximal esophagus. The patient was treated with a dose of 54 Gy in 30 fractions utilizing intensity-modulated radiation therapy. The tumor was located at 15–19 cm from the incisors and encompassed 40 % of the esophageal circumference. *Red* GTV, *yellow* CTV, *turquoise* PTV

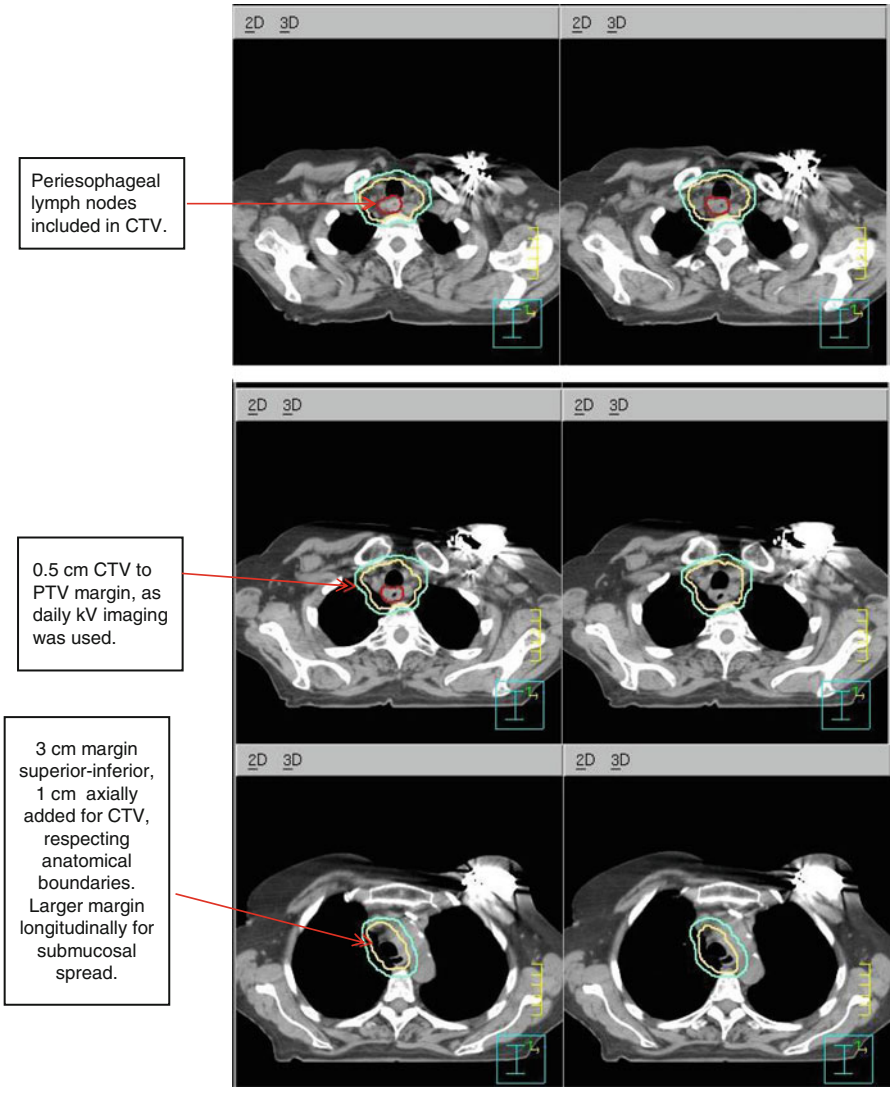

Fig. 13.1 (continued)

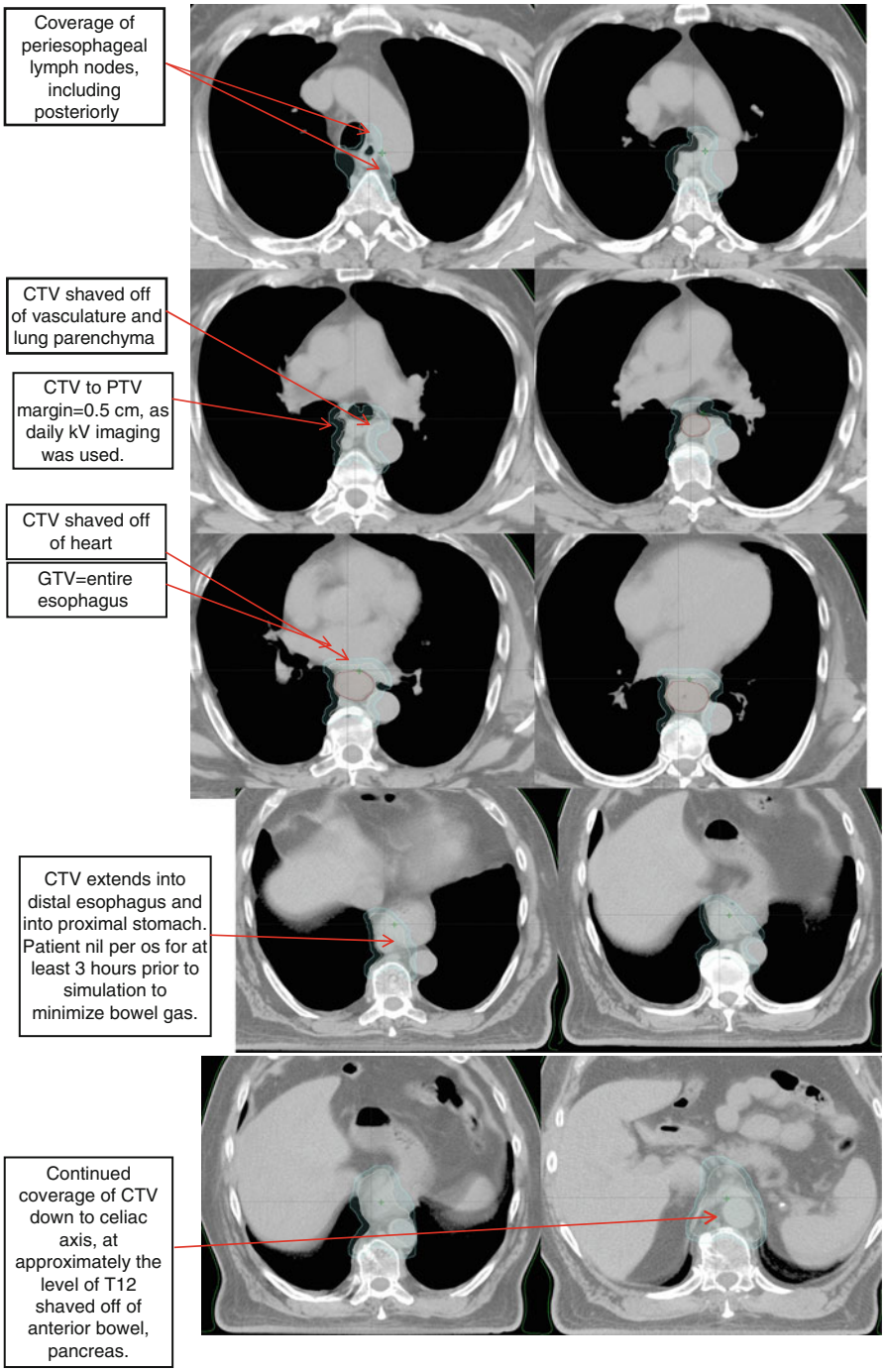

Fig. 13.2 Distal esophagus tumor. The patient had a history of uT3N0M0 adenocarcinoma of the distal esophagus, with a tumor located from 29 to 35 cm (GEJ at 38 cm). The coverage included the periesophageal lymph nodes, proximal portion of the stomach near the GEJ, and the celiac lymph nodes. *Red* GTV, *yellow* CTV, *turquoise* PTV

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Gastric Cancer

14

Jeremy Tey and Jiade J. Lu

General Principles of Planning and Target Delineation for Adjuvant Radiation for Adenocarcinomas of the Gastroesophageal Junction and the Stomach

- Prior to radiotherapy planning, it is imperative to review surgical and pathology reports and discuss with the surgeon to identify the areas considered to be the highest risk for recurrence; type of operation, i.e., total vs. partial gastrectomy, needs to be noted.
- Radiotherapy planning CT scans of 3–5 mm thickness should be obtained with patient in the supine position with arms overhead, from top of diaphragm (for stomach) or carina (for tumor of GE junction or cardia) to the bottom of L4. Patients should be fasted for 2–3 h.
- Intravenous contrast is preferred to demonstrate blood vessels and guide clinical target volume (CTV) delineation, particularly for lymph nodes; preoperative CT scans should be used to aid identification of preoperative tumor volume and nodal groups to be treated (Tables 14.1 and 14.2).
- CTV for adjuvant radiation therapy for gastric cancer depends on the position of the primary disease as well as the status of lymph node metastasis. Suggested target volumes for CTV coverage depending on subsite are detailed in Tables 14.4–14.6, Figs. 14.2–14.5.

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Table 14.1 Target volume definition and description

Target volumes	Definition and description
GTV	Gross residual disease defined by CT imaging and surgical findings
PTV (residual disease)	GTV/positive margins + 1.5 cm. Cone down boost after 45 Gy to a total dose of 50.4–54 Gy in 1.8 Gy/fraction
CTV_{45}	Coverage of nodal groups according to subsite (see Table 14.3). Also includes remnant stomach, anastomosis (gastrojejunal, esophagojejunal), duodenal stump
PTV_{45}	CTV_{45} + 1 cm margin. A larger margin may be required for organ motion and setup uncertainties

Table 14.2 General considerations for clinical target volume

Target volumes	Definition and description
Duodenal stump	Should preferably be covered in patients who have had a partial gastrectomy for distal/antral tumors
	Should not be covered in patients with proximal/cardia tumors who have had a total gastrectomy
Anastomosis	Gastrojejunal anastomosis (partial gastrectomy) and esophagojejunal anastomosis (total gastrectomy) should be treated
Para-aortic nodes	Should be included for the entire length of the CTV
Paraesophageal nodes	4 cm margin of the esophagus should be included in the clinical target volume for tumors of the gastroesophageal junction

- Three areas must be identified as CTV for adjuvant radiotherapy: the gastric tumor bed, the anastomosis or stumps, and the regional lymphatics.
- In addition, the hepatogastric ligament should preferably be treated in all cases as it is at high risk of recurrence. It represents the part of the lesser omentum that runs between the lesser curvature of the stomach and liver and contains the left and right gastric nodes that are not always completely removed at surgery.
- The benefits of intensity-modulated radiotherapy (IMRT) have been suggested by many publications. If used, tumor bed and subclinical target volumes including lymphatic draining regions should be delineated.
- Planning Target Volume (PTV): CTV+ margin considering organ motion and setup uncertainties. A minimum expansion of 1 cm is suggested.
- A total dose of 45 Gy in 25 fractions is recommended for adjuvant radiotherapy with concurrent chemotherapy, using high-energy (≥6MV) photons. Boosts to 50.4–54 Gy for positive margins or residual disease should be given, if doses to surrounding critical organs are within tolerance.

Lymph Nodes Groups Surrounding the Stomach Fig. 14.1, Table 14.3

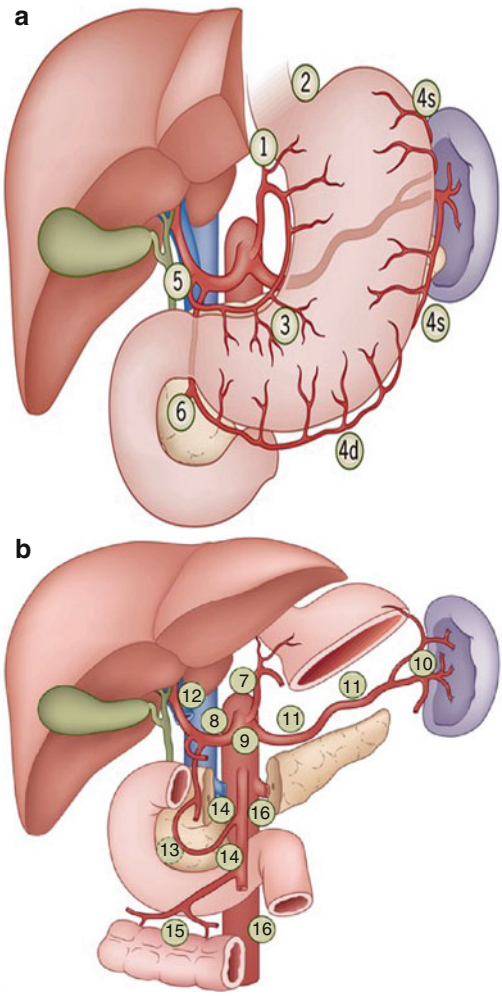

Fig. 14.1 (**a**) Lymph nodes groups 1-6, (**b**) Lymph nodes groups 7-16 surrounding the stomach

Table 14.3 Lymph node stations commonly involved in gastric cancer

1. Right cardial nodes	9. Nodes along the celiac axis
2. Left cardial nodes	10. Nodes at the splenic hilus
3. Nodes along the lesser curvature	11. Nodes along the splenic artery
4. Nodes along the greater curvature	12. Nodes in the hepatoduodenal ligament
5. Suprapyloric nodes	13. Nodes at the posterior aspect of pancreatic head
6. Infrapyloric nodes	14. Nodes at the root of the mesenterium
7. Nodes along left gastric artery	15. Nodes in the mesocolon of the transverse colon
8. Nodes along the common hepatic artery	16. Para-aortic lymph nodes

Source: Figure and table adapted from Hartgrink and Van De Velde [1]. Used with permission from Wiley Inc. Japanese Research Society for the Study of Gastric Cancer, JRSGC

Nodal Distribution and Clinical Target Volumes for Adjuvant Radiotherapy for Gastric Cancer

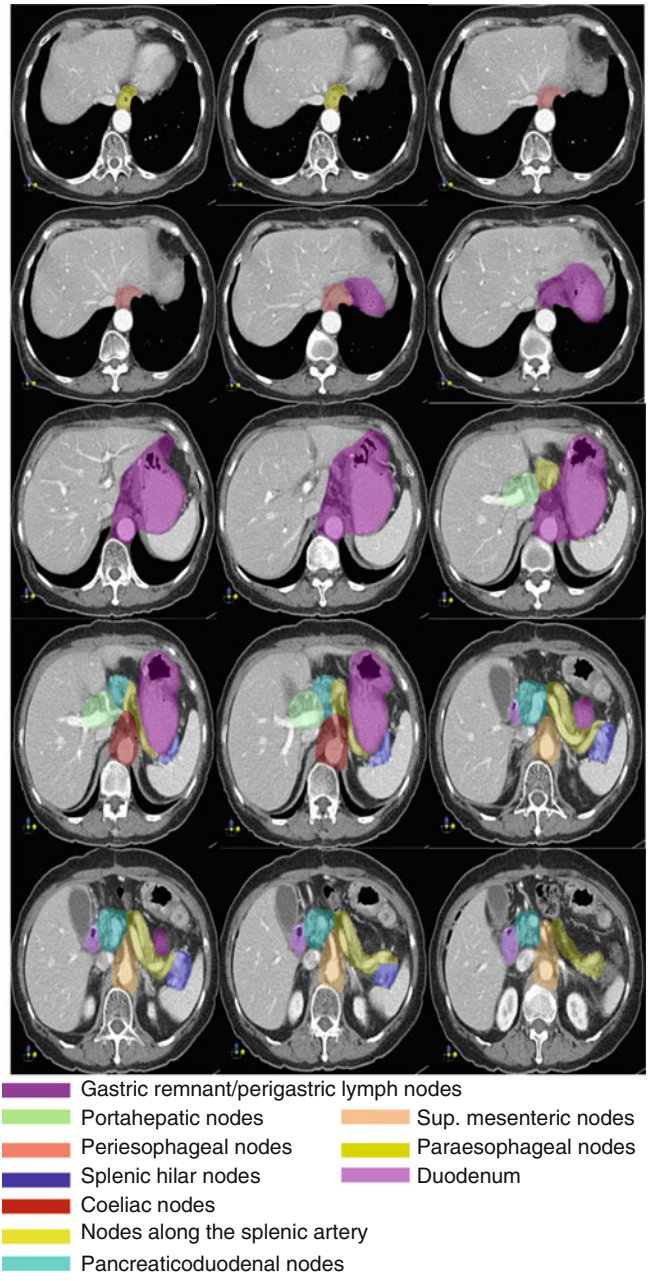

Fig. 14.2 Nodal distribution and clinical target volumes for adjuvant radiotherapy for gastric cancer

Table 14.4 Recommended nodal coverage depending on site of primary tumor in stomach: esophagogastric junction

Origin and stage (AJCC 7th edition)	Remaining stomach	Tumor bed volumes[a]	Nodal volume
EG junction	If allows exclusion of 2/3 right kidney	T stage dependent	N stage dependent
T3N0, invasion of subserosa, especially posterior wall	Variable, dependent on surgical pathological findings[b]	Medial left hemidiaphragm; adjacent body of pancreas	None or PG, PEN[c]
T4aN0	Variable, dependent on surgical pathological findings[b]	Medial left hemidiaphragm; adjacent body of pancreas	None or PG, PEN, MN, CN[c]
T4bN0	Preferable but dependent on surgical pathological findings[b]	As for T4aN0 plus sites of adherence with 3–5 cm margin	Nodes related to sites of adherence ±PG, PEN, MN, CN
T1–3 N+	Preferable	Not indicated for T1–2, as above for T3	PEN, MN, prox PG, CN
T4a/bN+	Preferable	As for T4a/bN0	As for T1–3 N+ and T4bN0

Modified from Gunderson and Tepper [2]

PG perigastric, *CN* celiac, *PEN* periesophageal, *MN* mediastinal

[a]Use preoperative imaging (CT, barium swallow), surgical clips, and postoperative imaging (CT, barium swallow)

[b]For tumors with >5-cm margins confirmed pathologically, treatment of residual stomach is optional, especially if this would result in substantial increase in normal tissue morbidity

[c]Optional node inclusion for T3–4a N0 lesions if adequate surgical node dissection (D2) and at least 10–15 nodes are examined pathologically

Clinical Target Volumes for a Patient with T1N1M0 Adenocarcinoma of the Gastric Cardia Post-total Gastrectomy

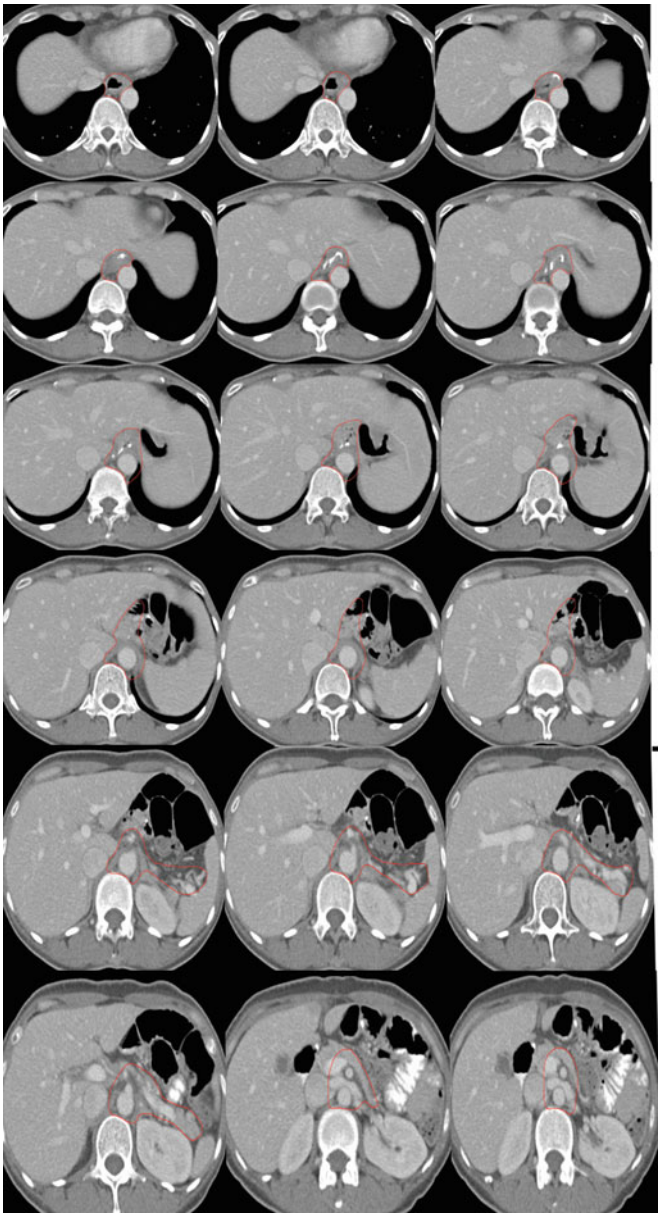

Fig. 14.3 Clinical target volumes for a patient with T1N1M0 adenocarcinoma of the gastric cardia post-total gastrectomy

Fig. 14.3 (continued)

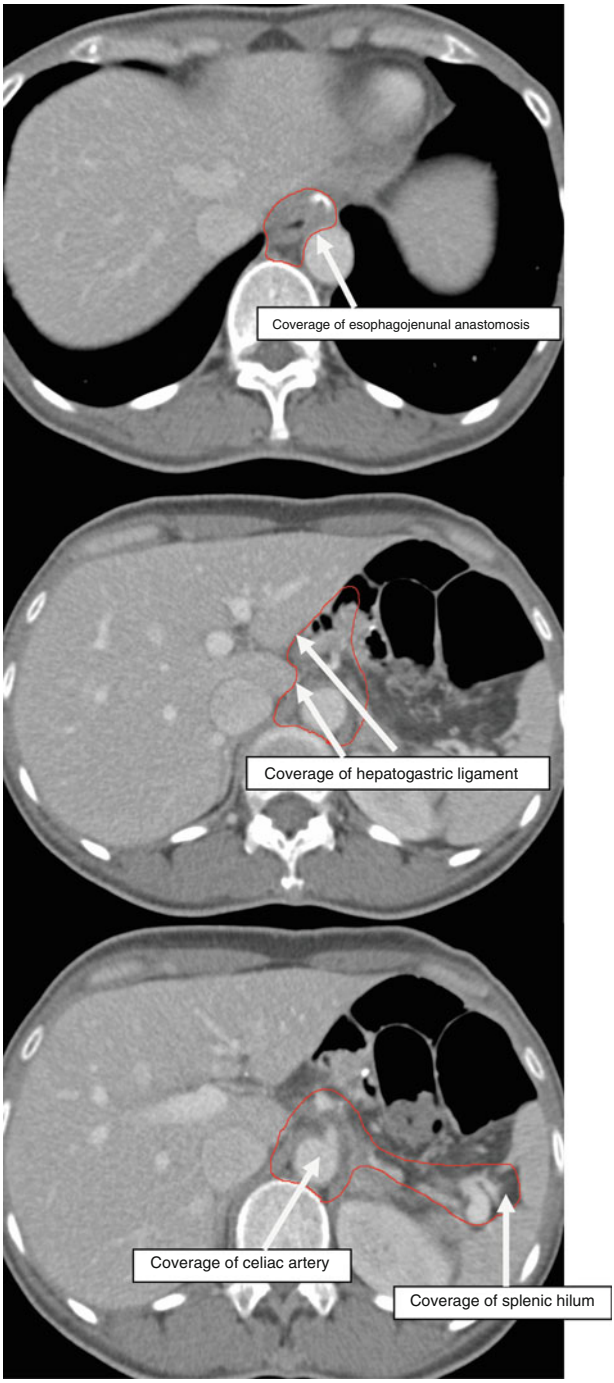

Table 14.5 Recommended nodal coverage depending on site of primary tumor in stomach: body/middle third of stomach

Site of primary and TN stage	Remaining stomach	Tumor bed volumes[a]	Nodal volume
Body/middle third of stomach	Yes, but spare 2/3 one kidney	T stage dependent	N stage dependent, spare 2/3 of one kidney
T3N0, especially posterior wall	Yes	Body of pancreas (±tail)	None or PG
			Optional: CN, SplN, SplNs, HNpd, PHN[b]
T4aN0	Yes	Body of pancreas (±tail)	None or perigastric
			Optional: CN, SplN, SplNs, HNpd, PHN[b]
T4bN0	Yes	As for T4aN0 plus sites of adherence with 3–5-cm margin	Nodes related to sites of adherence ±PG, SplNs, SplN, HNpd, CN, PHN
T1–3N+	Yes	Not indicated for T1–2, as above for T3	PG, CN, SplN, SplNs, HNpd, PHN
T4a/bN+	Yes	As for T4a/bN0	As for T1–3N+ and T4bN0

Modified from Gunderson and Tepper [2]

PG perigastric, *CN* celiac, *SplN* splenic, *SplNs* suprapancreatic, *PHN* porta hepatic, *HNpd* pancreaticoduodenal, *PEN* periesophageal, *MN* mediastinal

[a]Use preoperative imaging (CT, barium swallow), surgical clips, and postoperative imaging (CT, barium swallow)

[b]Optional node inclusion for T3–4a N0 lesions if adequate surgical node dissection (D2) and at least 10–15 nodes are examined pathologically

Clinical Target Volumes for a Patient with T3N3M0 Adenocarcinoma of the Gastric Body Post-distal Gastrectomy

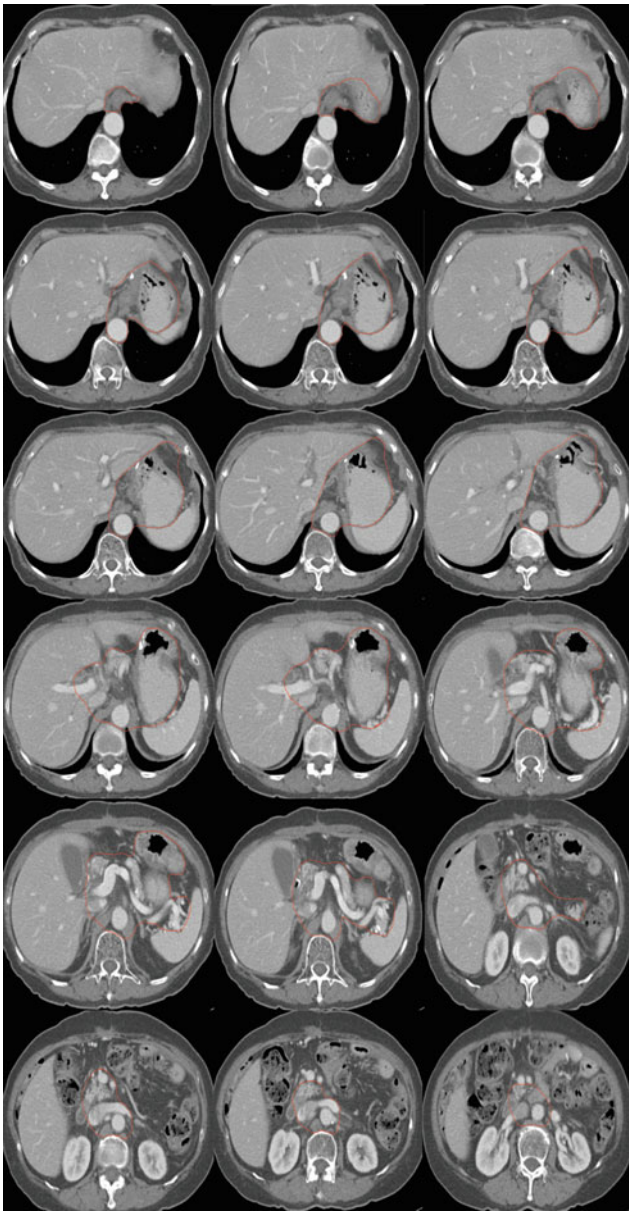

Fig. 14.4 Clinical target volumes for a patient with T3N3M0 adenocarcinoma of the gastric body post-distal gastrectomy

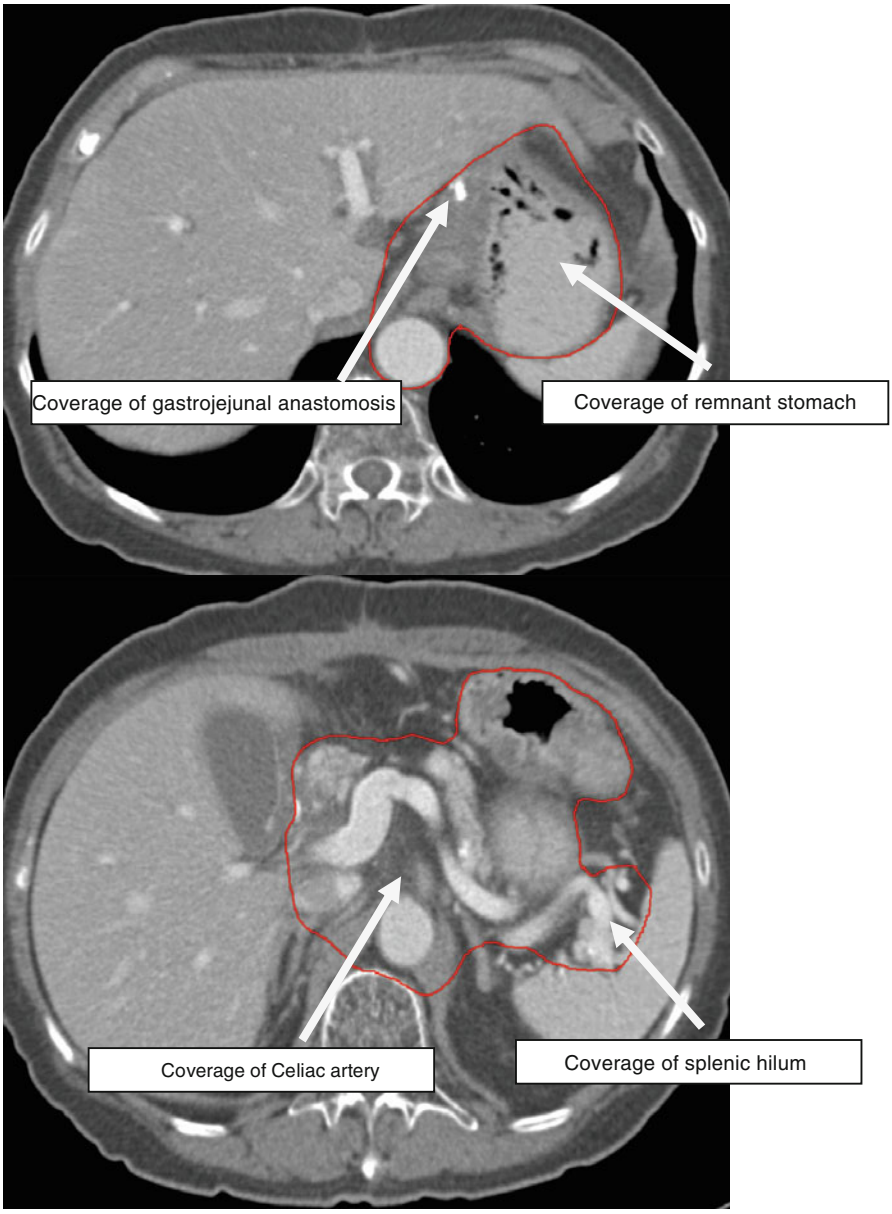

Fig. 14.4 (continued)

Table 14.6 Recommended nodal coverage depending on site of primary tumor in stomach: cardia/proximal third of stomach (*prox*) and antrum/pylorus/distal third of stomach (*distal*)

Origin and stage (AJCC 7th edition)	Remaining stomach	Tumor bed volumes[a]	Nodal volume
Cardia/prox third of stomach	Preferred, but spare 2/3 of one kidney (usually right)	T category dependent	N classification dependent
Antrum/distal third of stomach	Yes, but spare 2/3 of one kidney (usually left)		
T3N0,	Variable, dependent on surgical pathological findings[b]	*Prox:* medial left hemidiaphragm, adjacent body of pancreas (±tail)	*Prox:* none or PG[c]
		Distal: head of pancreas (±body), first and second part of duodenum	*Distal:* none or PG Optional: CN, SplNs, HNpd, PHN[c]
T4aN0	Variable, dependent on surgical pathological findings[b]	*Prox:* medial left hemidiaphragm, adjacent body of pancreas (±tail)	*Prox: n*one or PG Optional: PEN, MN, CN[c]
		Distal: head of pancreas (±body), first and second part of duodenum	*Distal*: none or PG Optional: CN, SplNs, HNpd, PHN[c]
T4bN0	Prox: variable, dependent on surgical pathological finding[b] Distal: preferable, dependent on surgical pathological finding[b]	As for T4aN0 plus sites of adherence with 3–5-cm margin	*Prox:* nodes related to sites of adherence ±PG,PEN, MN, CN *Distal:* nodes related to sites of adherence ±PG, SplNs, HNpd, CN, PHN
T1–3 N+	Preferable	Not indicated for T1–2, as above for T3	*Prox:* PG, CN, SplN, SplNs, ±PEN, MN, HNpd, PHN[d] *Distal:* PG, CN, HNpd, PHN, SplNs Optional: splenic hilum
T4a/bN+	Preferable	As for T4a/bN0	As for T1–3 N+ and T4bN0

Modified from Gunderson and Tepper [2]

PG perigastric, *CN* celiac, *SplN* splenic, *SplNs* suprapancreatic, *PHN* porta hepatic, *HNpd* pancreaticoduodenal, *PEN* periesophageal, *MN* mediastinal

[a]Use preoperative imaging (CT, barium swallow), surgical clips, and postoperative imaging (CT, barium swallow)

[b]For tumors with >5-cm margins confirmed pathologically, treatment of residual stomach is not necessary, especially if this would result in substantial increase in normal tissue morbidity

[c]Optional node inclusion for T3–4a N0 lesions if adequate surgical node dissection (D2) and at least 10–15 nodes are examined pathologically

[d]Pancreaticoduodenal and porta hepatis nodes are at low risk of nodal positivity is minimal (1–2 positive nodes with 10–15 examined), and this region does not need to be irradiated. Periesophageal and mediastinal nodes are at risk if there is esophageal extension

Clinical Target Volumes for a Patient with T2N1M0 Adenocarcinoma of the Antrum/Pylorus Post-distal Gastrectomy

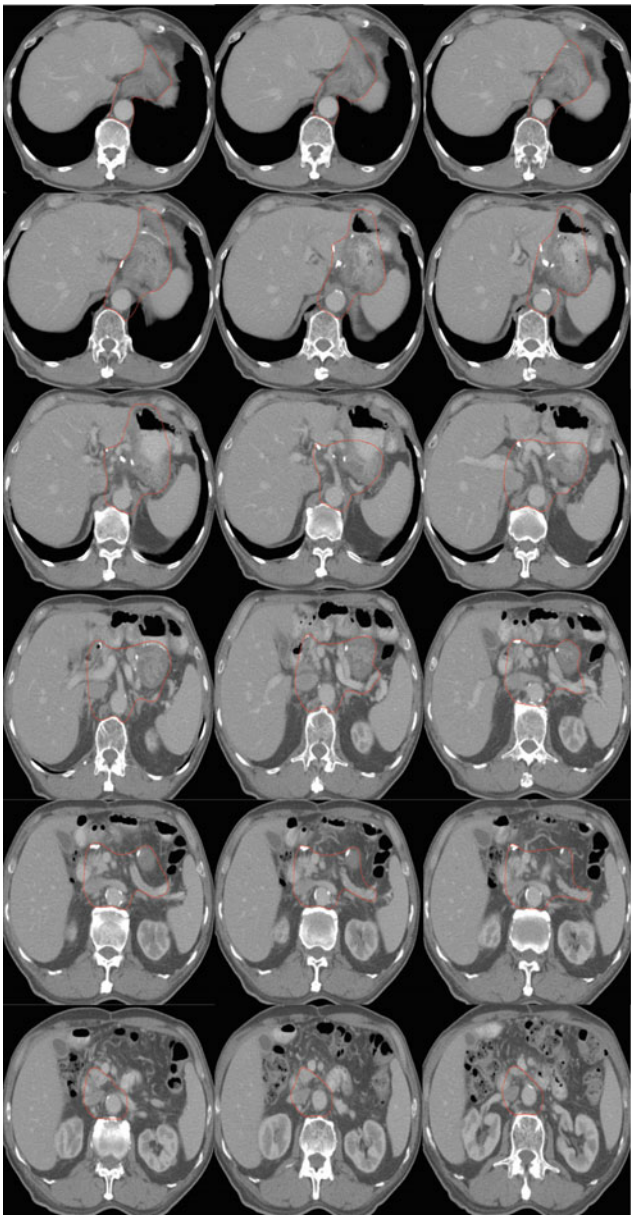

Fig. 14.5 Clinical target volumes for a patient with T2N1M0 adenocarcinoma of the antrum/pylorus post-distal gastrectomy

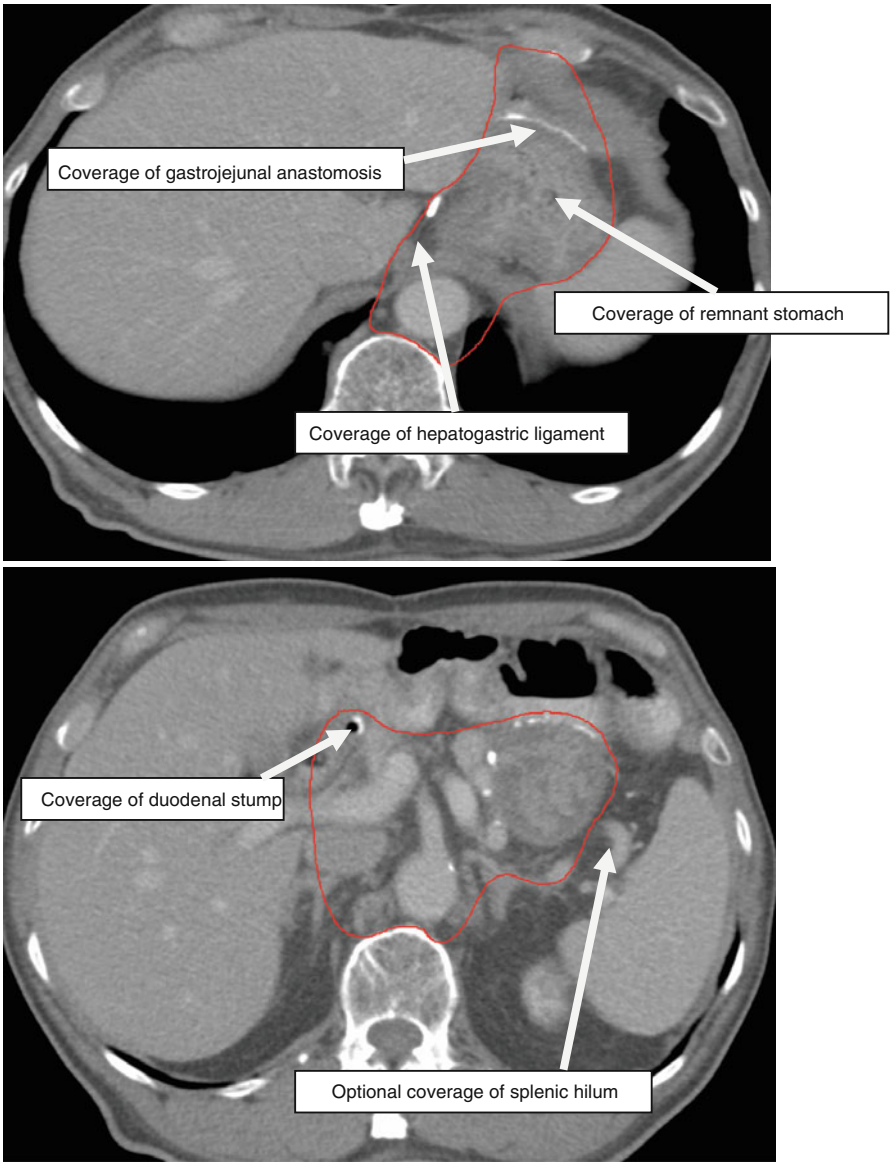

Fig. 14.5 (continued)

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Contouring Guidelines for Pancreatic Adenocarcinoma

15

Karyn A. Goodman and Michael R. Folkert

Unresectable Pancreatic Adenocarcinoma

General Principles of Planning and Target Delineation

- Intensity-modulated radiation therapy (IMRT) is becoming a standard technique for definitive or neoadjuvant radiation therapy for unresectable and borderline-resectable pancreatic adenocarcinoma.
- In addition to physical examination, adequate imaging studies should be obtained for diagnosis, staging, and planning. Unless contraindicated (renal disease/allergy), all patients should undergo a CT-angiogram (pancreas protocol) to fully identify the major vessels and involvement by tumor. Alternatively, MRI may be considered if an iodinated contrast allergy is present. PET/CT may be considered but its contribution to target delineation has not been fully characterized.
- Motion management is highly recommended due to the significant amount of motion of the pancreas. Fiducials should be placed prior to simulation to assist in motion management using percutaneous, intraoperative, or endoscopic techniques; motion management may be addressed using respiratory gating, breath-holding (ABC), respiratory tracking, or abdominal compression.
- CT simulation with IV contrast (unless contraindicated) should be performed to help guide the GTV target as well as lymph node coverage:
  - Arms above head in Alpha Cradle, oral and IV contrast (generally 100 cc Omnipaque), 4DCT pancreatic protocol with scan from carina to iliac crest.

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– If using respiratory gating, plan on end-expiration breath-hold scan and assess motion of implanted fiducials with 4DCT scan (Tables 15.1 and 15.2, Figs. 15.1 and 15.2).

Table 15.1 Target volumes for locally advanced or borderline resectable pancreatic cancer

Target volumes	Definition and description
GTV	Consists of the hypodense area corresponding to biopsy-proven disease in the pancreas and any positive lymph nodes visualized on diagnostic pancreatic protocol CT, arterial phase (contoured on expiration phase)
CTV	The CTV encompasses all relevant nodal regions including the porta hepatis, celiac/SMA, and PA/RP lymph nodes approximately from T11 to bottom of L2 (may adjust based on location of primary tumor) [2]; the superior-inferior extent is primarily determined by overlapping coverage of the appropriate nodal regions and tumor location.
	In general, the GTV is also expanded by 1 cm; this expansion is then added to the nodal CTV [1]
PTV5040	Expansion on the CTV by 5 mm (receives 5,040 cGy in 180 cGy fractions)
PTV5600	Expansion on the GTV by 3–5-mm margin, minimizing overlap with the duodenum (receives 5,600 cGy in 200 cGy fractions). Note that this is an integrated boost guideline based on Memorial Sloan-Kettering Cancer Center standard practice

CTV clinical target volume; *SMA* superior mesenteric artery; *PA* paraaortic; *RP* retroperitoneal; *GTV* gross tumor volume

Table 15.2 Normal tissue constraints

Organ	Dose constraint
Liver	Mean dose < 25 Gy, 70 % < 20 Gy
Kidney	2/3 < 18 Gy or 70 % < 15 Gy
Cord	dmax < 40 Gy if using respiratory gating; dmax <45Gy for non-gated treatments
Duodenum	50 % < 30 Gy; Dmax <102% of prescription dose
Heart	V20 < 30 %, V30 < 20 %, 70 % < 15 Gy

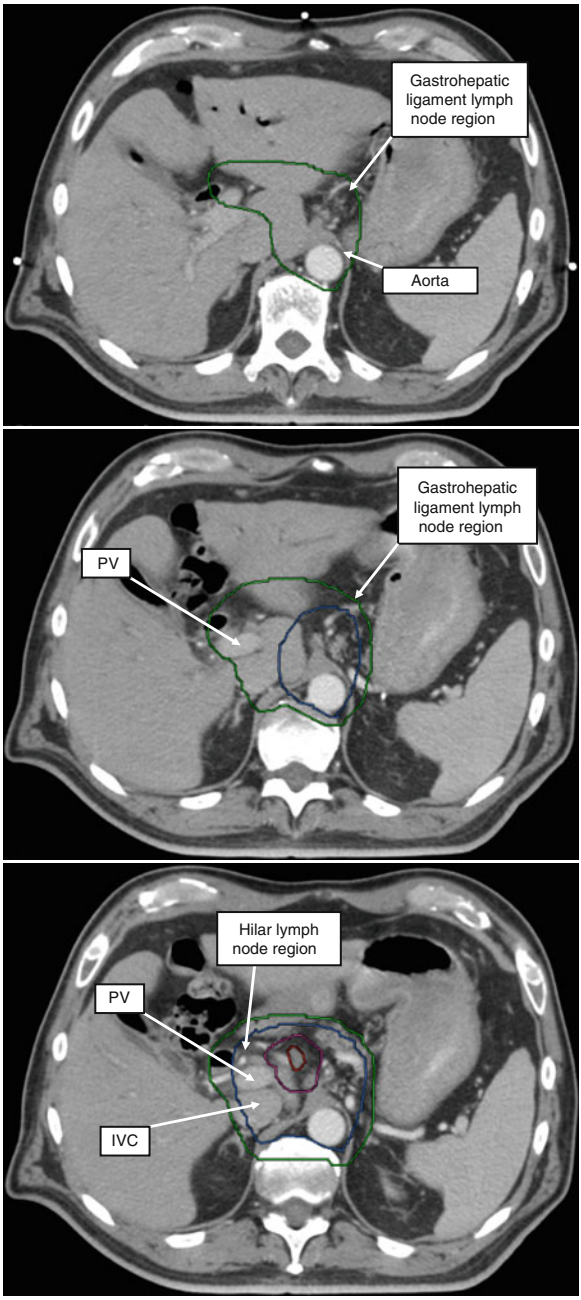


Fig. 15.1 A patient with T4N0 unresectable pancreatic adenocarcinoma with a 5-cm mass in the pancreatic head, extensive compression of the main portal vein, encasement of the common hepatic and gastroduodenal arteries, and abutment of the celiac, proper hepatic, and superior mesenteric artery. Patient was simulated with 4DCT, 2.5-mm slice thickness on each slice. GTV is in *red*, CTV is in *blue*, PTV5040 is in *green*, and PTV5600 is in *pink*. Please note that these are representative slices and not all slices are included. *PV* portal vein; *IVC* inferior vena cava; *SMV* superior mesenteric vein; *SMA* superior mesenteric artery; *GTV* gross tumor volume

Fig. 15.1 (continued)

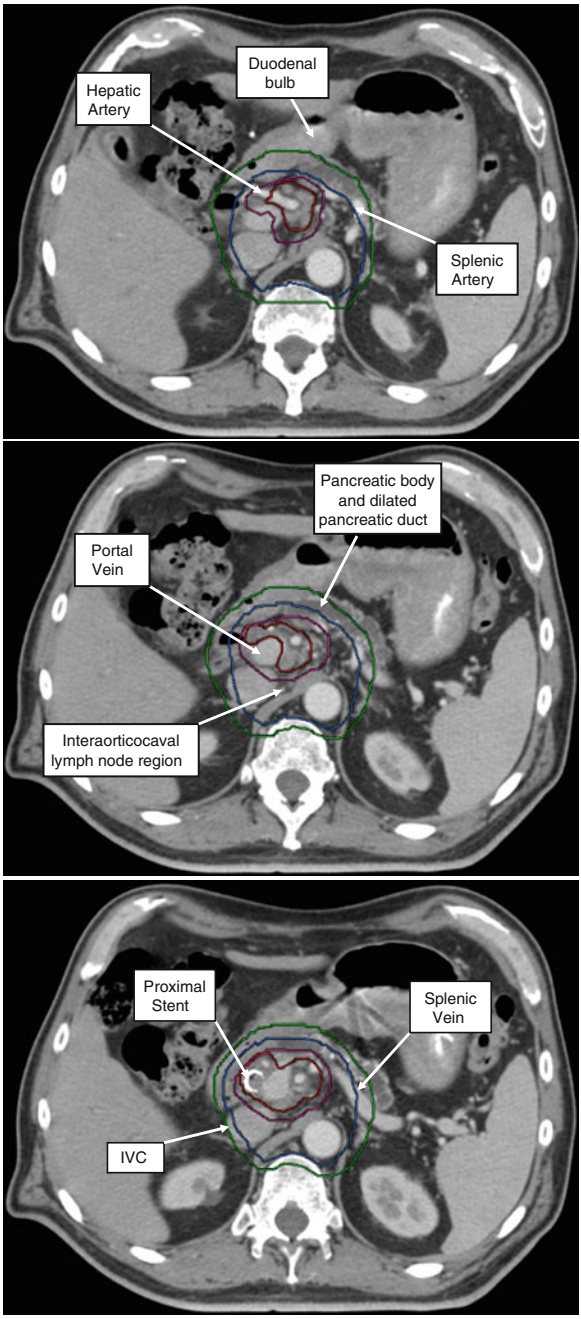


Fig. 15.1 (continued)

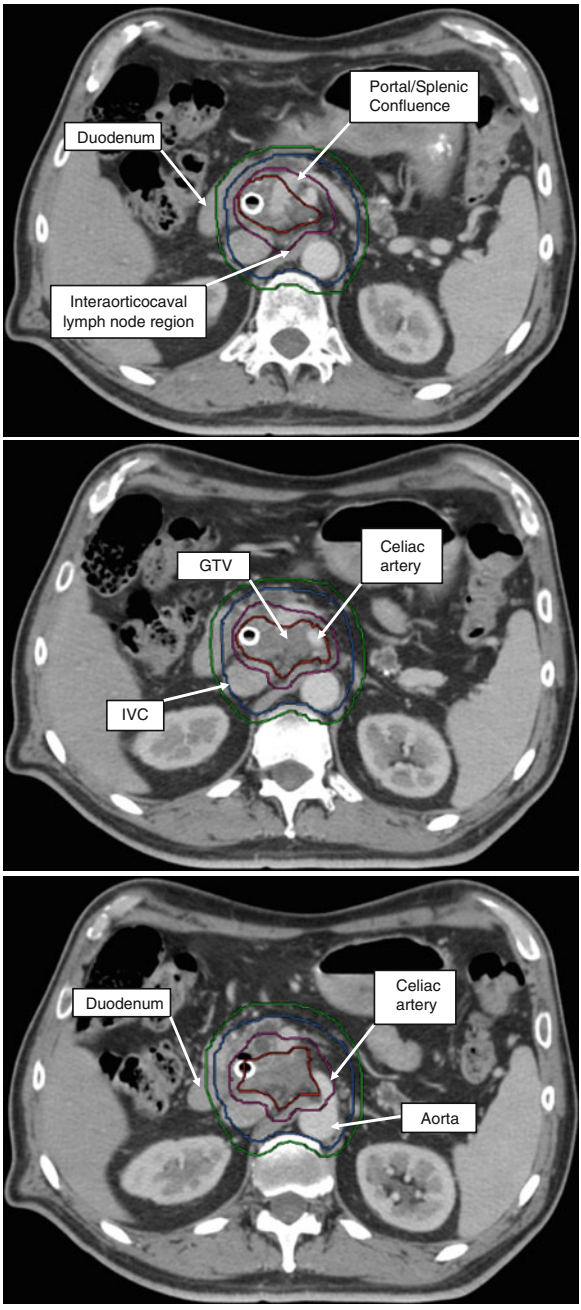


Fig. 15.1 (continued)

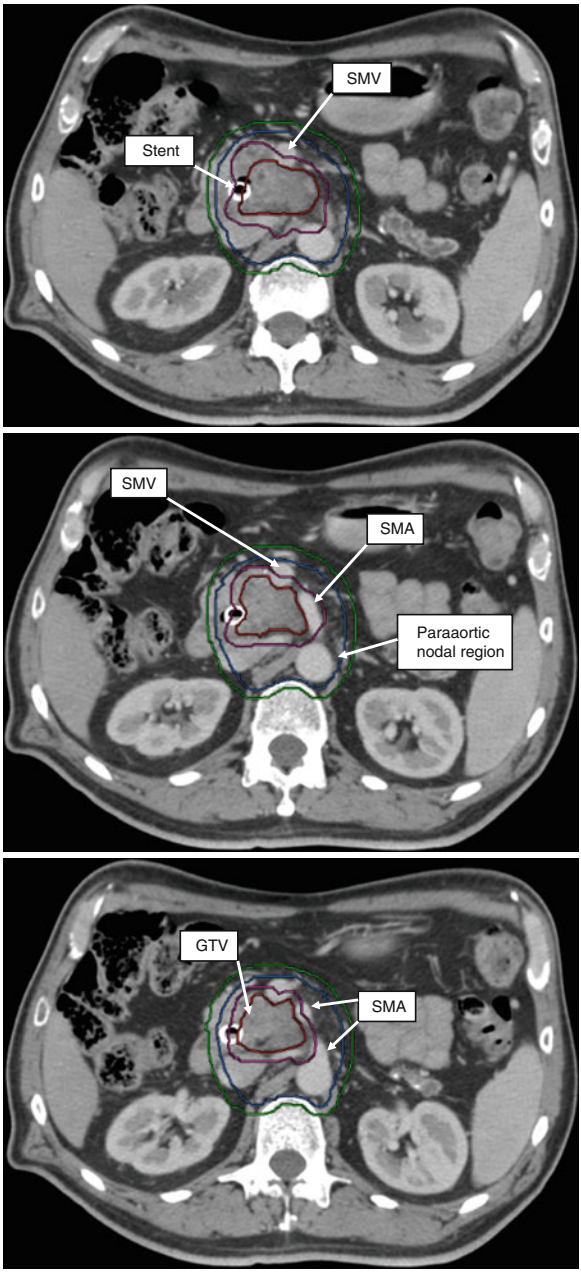


Fig. 15.1 (continued)

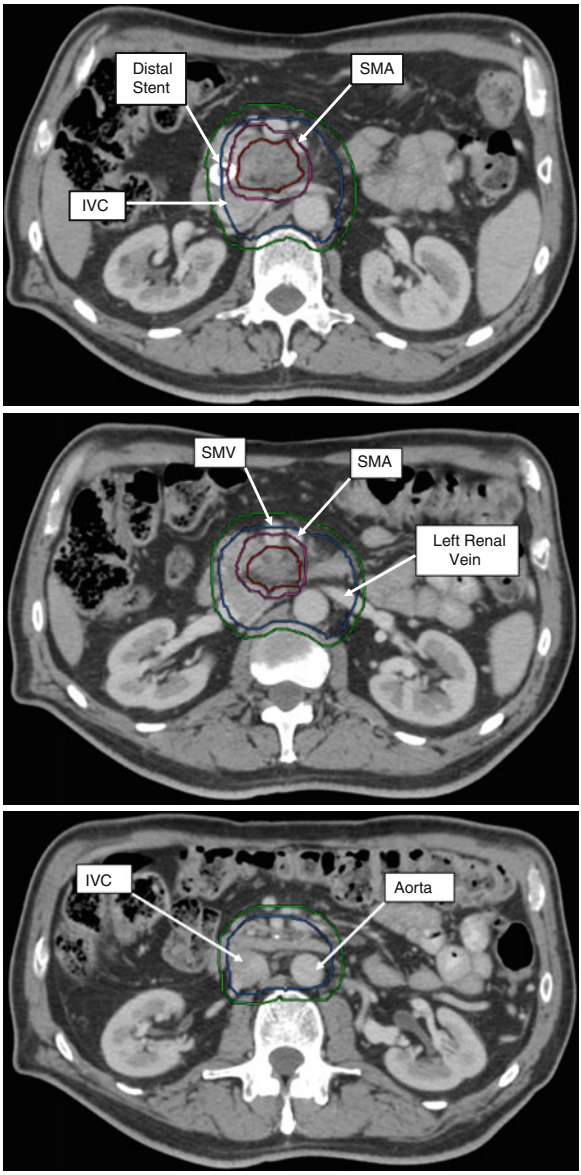
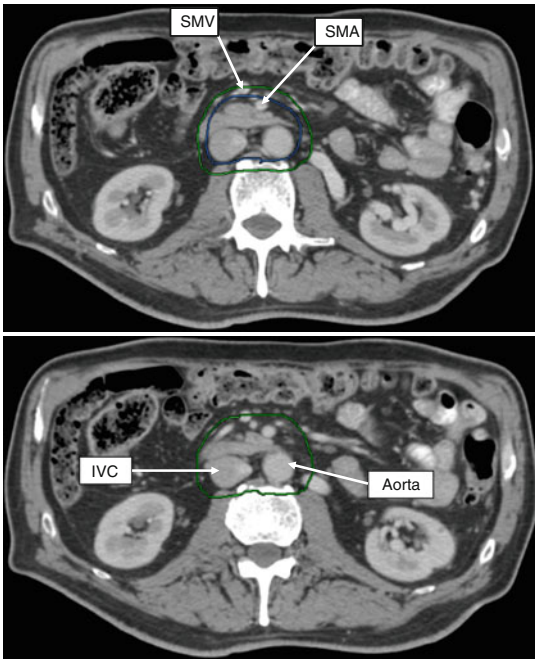


Fig. 15.1 (continued)



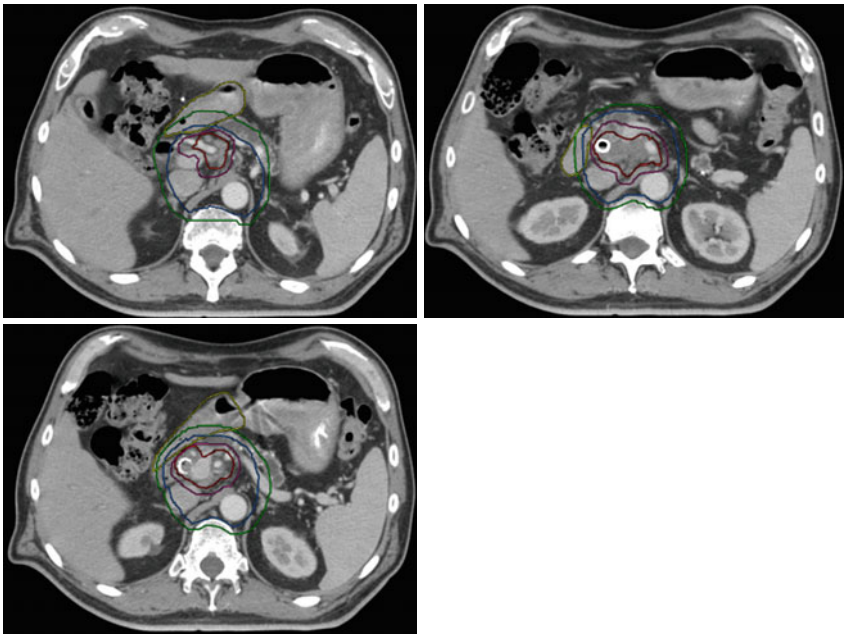


Fig. 15.2 Detail for PTV5600, inoperable pancreatic adenocarcinoma. The GTV (*red*) is expanded by 3–5 mm, and the resulting PTV (pink) is then modified to minimize overlap with the duodenum (*yellow*). As with Fig. 15.1, the CTV is in blue and the PTV5040 is in green

Adjuvant Chemoradiation Pancreatic Adenocarcinoma (Postoperative)

General Principles of Planning and Target Delineation

- Intensity-modulated radiation therapy (IMRT) is becoming the standard technique for adjuvant radiation therapy for pancreatic adenocarcinoma in the postoperative setting.
- Preoperative imaging should be obtained to facilitate contouring of the tumor bed; in addition, postoperative imaging should be obtained to:
  - Evaluate for metastases, in which case postoperative radiation therapy may not provide significant benefit, and
  - Evaluate for recurrent disease, which may receive additional radiation in the form of an integrated boost or cone-down field.
- CT simulation with IV contrast (unless contraindicated) should be performed to assist with delineation of the lymph nodes:
  - Arms above head in Alpha Cradle, oral and IV contrast (generally 100 cc Omnipaque), 4DCT pancreatic protocol with scan from carina to iliac crest.
  - If using respiratory gating, will plan on end-expiration breath-hold scan and assess motion of operative clips with 4DCT scan.

Table 15.3 Target volumes for Adjuvant Therapy

Target volumes	Definition and description
GTV	Positive margin region (based on operative report and pathology report) visualized on pancreatic protocol planning CT scan (arterial phase, contour on expiration phase if using 4DCT) or any targetable residual/and or recurrent disease
CTV	The CTV includes the para-aortic nodes (Ao), pancreaticojejunostomy (PJ), portal vein segment (PV), celiac artery (CA), superior mesenteric artery (SMA), and post-operative tumor bed (Postop), which are identified on the planning CT: Ao extends from the top of the uppermost PV, CA, or SMA slice to the bottom of L2, or L3 if there is a low-lying tumor Fig. (15.4) PJ usually is identified by following the pancreatic remnant medially and anteriorly until the junction with the jejunal loop is noted PV is the portion of the vein running anterior and medial to the IVC and stops prior to the confluence of the SMV or splenic vein SMA is the proximal 2.5–3.0 cm of the vessel CA is the most proximal 1.0–1.5 cm of the vessel Postop is the area occupied by the tumor on preoperative scans Ao is expanded 2.5 cm to the right, 1 cm to the left, 0.2 cm posteriorly, and 2 cm anteriorly; PJ, PV, SMA, CA, and Postop are generally expanded by 1 cm; these two expansions are then added to make the CTV, which is then adjusted to ensure coverage of the draining nodal regions while limiting overlap with the kidneys *Special case*: the above guidelines are meant for pancreatic head lesions; in the setting of a tail lesion, coverage of the PV should be replaced with coverage of the splenic hilar lymph nodes Fig. (15.5)
PTV5040	Expansion on the CTV by 5 mm (receives 5,040 cGy in 180 cGy fractions)
PTV5600	Expansion on the GTV by 3–5-mm margin (receives 5,600 cGy in 200 cGy fractions via integrated boost); minimize overlap with bowel

- Comprehensive guidelines have been established by the RTOG and may be found at http://www.rtog.org/CoreLab/ContouringAtlases/PancreasAtlas.aspx (Tables 15.3 and 15.4, Fig. 15.3).

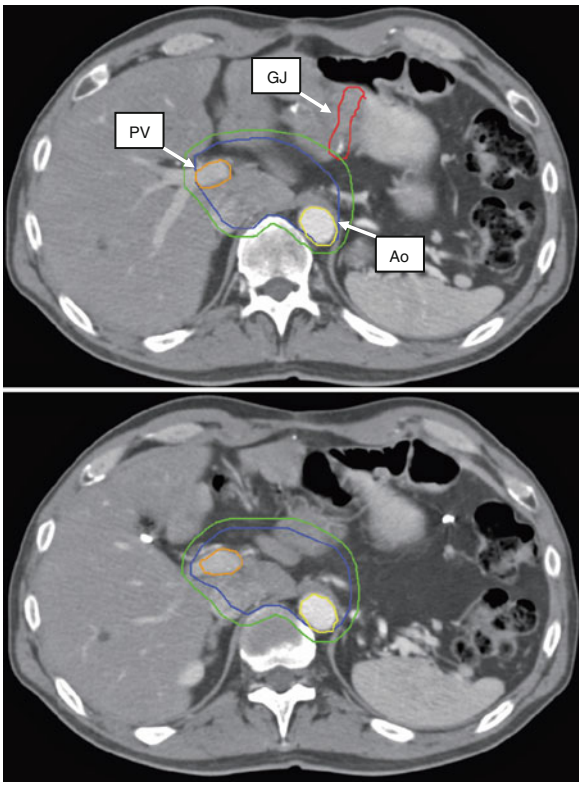


Fig. 15.3 Postoperative case; a patient with pT1N1 resected pancreatic adenocarcinoma with a 1.8-cm lesion in the head of the pancreas, positive distal margin, and 3/13 nodes positive for involvement. Images below show PTV in *green*, CTV in *blue*, and postoperative bed in *red*. Relevant structures including the gastrojejunostomy (*GJ*), pancreaticojejunostomy (*PJ*), aorta (*Ao*), celiac artery (*CA*), and superior mesenteric artery (*SMA*) are labeled. Please note that these are representative slices and not all slices are included

Fig. 15.3 (continued)

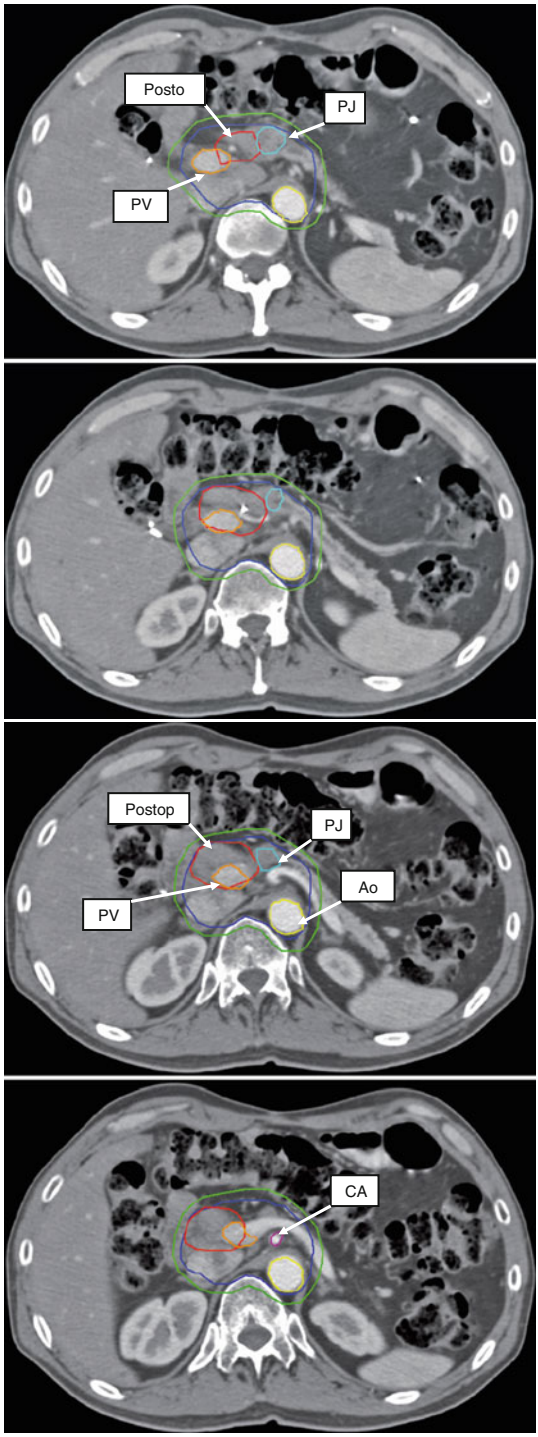


Fig. 15.3 (continued)

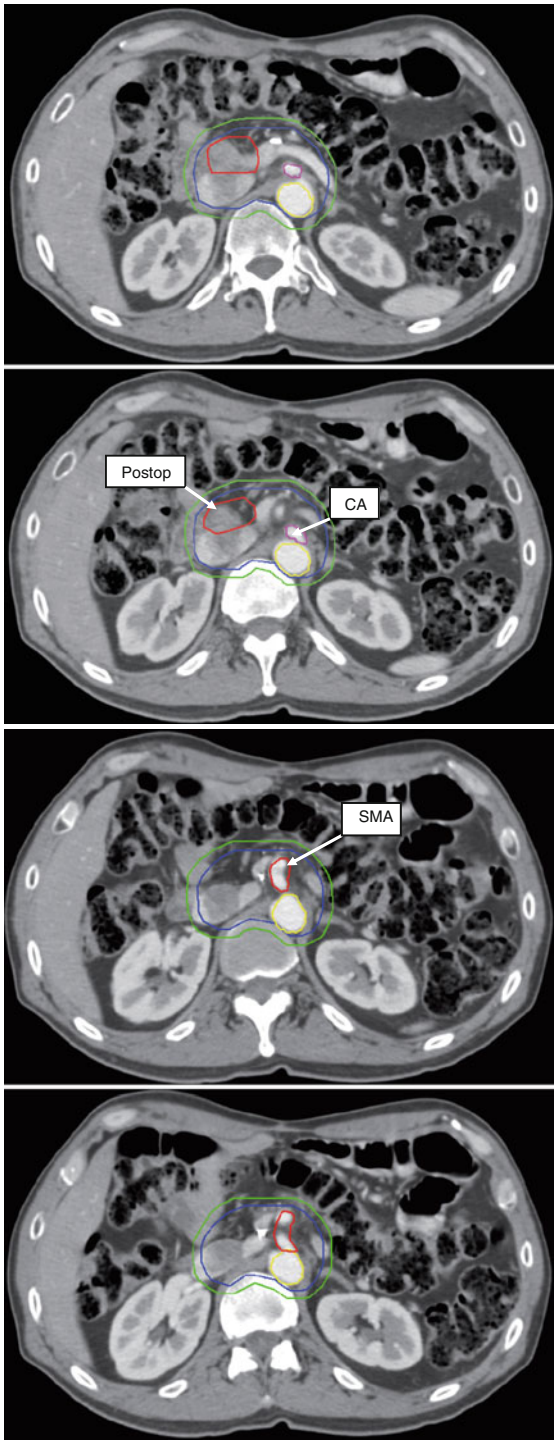


Fig. 15.3 (continued)

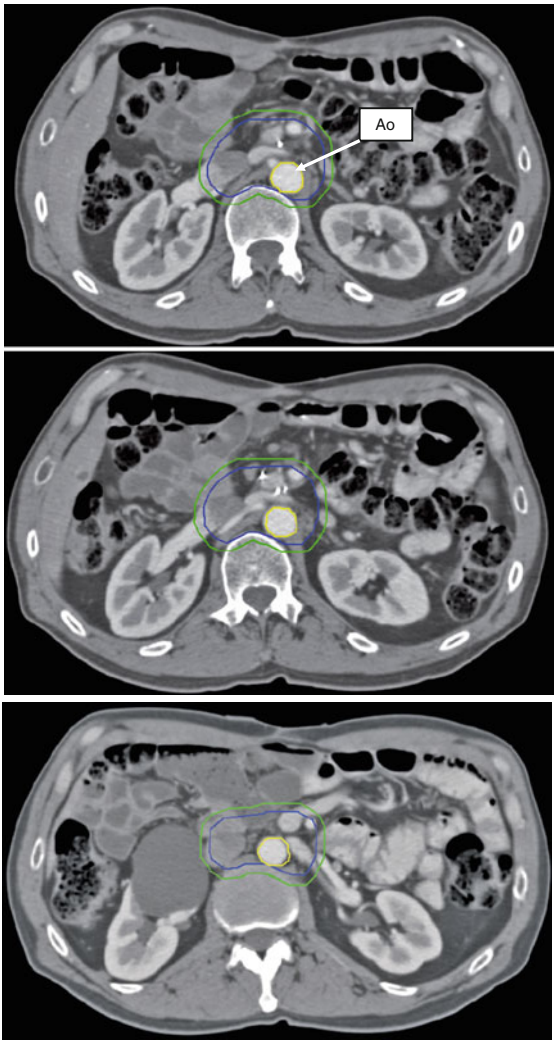


Table 15.4 Normal tissue constraints

Organ	Dose constraint
Liver	Mean dose < 25 Gy, 70 % < 20 Gy
Kidney	2/3 < 18 Gy or 70 % < 15 Gy
Cord	dmax < 40 Gy
Duodenum	50 % < 30 Gy
Heart	V20 < 30 %, V30 < 20 %, 70 % < 15 Gy

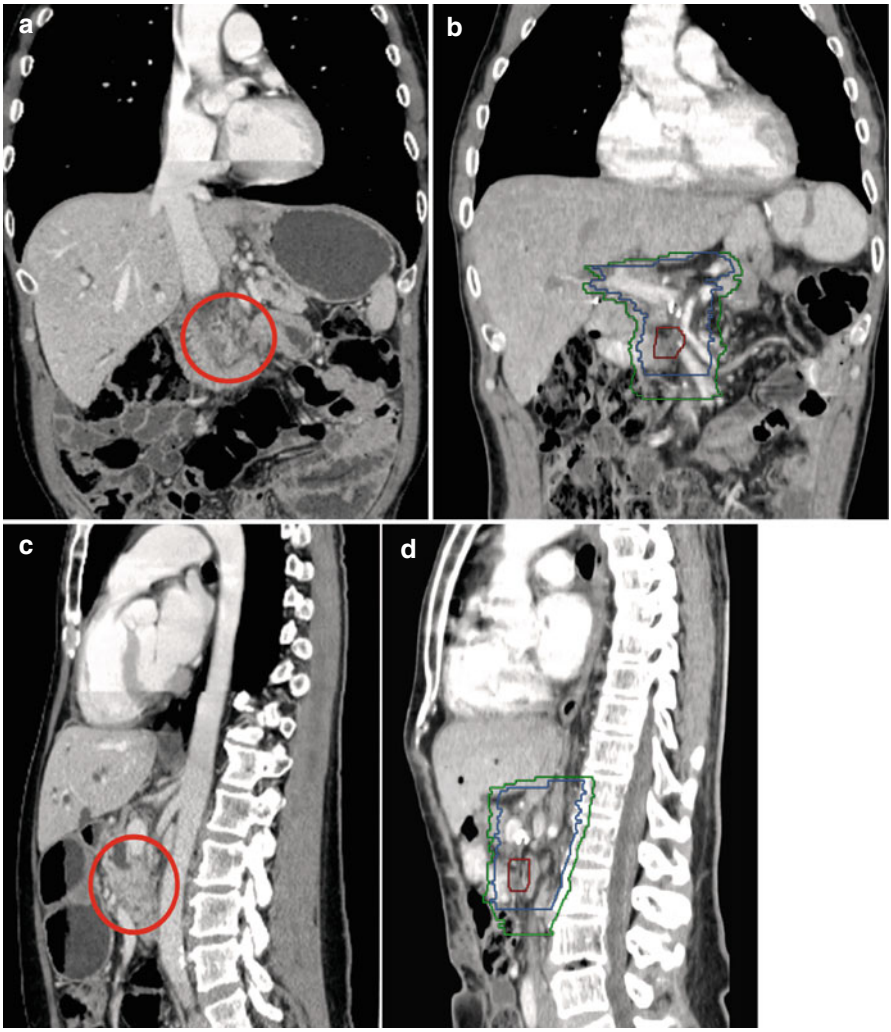
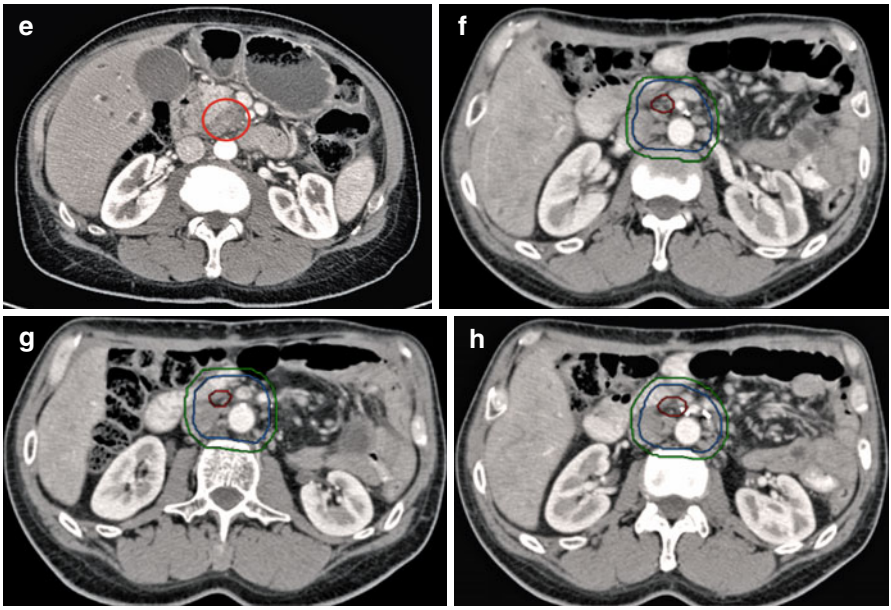


Fig. 15.4 Postoperative case; example of a low-lying tumor. A patient with pT3N1 resected pancreatic adenocarcinoma with a 2.3-cm lesion in the head/uncinate, close <1-mm margins posteriorly and inferiorly, and 14/25 nodes positive for involvement. (**a**) Coronal preoperative CT with tumor marked in *red*; (**b**) coronal planning images with PTV in *green*, CTV in *blue*, and postoperative bed in *red*; (**c**) sagittal preoperative CT with tumor marked in *red*; (**d**) sagittal planning images with PTV in *green*, CTV in *blue*, and postoperative bed in *red*; (**e**) axial preoperative CT with tumor marked in *red*; (**f–h**) axial planning images with PTV in *green*, CTV in *blue*, and postoperative bed in *red*



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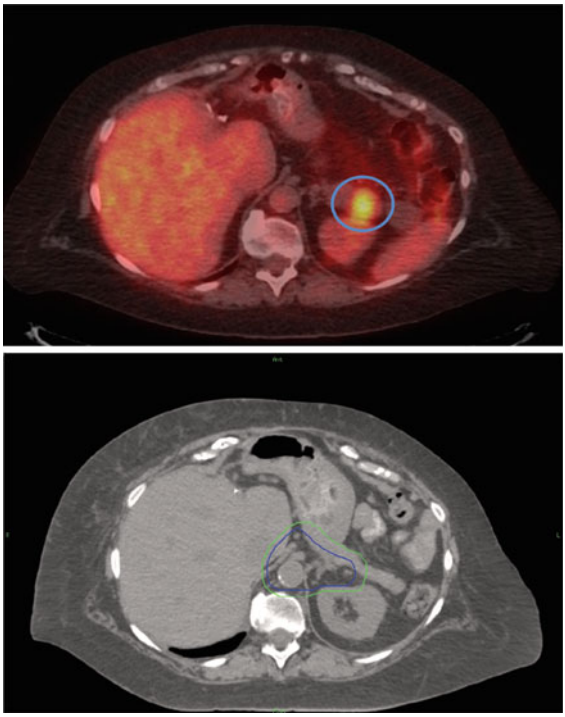
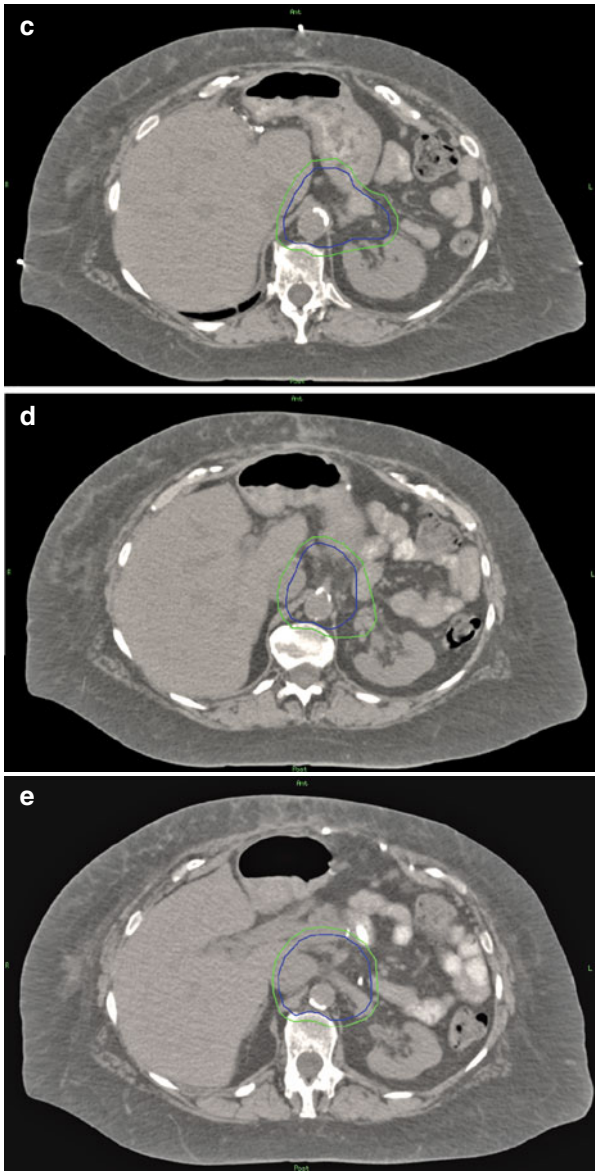


Fig. 15.5 Postoperative case; example of a distal pancreatic cancer. A patient with stage IIA (pT3N0) pancreatic adenocarcinoma, 2.5-cm lesion in pancreatic tail with +PNI/VI and negative margins, and 0/9 nodes involved. (**a**) Preoperative PET CT scan showing FDG-avid pancreatic tail lesion and (**b**–**e**) planning images show PTV in *green*, CTV in *blue*, showing coverage of postoperative bed, splenic hilar lymph nodes, para-aortic nodes, and celiac/SMA nodes. Note that this patient was unable to receive iodinated contrast due to allergy, so disease was characterized with PET; comparison of this patient's vessels to the patients shown in Figs. 15.3 and 15.4 illustrates the importance of IV contrast in defining the vessels on which the CTV is based. *PNI/VI*; *PNI* perineural invasion, *VI* vascular invasion

Fig. 15.5 (continued)



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Hepatocellular Carcinoma

16

Jason Chia-Hsien Cheng, Che-Yu Hsu, Sameh A. Hashem, and Laura A. Dawson

General Principles of Planning and Target Delineation

- Three-dimensional conformal radiation therapy (3DCRT) has been the standard technique for hepatocellular carcinoma (HCC). Intensity-modulated radiation therapy (IMRT) may be useful to improve target coverage and for normal organ sparing, especially in the setting of unusual-shaped target volumes. Stereotactic body radiation therapy (SBRT) has been used more recently. Individualized prescription doses are commonly used due to variable liver volume irradiated and proximity to luminal gastrointestinal tissues.
- In addition to a history and physical examination, laboratory examinations, liver function assessment, and imaging studies should be obtained for diagnosis, staging, and planning. Patients should undergo contrast-enhanced (preferably triphasic [arterial, portal-venous, and delayed phases]) CT scan of the liver, with 3–5-mm slice thickness. Multiphase dynamic MRI scans can be used if CT contrast is contraindicated and may be complimentary to CT scans for target delineation.

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- A half-body or whole-body immobilization, using vacuum bag preferably with arms up, may be done during simulation and used throughout radiotherapy course to reproduce the position and to allow spatial freedom of beam directions. The systems for respiratory coordination should be made of materials not attenuating radiation doses and should not interfere with the gantry positions that may be required for coplanar and noncoplanar beams.
- Respiratory coordination using a number of techniques is frequently needed for breathing motion of the liver (e.g., active breath hold, abdominal compression). Delineation of target volumes is most often done on multiphasic, multimodality imaging, obtained in breath hold (i.e., similar to diagnostic imaging for HCC). Image-guided radiation therapy (IGRT) is required to account for changes in the liver position day to day.
- CT simulation with IV contrast to obtain multiphase imaging is required. This should be obtained with the patient in the treatment position. Fusion of the different phase imaging and/or diagnostic images will aid in the delineation of the gross tumor volume (GTV). Usually, the viable HCC is best visualized (brightest) on the arterial-phase CT scan, with less enhancement seen relative to the liver on venous and delayed phase imaging. Tumor invasion into the vascular structures (e.g., portal vein or inferior vena cava) is often best observed on either portal-venous or delayed-venous phase CT scans.
- The GTV should be delineated on every slice of the planning CT. An additional margin of 4–8 mm around the GTV, confined to the liver to form a clinical target volume (CTV), is optional on the basis of individualized protocol. The expanded margin from vascular thrombus for CTV may be smaller and confined to the vascular structure. Alternatively, the CTV for vascular thrombus may be larger to include some bland thrombus that may contain subclinical HCC.
- Planning target volume (PTV) is expanded from CTV (or GTV if no CTV designed) three-dimensionally, typically with the margins ranging from 5 to 20 mm, depending on the immobilization and respiratory coordination system used. The PTV includes a margin for setup uncertainty and internal target motion, which is based on liver motion observed on fluoroscopy and four-dimensional CT scan that form the basis for an internal target volume (ITV).
- Suggested target volumes for gross disease (GTV and CTV macroscopic) and high-risk regions (CTV microscopic) are detailed in Tables 16.1 (Figs. 16.1, 16.2, 16.3, and 16.4).

Table 16.1 Suggested target volumes at the GTV and CTV regions

Target volumes	Definition and description
GTV	Liver tumor: intrahepatic-enhancing tumor on arterial-phase contrast CT with washout on venous or delayed phase CT Lipiodol retaining tumor: lipiodol (white) contiguous to the enhancing tumor Vascular tumor thrombus: arterial enhancing thrombus with washout on venous phase CT
$CTV_{macroscopic*}$	Liver tumor: the intrahepatic enhancing tumor on arterial-phase contrast CT Lipiodol retaining tumor: TACE zone contiguous to the enhancing tumor included in GTV Enhancing tumor vascular thrombus
$CTV_{microscopic\ (elective)^{\wedge}}$ (optional based on individualized case and protocol)	4–5-mm margin around intrahepatic GTV (the additional margin around the intrahepatic HCC may be treated to macroscopic/higher doses if safe) 2–3-mm margin around the tumor thrombus GTV Bland thrombus adjacent to tumor thrombus GTV Radiofrequency ablation zone adjacent to GTV TACE zone not directly adjacent to the GTV
PTV	CTV + 5–20 mm (may be asymmetric), depending on immobilization and respiration control. The internal organ motion and the setup error form the basis of this margin

*Macroscopic/gross GTV. For example, to be treated to 39–54 Gy in 5–6 fractions. Note that the "safe" dose may need to be reduced if limited by normal tissues

^Elective/microscopic CTV. For example, to be treated to 27.5–30 Gy in 5–6 fractions

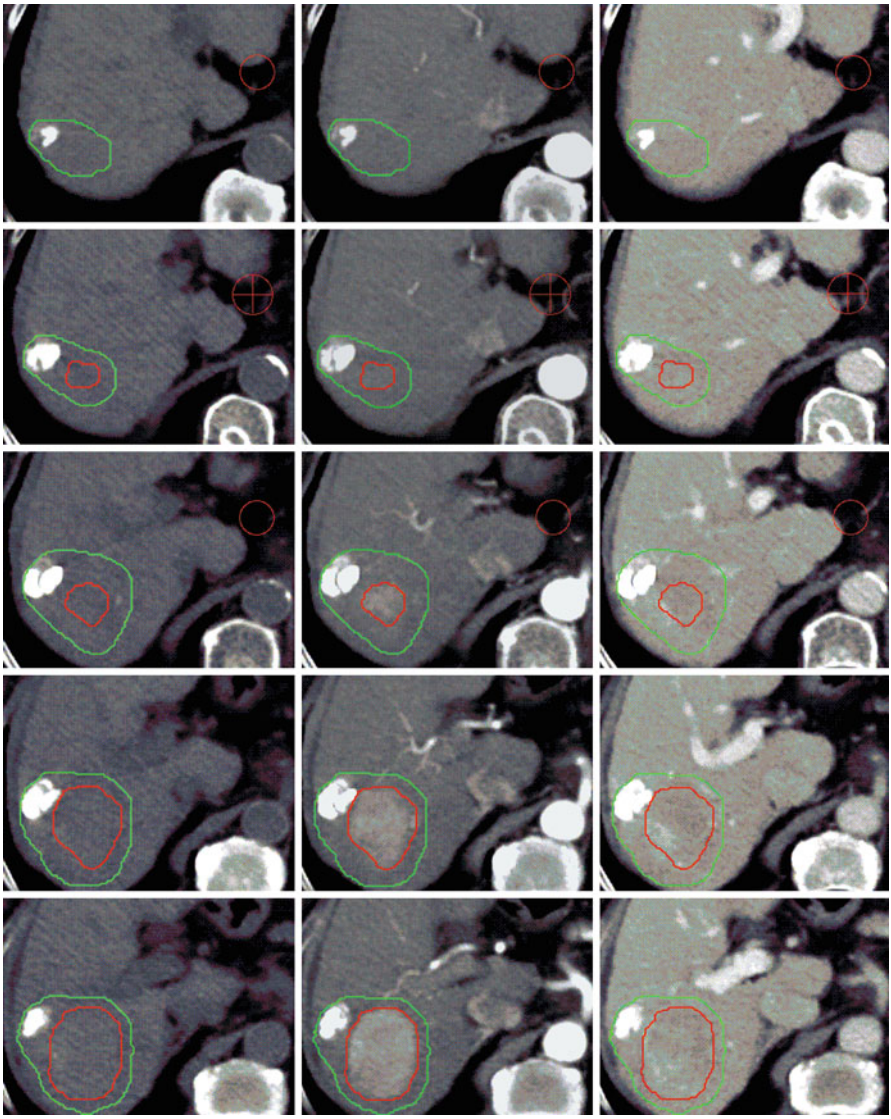


Fig. 16.1 Transcatheter arterial chemoembolization (TACE) refractory HCC. Triphasic contrast-enhanced CT simulation (from *left* to *right*: no contrast, arterial and portal-venous phases), obtained using active breath coordination for liver immobilization, with a 5-mm thickness. The CTV (in *green*) includes the contrast-enhancing tumor (GTV in *red*), the Lipiodol contiguous to the GTV, and a 5-mm margin around the GTV

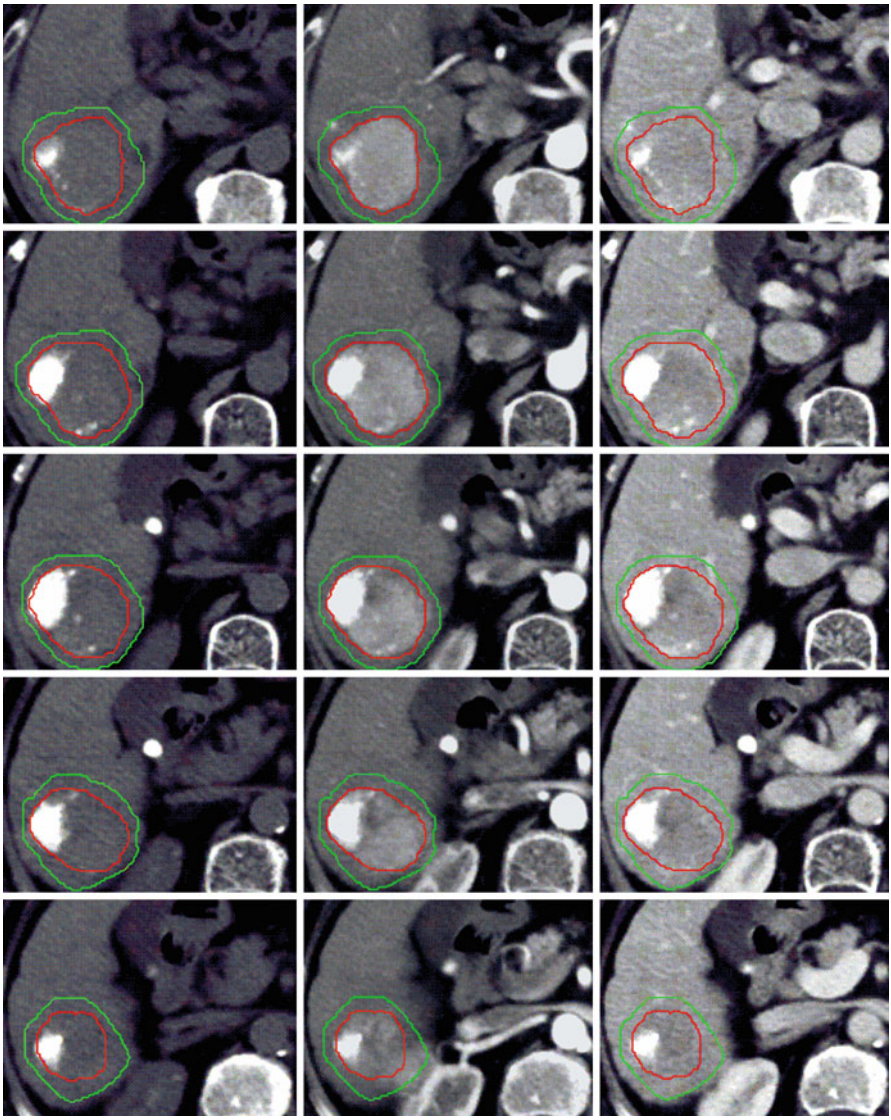
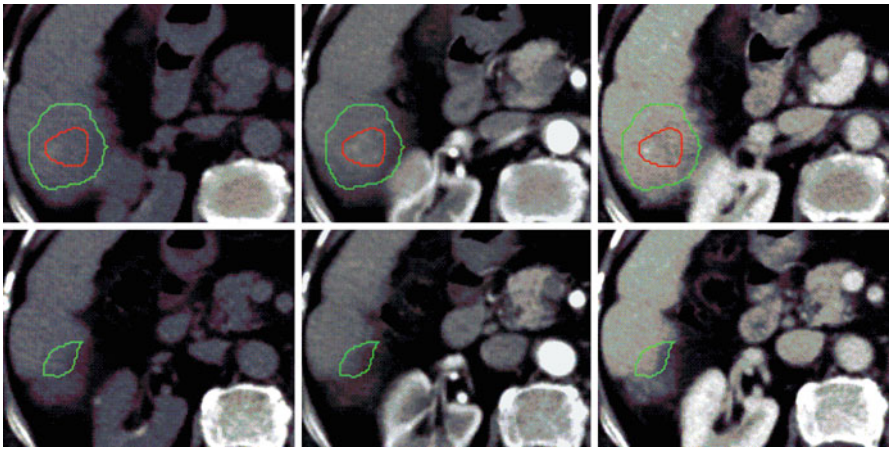


Fig. 16.1 (continued)



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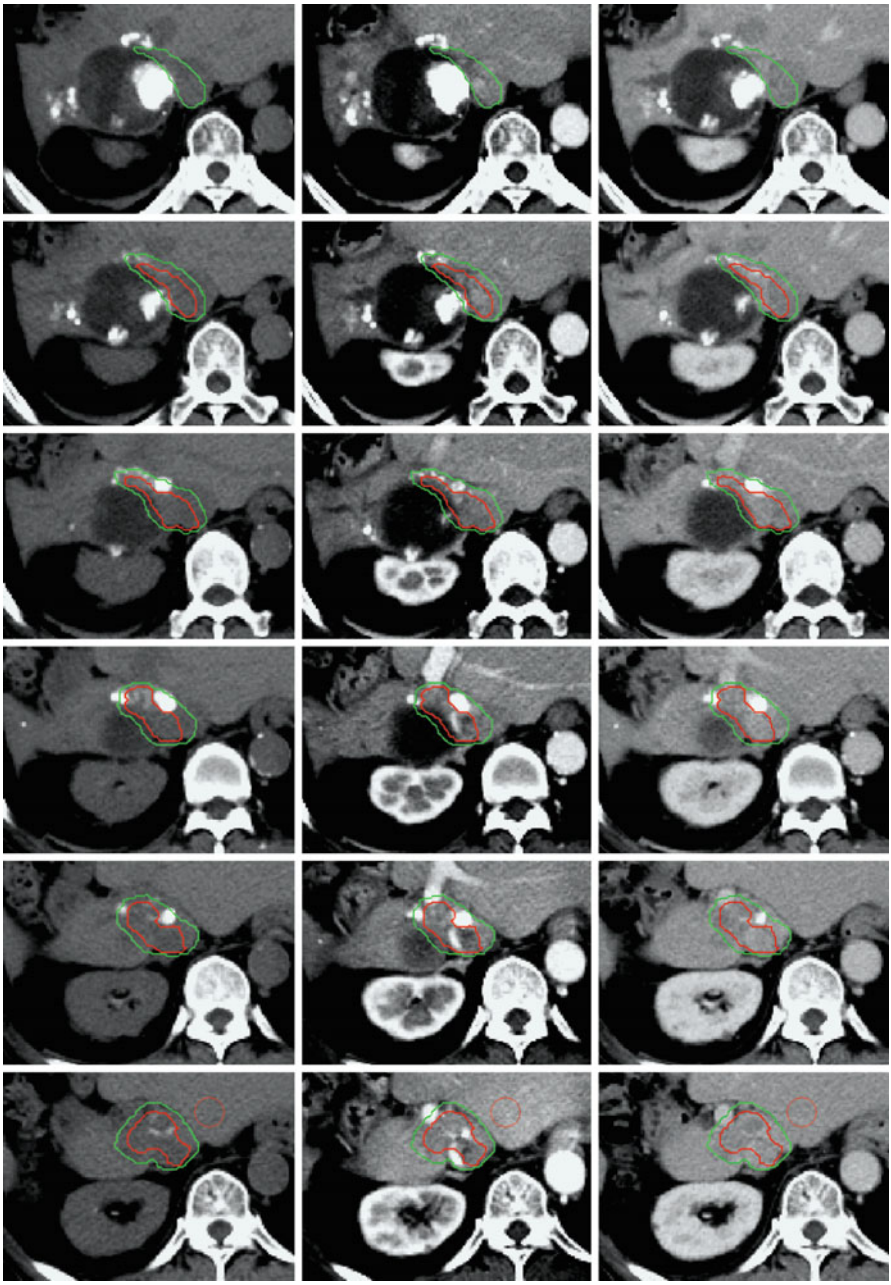
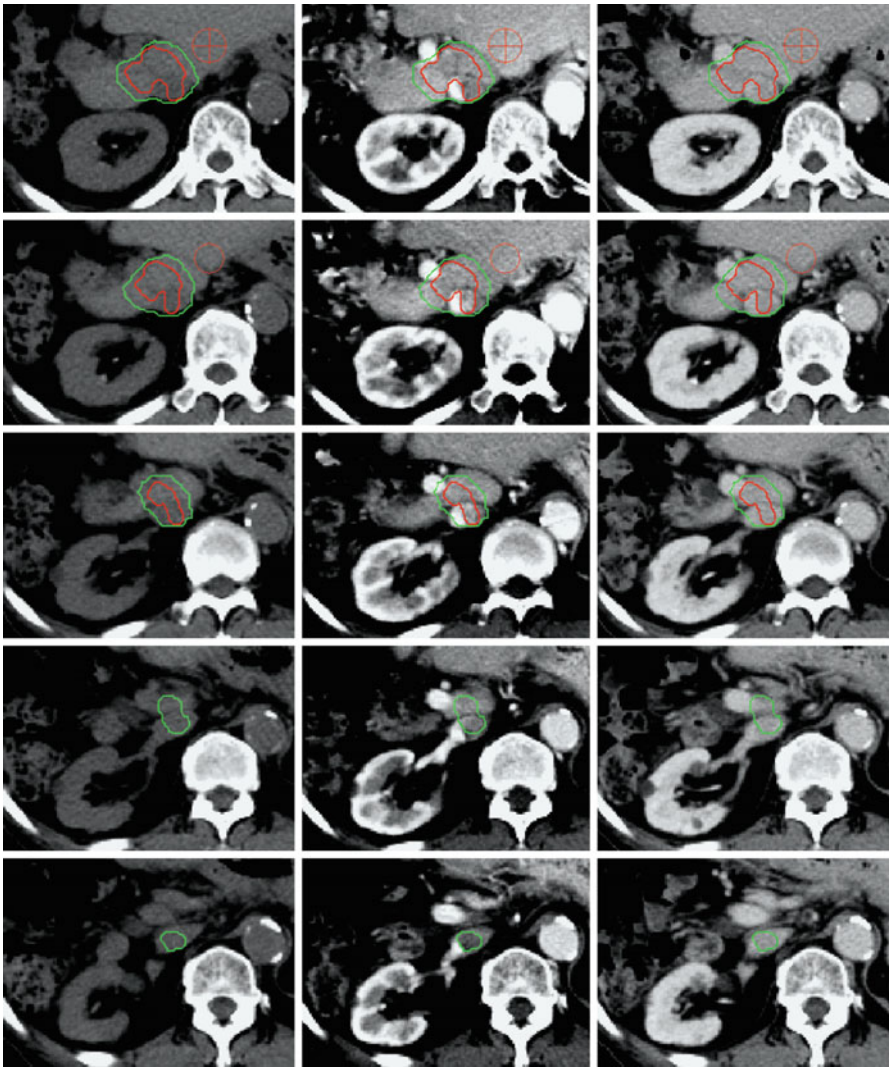


Fig. 16.2 Recurrent HCC after surgery and TACE, invading directly into the right portal vein and inferior vena cava. Triphasic contrast-enhanced CT simulation (from *left* to *right*: no contrast, arterial and portal-venous phases), obtained using active breath coordination for liver immobilization, with a 5-mm thickness. The CTV (in *green*) includes the contrast-enhancing tumor (GTV in *red*), the tumor thrombus, and a 5-mm margin around the GTV



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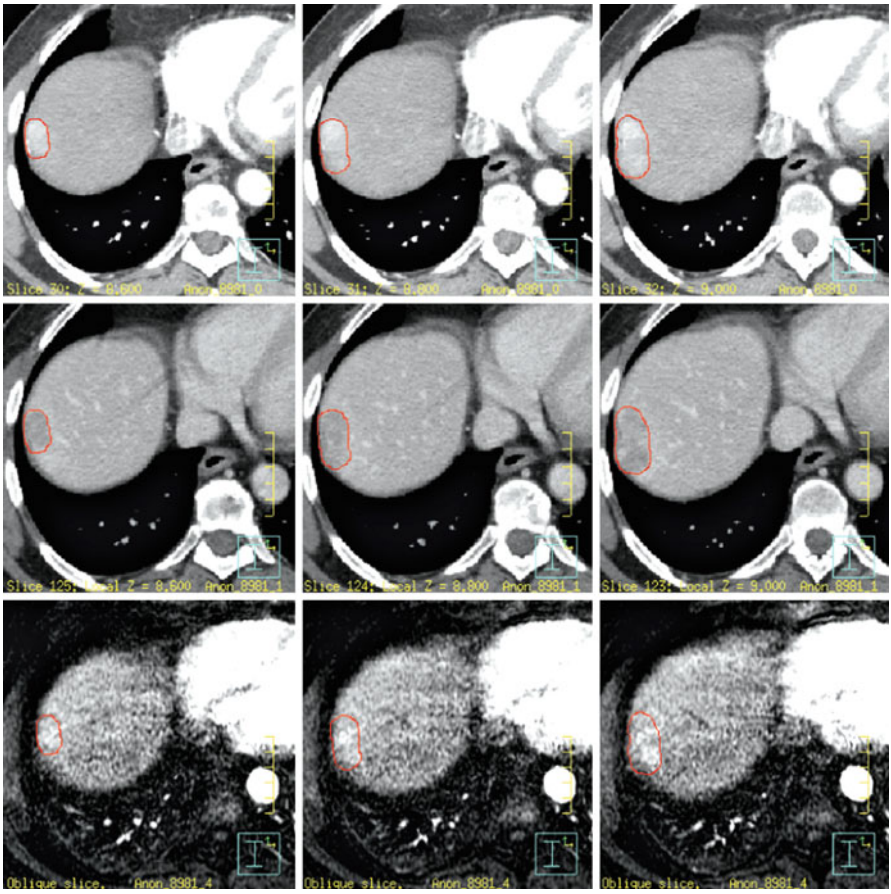
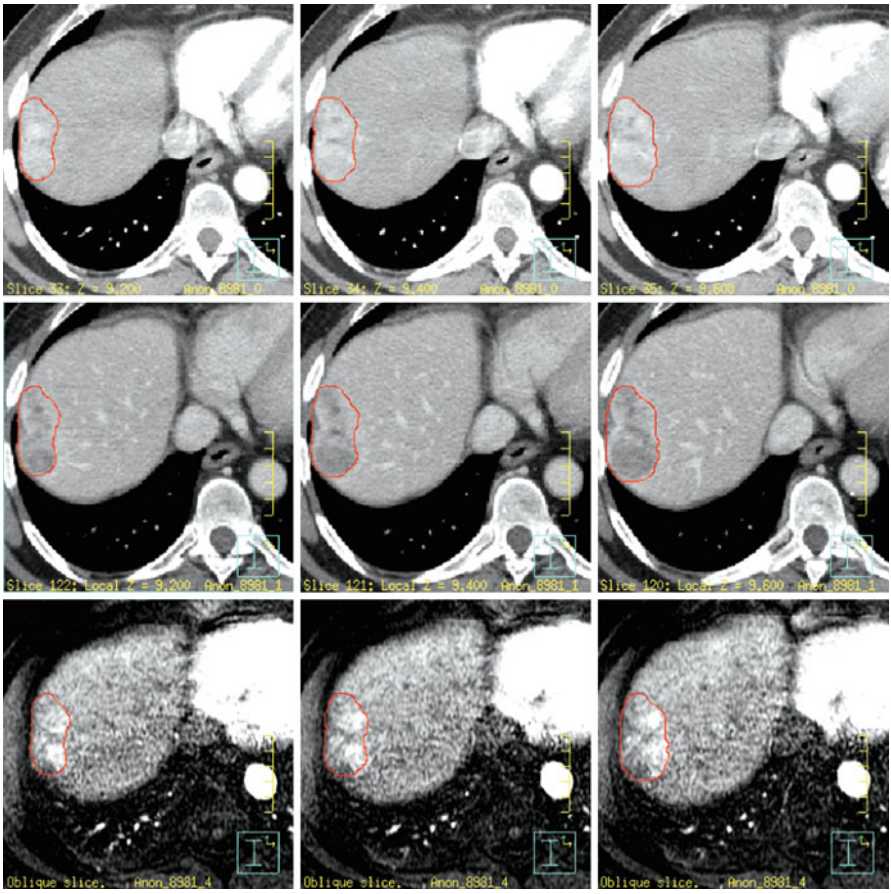


Fig. 16.3 Recurrent HCC post-liver transplant. Multiphase CT and MR obtained in exhale breath hold. GTV shown (in *red*) has typical enhancement on arterial-phase CT (first row), with washout on venous phase CT (second row). A fused arterial-phase T1 MR shown in the third row. Contouring and recording dose to the chest wall and ribs is optional but should be considered for lesions adjacent to the chest wall, especially if using SBRT



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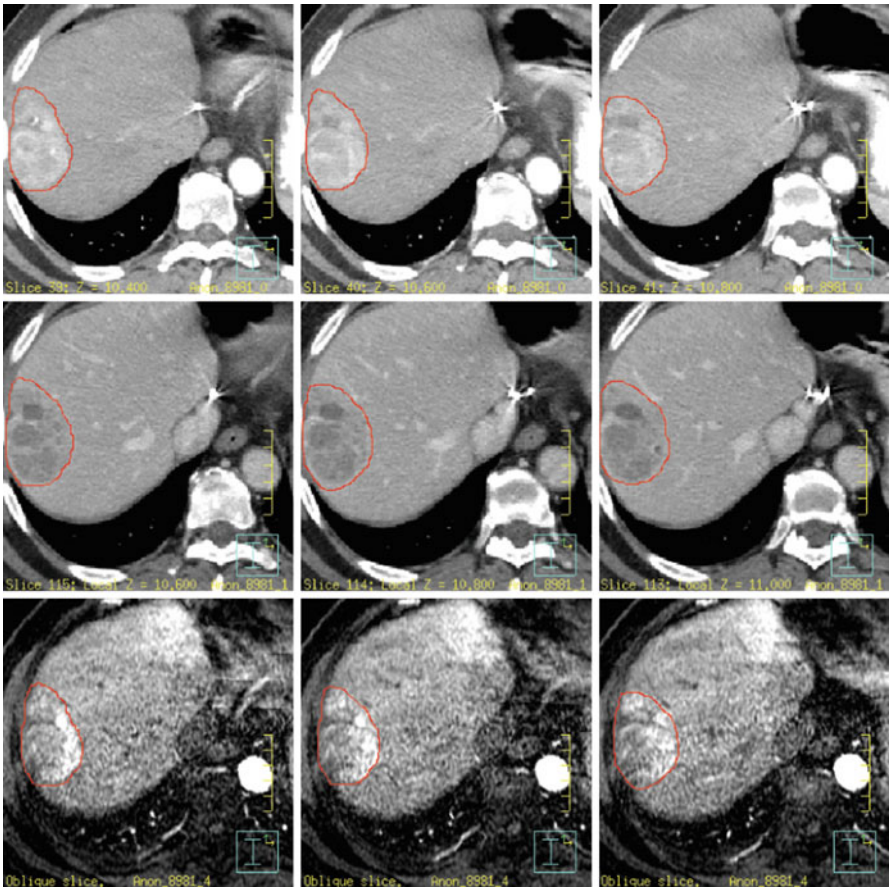

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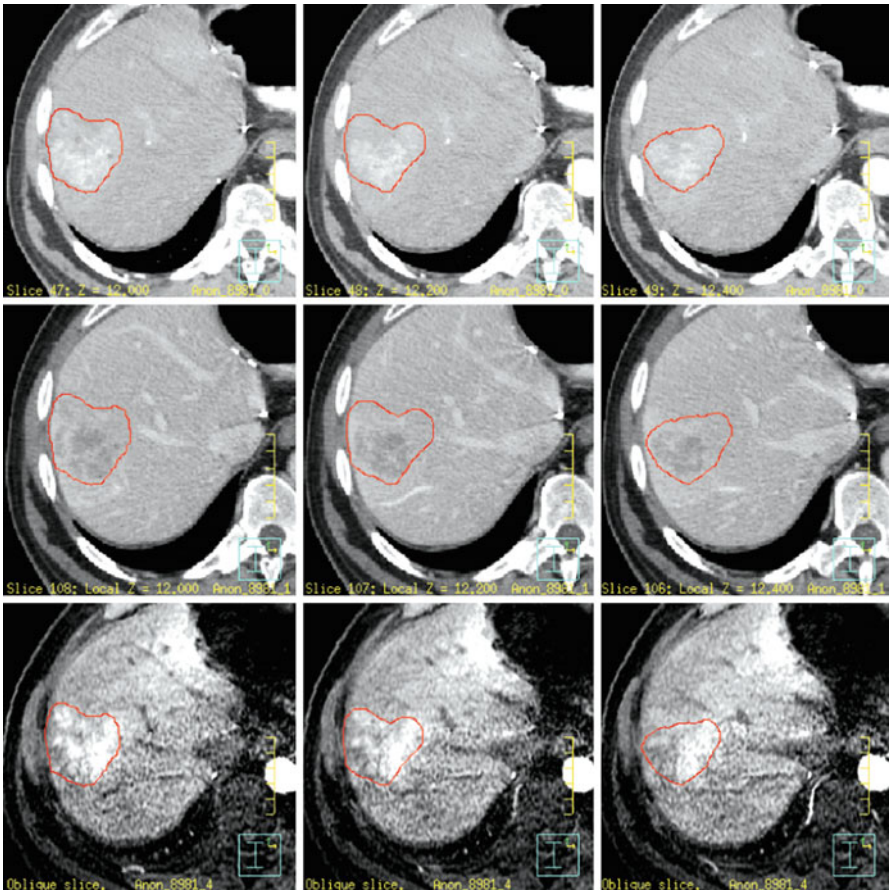

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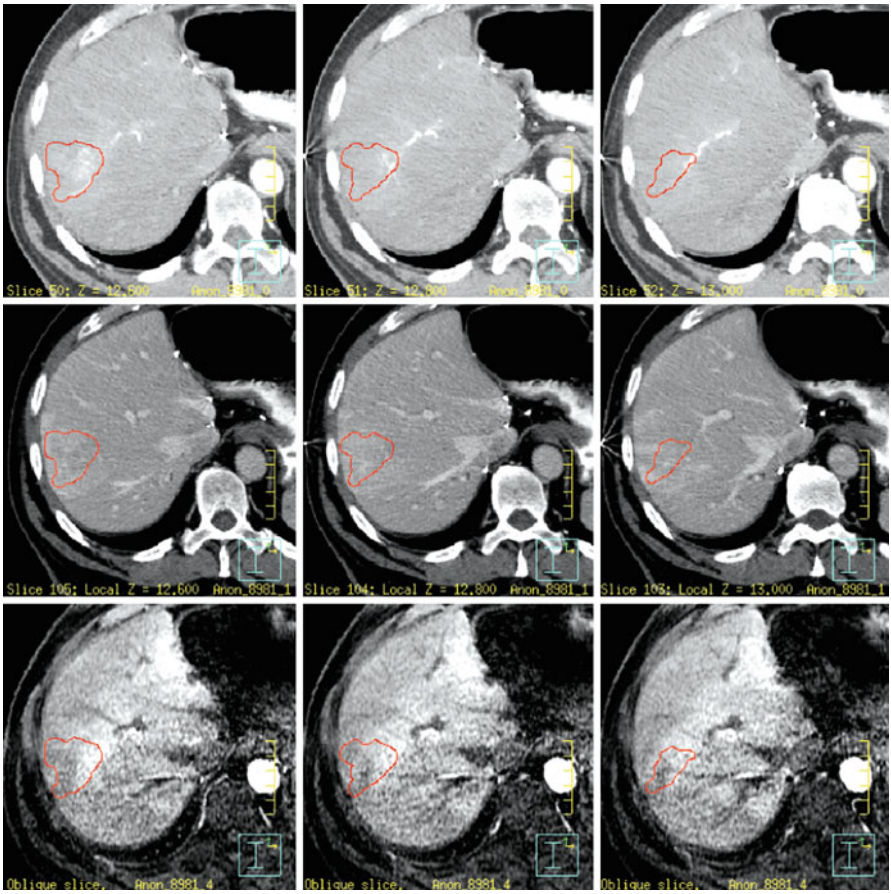

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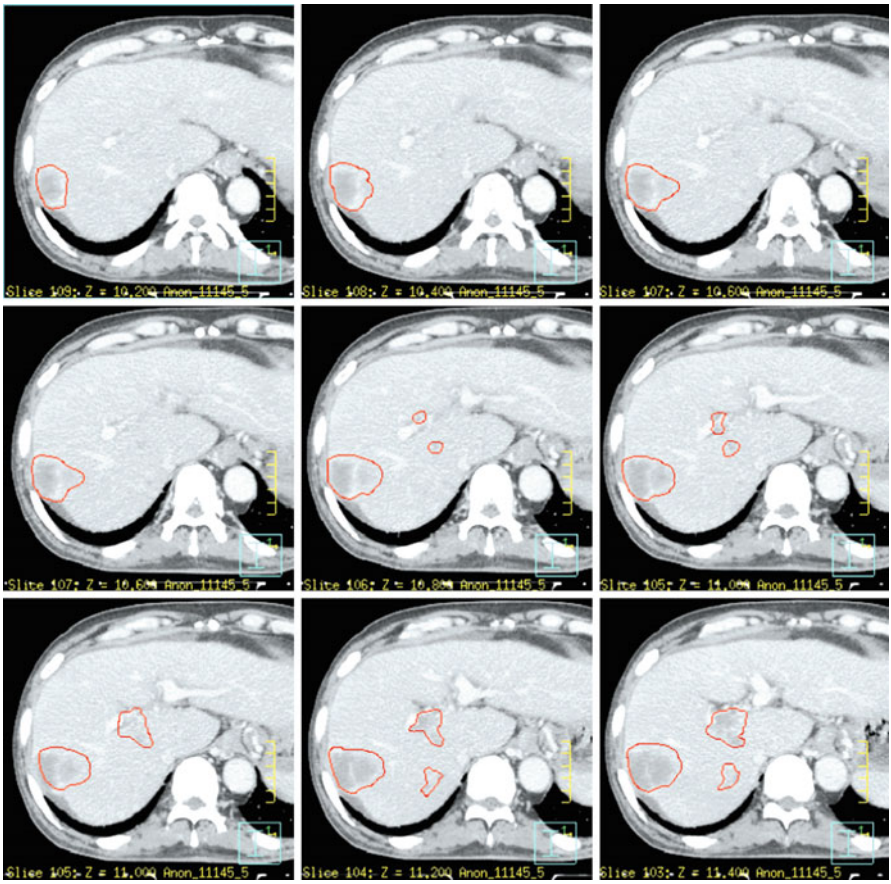
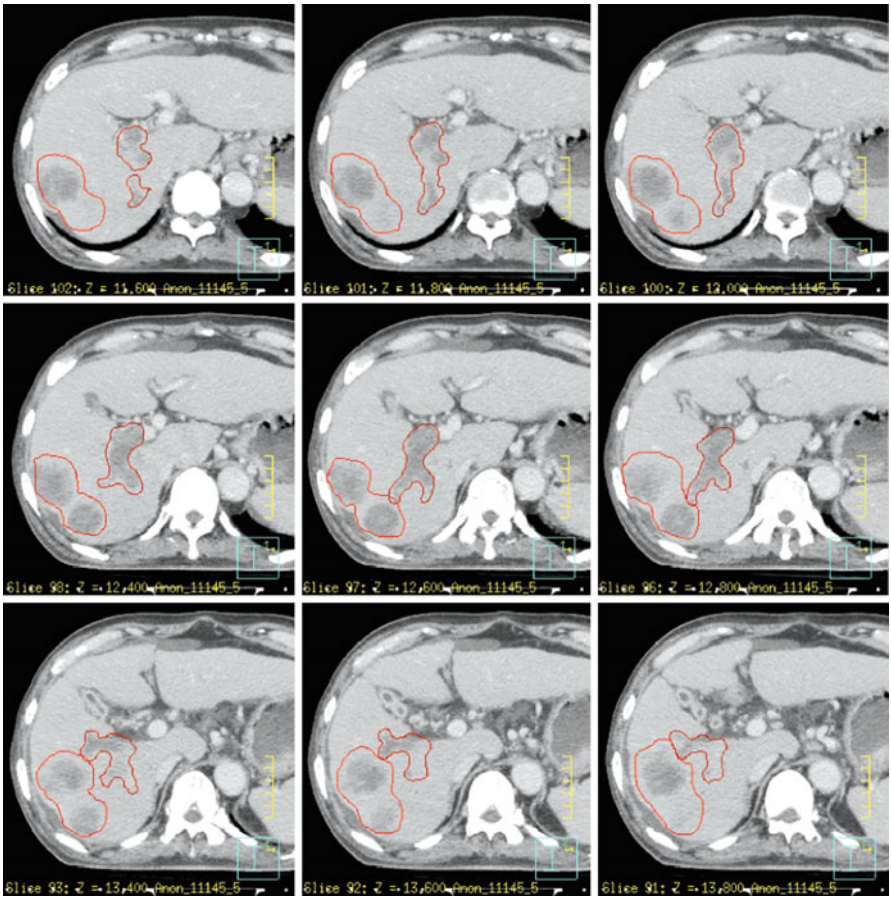


Fig. 16.4 HCC with extensive tumor thrombus (*red* contours), best seen on venous phase CT



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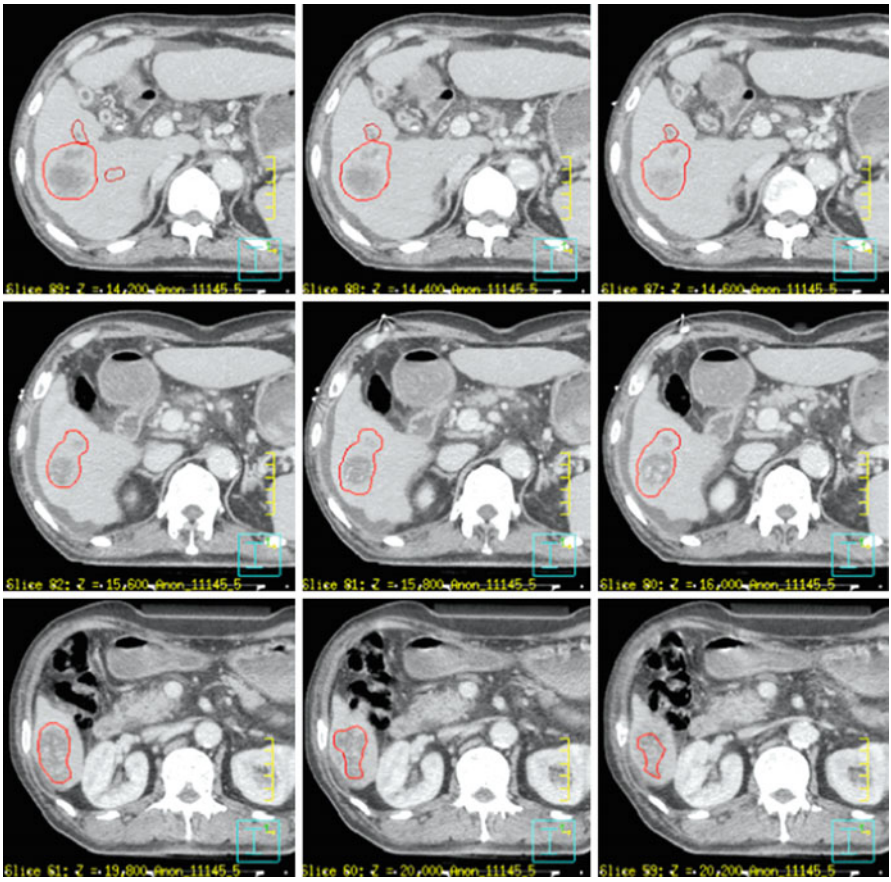

Fig. 16.4 (continued)

Further Reading

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Rectal Cancer

17

Joey G. Bazan, Albert C. Koong, and Daniel T. Chang

General Principles of Planning and Target Delineation

- Physical examination is an important part of the staging and planning process as well as adequate imaging studies. For tumors that are palpable, attention should be paid as to how far the tumor begins from the anal verge. Standard studies include CT of the pelvis to assess the primary tumor and the status of regional lymph nodes. These tumors can be well-visualized on PET, so a PET/CT scan is becoming a standard part of staging and planning to help delineate the extent of gross disease. However, areas of low uptake on PET should not supercede physical exam findings or abnormalities seen on CT.
- MRI is becoming a standard part of preoperative staging to determine invasion of tumor into the mesorectal fat (T3) and into adjacent organs (T4) and assess operability with negative margins. MR fusion could aide in treatment planning.
- CT simulation with IV contrast should be performed to delineate the pelvic blood vessels and gross tumor volume. If PET/CT is available, a PET/CT fusion can be performed to aid in target volume delineation. A radiopaque marker should be placed on the anus.
- The patient can be simulated in the supine position in a body mold or other immobilization device to ensure setup reproducibility. Prone position with the use of a belly board can be used to allow for anterior displacement of the bowel.
- Bladder filling/emptying may be considered, especially if IMRT is used. A full bladder may keep bowel from migrating in to the pelvis. An empty bladder may be more reproducible.
- Target volumes including gross tumor volume and clinical target volume (CTV) should be delineated on every slice of the planning the CT.

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Table 17.1 Suggested target volumes in the preoperative setting

Target volumes	Definition and description
GTV (gross tumor volume)	Primary: all gross disease on physical examination and imaging Regional nodes: all visible perirectal and involved iliac nodes; includes any lymph node in doubt as GTV in the absence of a biopsy
CTV (high risk)	Should cover the GTV with a minimum of 1.5–2-cm margin superiorly and inferiorly and should include the entire rectum, mesorectum, and presacral space axially at these levels but exclude uninvolved bone, muscle, or air. A 1–2-cm margin around areas of gross tumor invasion into adjacent organs should be added. Coverage of the entire presacral space and mesorectum should be considered. Any visible mesorectal nodes on CT and PET should also be included
CTV (standard risk)	Should cover the entire mesorectum and right and left internal iliac lymph nodes for T3 tumors. The right and left external iliac lymph nodes for T4 tumors with anterior organ involvement A 1–2-cm margin in adjacent organs with gross tumor invasion should be added for T4 lesions Superiorly, the entire rectum and mesorectum should be included (usually up to L5/S1) and at least 2-cm margin superior to gross disease, whichever is more cephalad Inferiorly, the CTV should extend to the pelvic floor or at least 2 cm below the gross disease, whichever is more caudad To cover the lymph nodes, a 0.7-cm margin around the iliac vessels should be drawn (excluding muscle and bone) To cover the external iliac vessels (for T4 lesions), an additional 1-cm margin anterolaterally is needed. Any adjacent small lymph nodes should be included Anteriorly, a 1–1.5-cm margin should be added into bladder to account for changes in bladder and rectal filling changes [3] A 1.8-cm wide volume between the external and internal iliac vessels is needed to cover the obturator nodes
PTV	Should be expanded by 0.5–1 cm, depending on the physician's comfort level with setup accuracy, frequency of imaging, and the use of IGRT

- Suggested target volumes of the various CTVs are described in Tables 17.1 and 17.2 [1, 2].
- Suggested dose to PTV (standard risk) is 1.8 Gy/fraction to 45 Gy.
- Suggested dose to PTV (high risk) is 1.8 Gy/fraction to 50.4 Gy (for T3 tumors, Fig. 17.1) and consider 54–55.8 Gy (for T4 tumors, Fig. 17.2).
- Simultaneous integrated boost using IMRT could also be considered. For example:
  - T3N0-1
    PTV (standard risk) – 45 Gy at 1.8 Gy/fraction
    PTV (high risk) – 50 Gy at 2.0 Gy/fraction

Table 17.2 Suggested target volumes in the postoperative setting

Target volumes	Definition and description
CTV (positive margin or gross disease)	Should include the area of known microscopically involved margin or macroscopic residual disease plus a 1–2-cm margin but exclude uninvolved bone, muscle, or air
CTV (high risk)	Should include the entire remaining rectum (if applicable), mesorectal bed, and presacral space axially at these levels but exclude uninvolved bone, muscle, or air. Coverage of the entire presacral space and mesorectum should be considered
CTV (standard risk)	Should cover the entire mesorectum and right and left internal iliac lymph nodes for T3 tumors. The right and left external iliac lymph nodes for T4 tumors with anterior organ involvement Superiorly, the entire remaining rectum and mesorectum should be included (usually up to L5/S1) and at least 1-cm margin superior to the anastomosis, whichever is more cephalad Inferiorly, the CTV should extend to the pelvic floor or at least 1 cm below the anastomosis or rectal stump, whichever is more caudad. If s/p abdominoperineal resection, the surgical bed extending down to the perineal scar should be included. The scar should be outlined with a radiopaque marker To cover the lymph nodes, a 0.7-cm margin around the iliac vessels should be drawn (excluding muscle and bone). To cover the external iliac vessels, an additional 1-cm margin anterolaterally is needed. Any nearby small lymph nodes should be included Anteriorly, a 1–1.5-cm margin should be added into bladder to account for changes in bladder and rectal filling changes A 1.8-cm wide volume between the external and internal iliac vessels is needed to cover the obturator nodes
PTV	CTV should be expanded by 0.5–1 cm, depending on the physician's comfort level with setup accuracy, frequency of imaging, and the use of IGRT

  - T4N0-1
    PTV (standard risk) – 45.9 Gy at 1.7 Gy/fraction
    PTV (high risk) – 54 Gy at 2.0 Gy/fraction
- In postoperative setting (Fig. 17.3), suggested dose to PTV (standard risk) is 1.8 Gy/fraction to 45 Gy.
- Suggested dose to PTV (high risk) is 1.8 Gy/fraction to a minimum of 50.4 Gy and should consider 54–55.8 Gy.
- Suggested dose to PTV (positive margin or gross disease) is 1.8 Gy/fraction to 54 – ≥59.4 Gy.
- Simultaneous integrated boost using IMRT could also be considered. For example:
  - PTV (standard risk) – 45.9 Gy at 1.7 Gy/fraction
  - PTV (high risk) – 54 Gy at 2.0 Gy/fraction

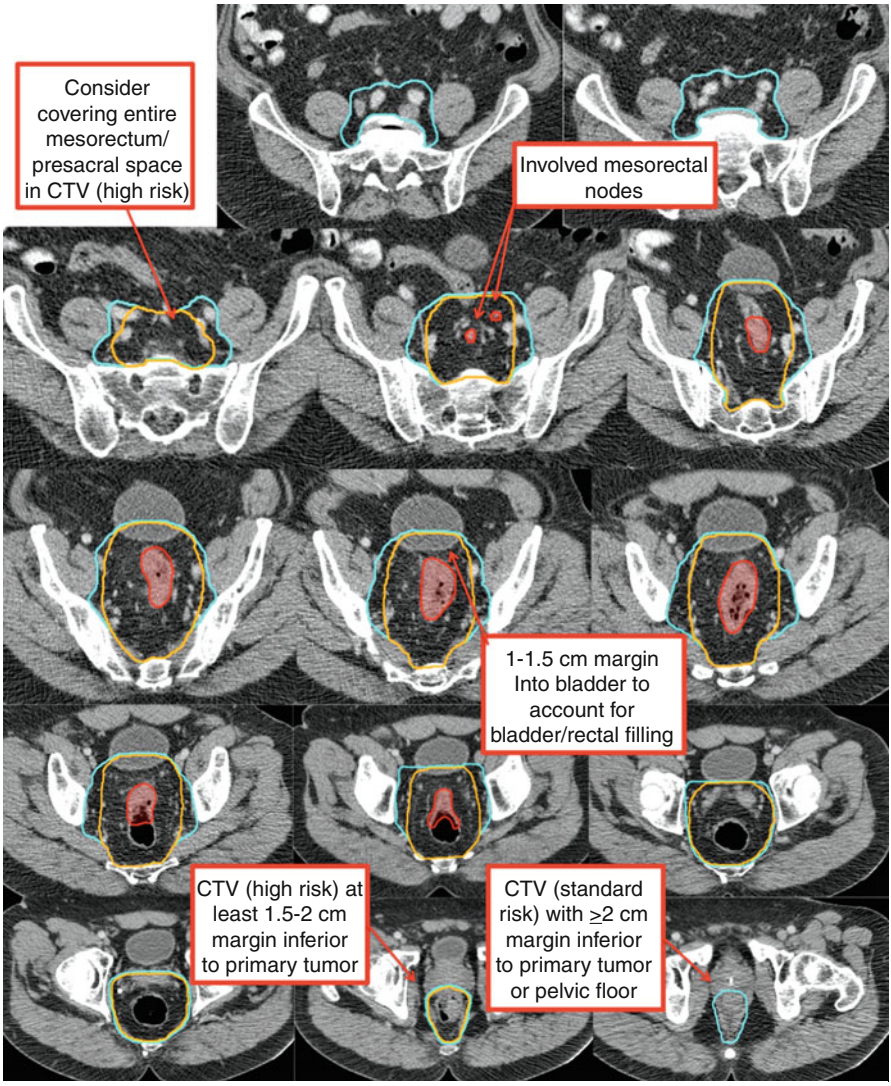
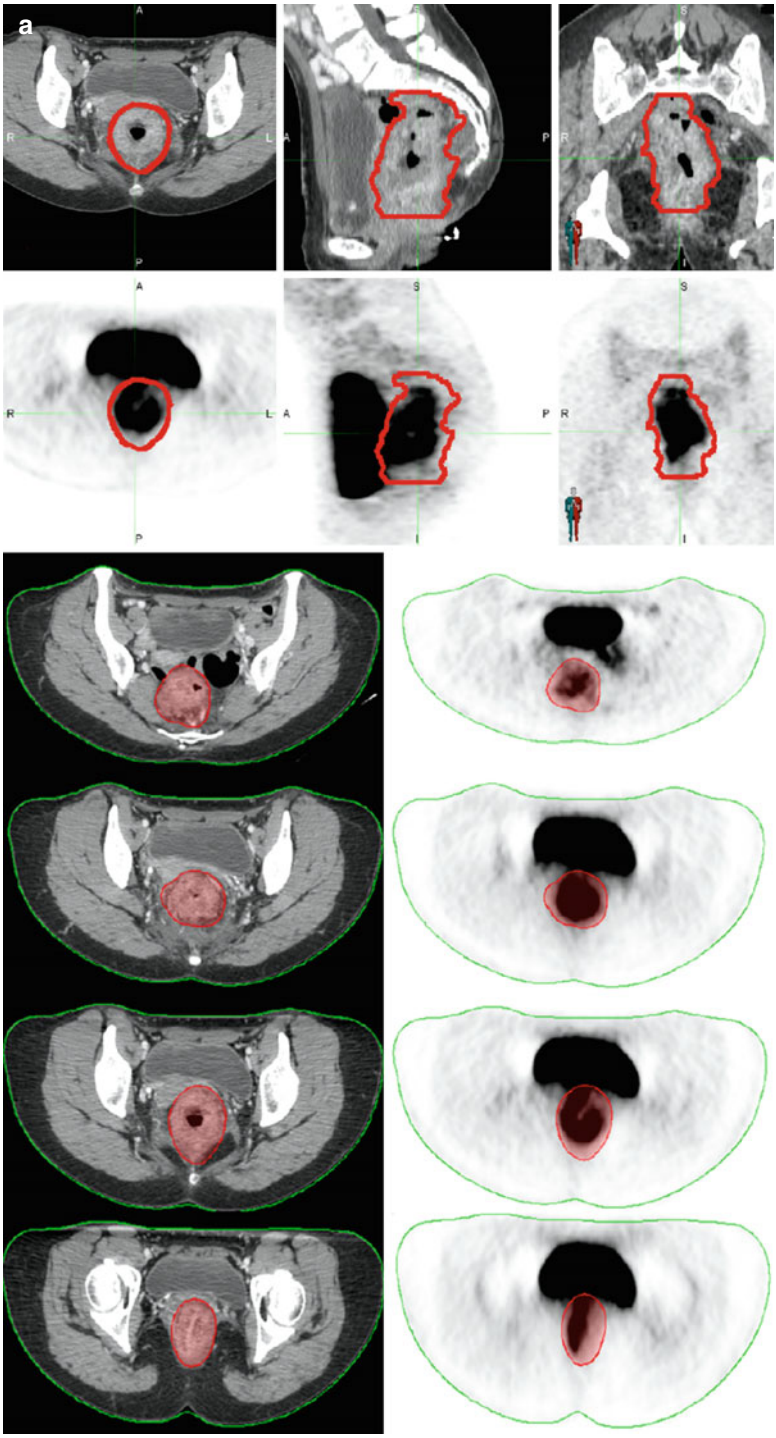


Fig. 17.1 A patient with T3N1 rectal adenocarcinoma. This patient was simulated prone (note the anterior displacement of the small bowel) with PET/CT simulation with 2.5-mm thickness on each slice. CTV (standard risk – *cyan*), CTV (high risk – *orange*), and GTV (*red*, *shaded*) are shown. Note that these are representative slices and not all slices are contoured. Also, the patient was simulated prone but the CT images are rotated 180° for viewer orientation

Fig. 17.2 (**a**) A patient with T4N0 rectal adenocarcinoma (invasion into the cervix). As in the prior case, the patient was simulated supine with PET/CT with slices of 2.5-mm thickness. GTV: These panels illustrate the utility of PET in target volume delineation. In the upper panel, the GTV (*red*) is seen on representative axial, sagittal, and coronal images, respectively, on both the treatment planning CT and PET. The lower panel shows additional axial slices. (**b**) A patient with T4N0 rectal adenocarcinoma (invasion into the cervix). Axial slices showing CTV (standard risk – *cyan*) in relation to the CTV (high risk – *orange*), and GTV (*red*, *shaded*). Note that in this case, the CTV (standard risk) covers the external iliac nodal region due to the T4 disease. Also note that these are representative slices and not all slices are contoured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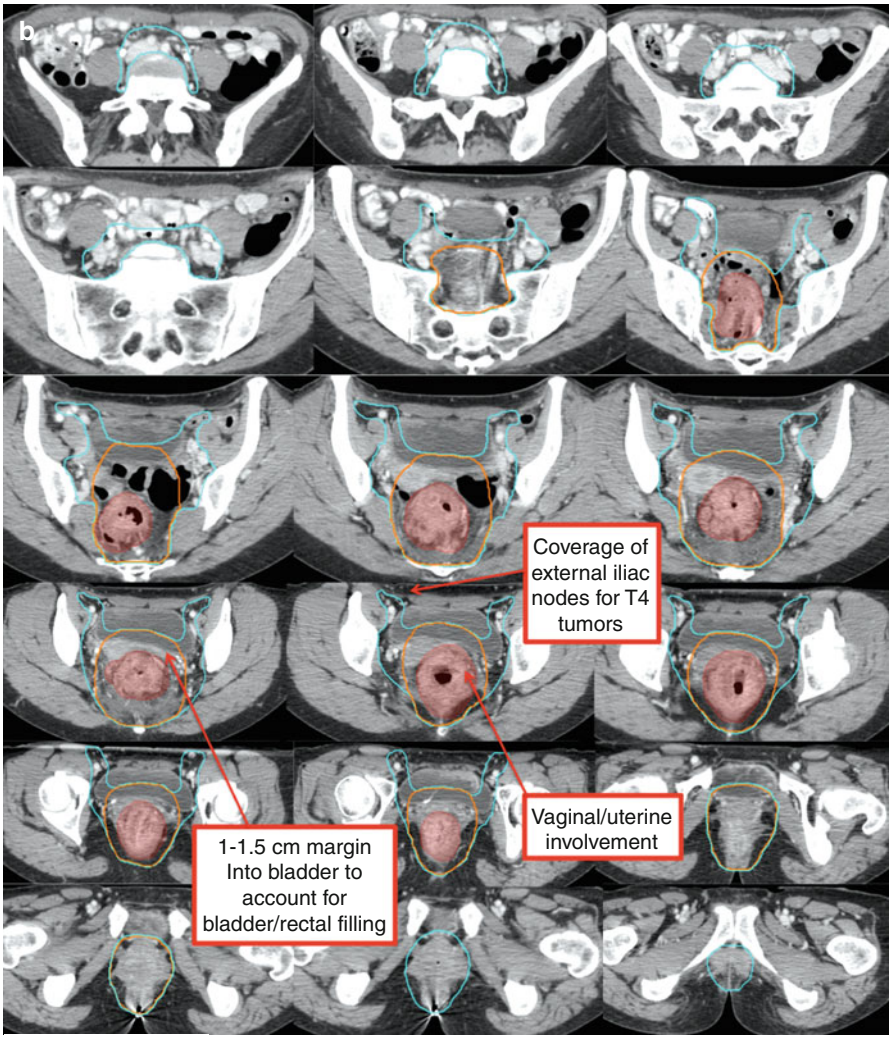

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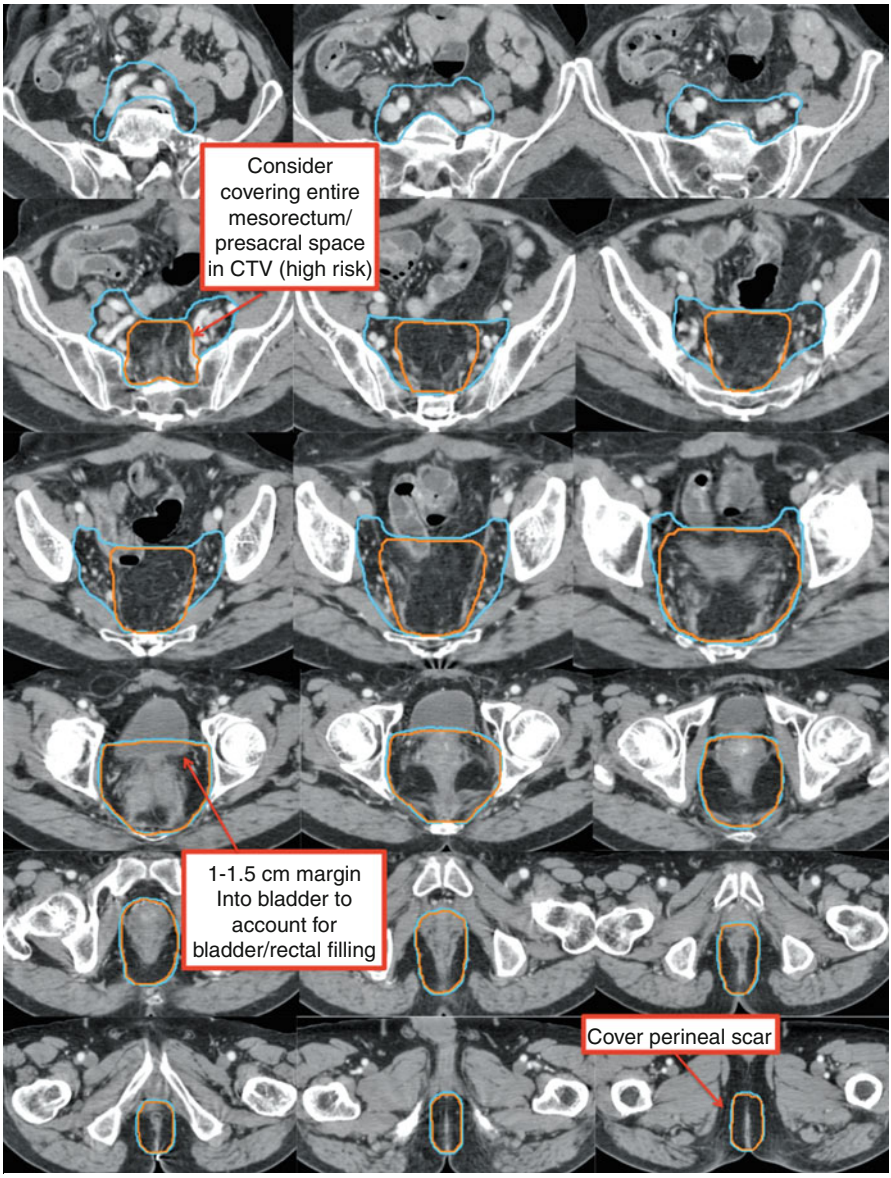

Fig. 17.3 A patient with pathologic T3N2a rectal adenocarcinoma. This patient underwent an abdominoperineal resection (APR) without neoadjuvant chemoradiotherapy. The primary tumor extended from 2 to 5 cm from the anal verge. The patient was simulated prone with CT with slices of 2.5-mm thickness. CTV (standard risk – *cyan*) and CTV (high risk – *orange*) are shown. In this case, due to the absence of small bowel near the postoperative bed, the total dose was 55.8 Gy. However, if a portion of bowel was near the boost volume, the dose could be reduced. Note that these are representative slices and not all slices are contoured. Also, the patient was simulated prone but the CT images are rotated 180° for viewer orientation

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Anal Canal Cancer

18

Joey G. Bazan, Albert C. Koong, and Daniel T. Chang

General Principles of Target Delineation

- Physical examination is an important part of the staging and planning process as well as adequate imaging studies. Standard studies include CT of the pelvis to assess the primary tumor and the status of regional lymph nodes. These tumors can be well visualized on PET, so a PET/CT scan is becoming a standard part of staging and planning to help delineate the extent of gross disease. However, areas of low uptake on PET should not supercede physical exam findings or abnormalities seen on CT.
- CT simulation with IV contrast should be performed to delineate the pelvic blood vessels and gross tumor volume. If PET/CT is available, a PET/CT fusion should be obtained to aid in target volume delineation. A radiopaque marker should be placed on the anus.
- The patient can be simulated in the supine position in a body mold or other immobilization device to ensure setup reproducibility. Prone position with the use of a belly board can be used to allow for anterior displacement of the bowel, but setup reproducibility is more variable and using bolus or additional electron fields to supplement dose to the inguinal regions would not be possible.
- Bladder filling/emptying should be considered. A full bladder may keep bowel from migrating into the pelvis. An empty bladder may be more reproducible.
- Lymph nodes in the inguinal region that are suspicious but borderline should be biopsied.
- Suggested target volumes of the various CTVs are described in Table 18.1 [1, 2]. Of note, there are multiple techniques and methods of dose prescription for anal cancer, and the exact dose fractionation will vary based on which technique is used. The current recommendations are based on the treatment plan used in RTOG 98-11 [3]. RTOG 0529 has recommendations on contouring for IMRT [4].

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Table 18.1 Suggested target volumes at the gross disease region

Target volumes	Definition and description
GTV (gross tumor volume)	Primary: all gross disease on physical examination and imaging Regional nodes: all nodes ≥1.5 cm, PET-positive, or biopsy-proven; include any lymph node in doubt as GTV in the absence of a biopsy
CTV (gross disease)	Should cover the GTV with 1.5–2.5-cm margin expansion but exclude uninvolved bone, muscle, or air
CTV (high risk)	Should cover the entire mesorectum, the right and left internal iliac lymph nodes inferior to the inferior-most level of the sacroiliac joint, and the inguinal or external iliac lymphatics if the inguinal nodes are involved To cover the iliac lymphatics, a 0.7-cm margin around the iliac vessels should be drawn (excluding muscle and bone). To cover the external iliac vessels, an additional 1-cm margin anterolaterally is needed. Any adjacent small lymph nodes should be included Anteriorly, a 1–1.5-cm margin should be added into bladder to account for changes in bladder and rectal filling changes [5] A 1.8-cm wide volume between the external and internal iliac vessels is needed to cover the obturator nodes
CTV (low risk)	Should include the uninvolved inguinal, external iliac, and internal iliac nodes superior to the inferior-most level of the sacroiliac joint To cover the lymph nodes, a 0.7-cm margin around the iliac vessels should be drawn (excluding muscle and bone). To cover the external iliac vessels, an additional 1-cm margin anterolaterally is needed. Any nearby small lymph nodes should be included Anteriorly, a 1–1.5-cm margin should be added into bladder to account for changes in bladder and rectal filling changes [5] A 1.8-cm wide volume between the external and internal iliac vessels is needed to cover the obturator nodes
PTV	CTV should be expanded by 0.5–1 cm, depending on the physician's comfort level with setup accuracy, frequency of imaging, and the use of IGRT

- Suggested dose to PTV (high risk) is 1.8 Gy/fraction to 45 Gy.
- Suggested dose to PTV (low risk) is 1.8 Gy/fraction to 36 Gy or 1.6 Gy/fraction to 40 Gy (if using simultaneous integrated boost with IMRT).
- Suggested PTV (gross disease) dose is 1.8 Gy/fraction to 50.4 Gy for T2N0 tumor and 54–59.4 Gy for T2N+ or T3–4 N0–1 disease (sequential cone down after 45 Gy).
- Suggested dose for T1N0 tumors is 45–50.4 Gy at 1.8 Gy/fraction.
- Additional dose scheduling regimens can be used with IMRT using simultaneous integrated boost technique. However, caution should be used when using >2 Gy per fraction to the primary tumor. The authors recommend 1.8 Gy per fraction as the maximum daily dose to the primary tumor (Figs. 18.1, 18.2, and 18.3).

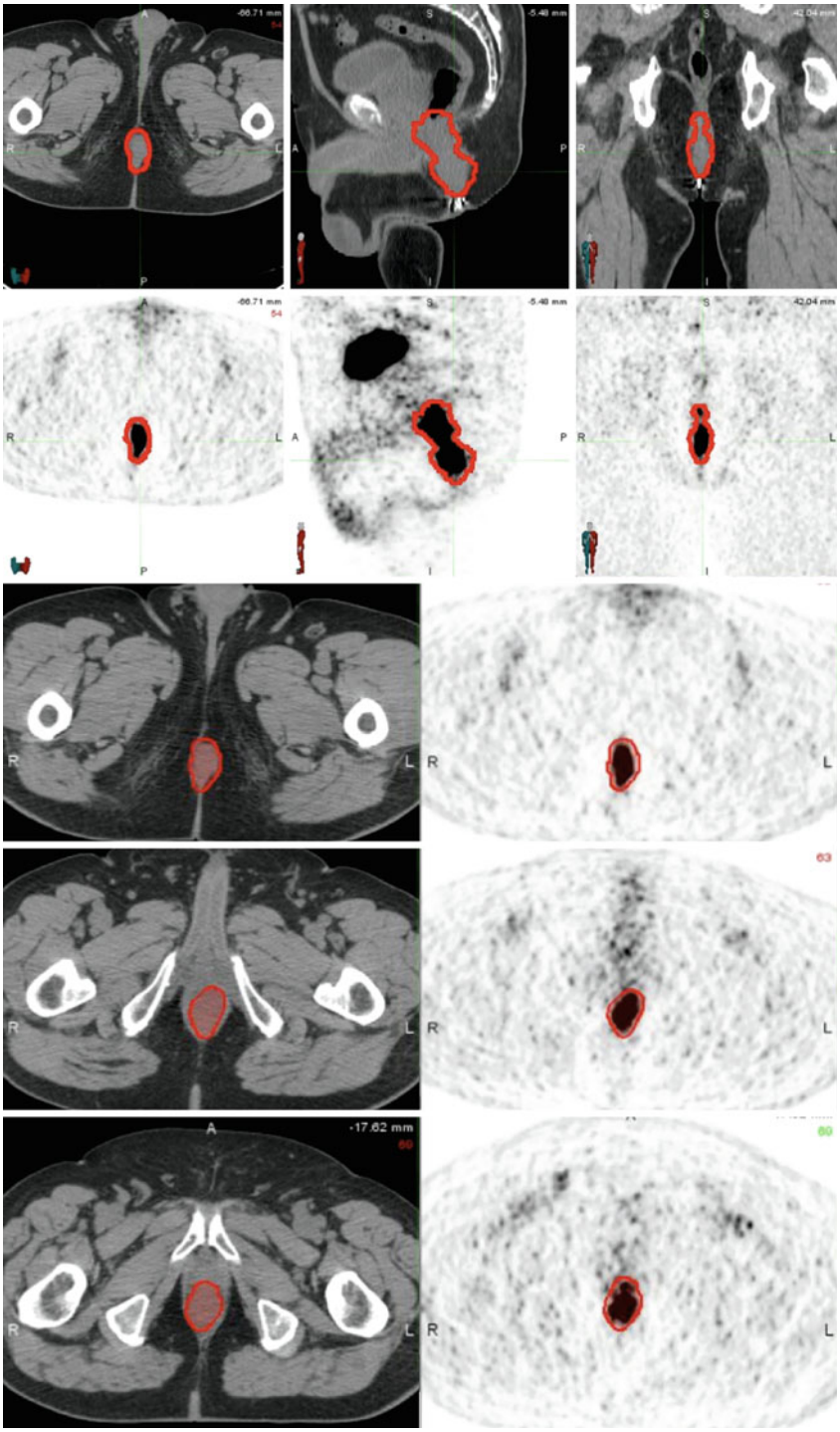

Fig. 18.1 An example of how PET can help delineate GTV. The GTV (*red*) is seen on representative axial, sagittal, and coronal images, respectively, on both the treatment planning CT and PET in the upper panels. Additional representative axial slices are shown below in the lower panels

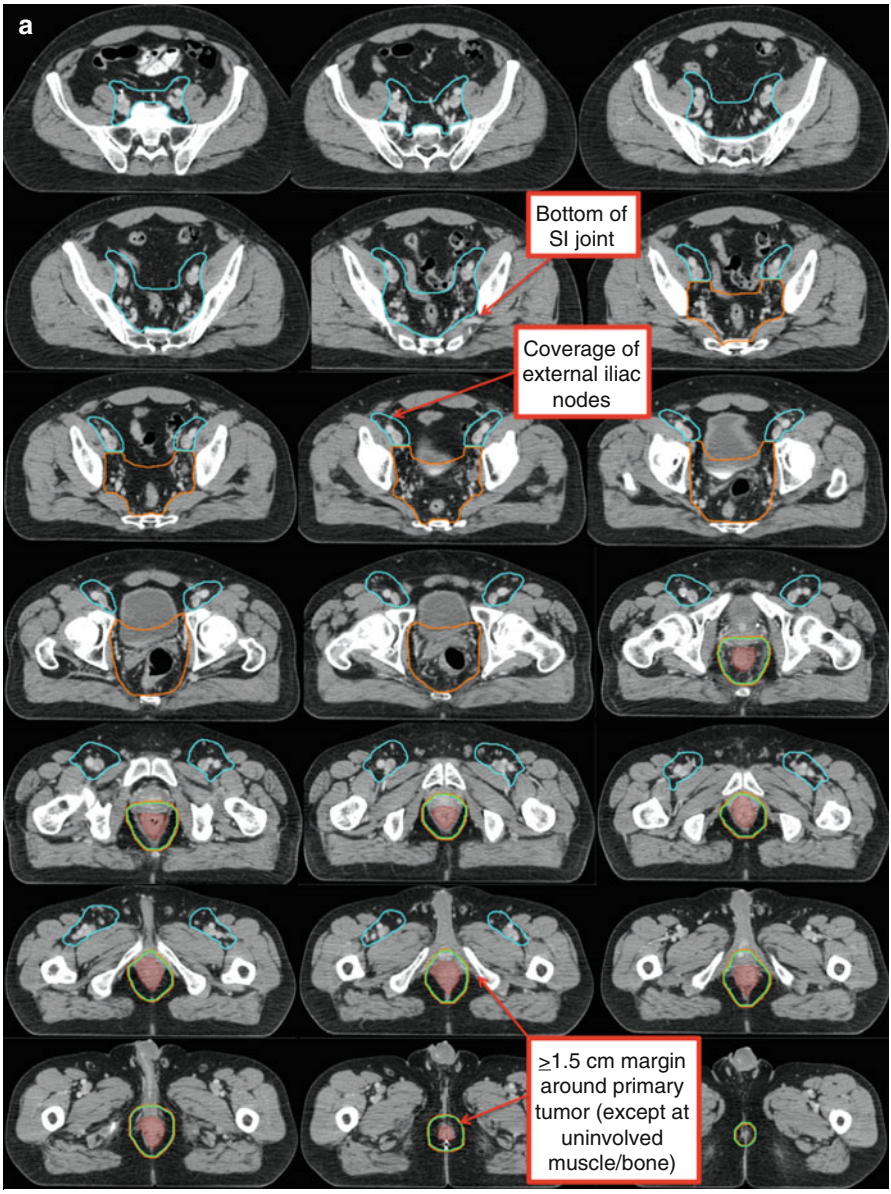

Fig. 18.2 (**a**) A patient with T2N0 anal canal cancer. This patient was simulated supine using PET/CT simulation with a 2.5-mm thickness on each slice. CTV is shown. Note that these are representative slices and not all slices are included. CTV (low risk – *cyan*), CTV (high risk – *orange*), CTV (gross disease – *green*), and GTV (red, shaded) are shown. (**b**) Enhanced view of lower pelvis showing CTV (low risk – *blue*), CTV (high risk – *orange*), CTV (gross disease – *green*), and GTV (*red*, *shaded*)

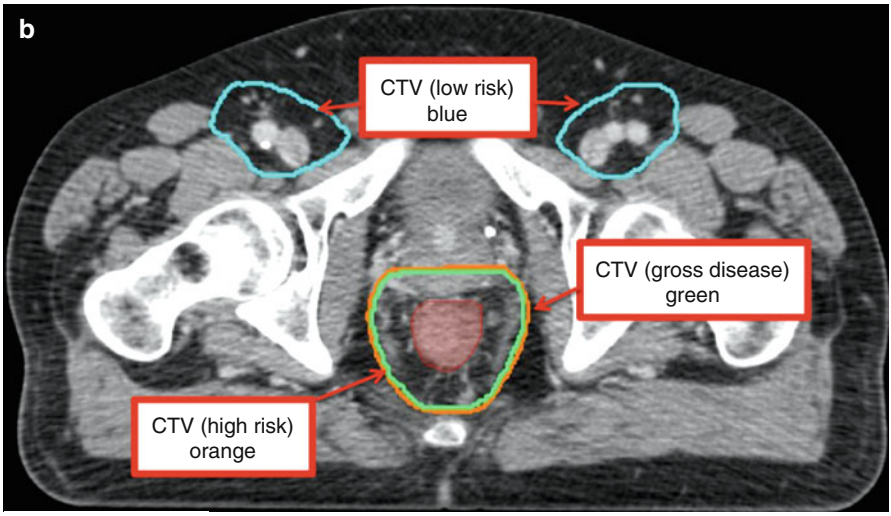

Fig. 18.2 (continued)

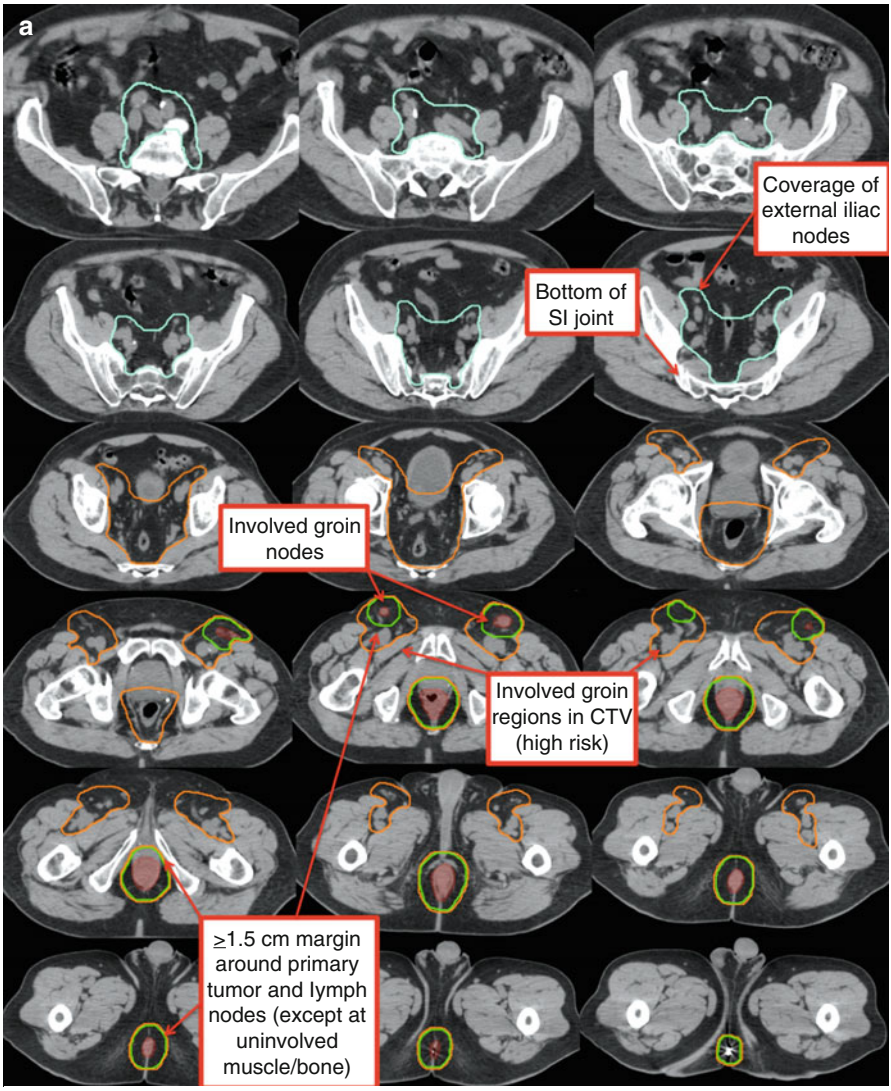

Fig. 18.3 (**a**) A patient with T3N3 anal canal cancer with bilateral inguinal lymph node involvement. This patient was simulated supine using PET/CT simulation with a 2.5-mm thickness on each slice. CTV (low risk – *cyan*), CTV (high risk – *orange*), CTV (gross disease – *green*), and GTV (*red*, *shaded*) are shown. Note that these are representative slices and not all slices are included. (**b**) Enhanced view of lower pelvis showing CTV (high risk – *orange*), CTV (gross disease – *green*), and GTV (*red*, *shaded*)

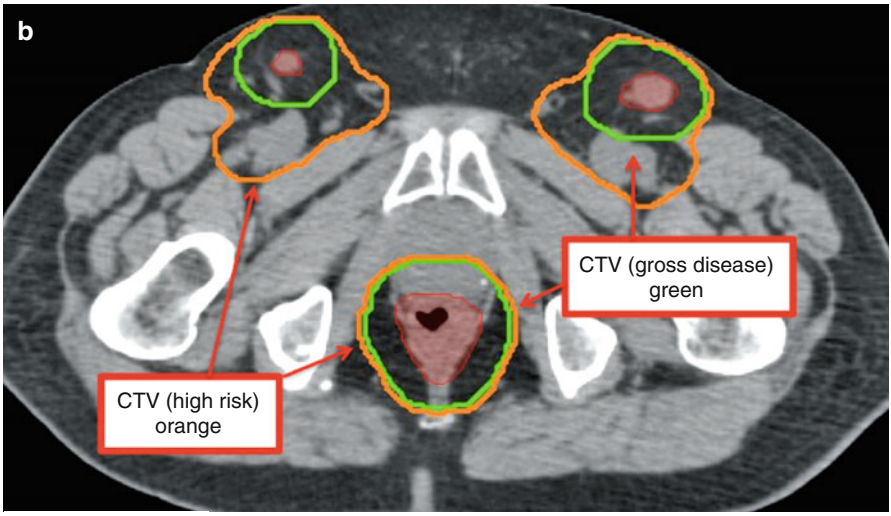

Fig. 18.3 (continued)

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Cervical Cancer

19

Arno J. Mundt, Catheryn Yashar, and Loren K. Mell

General Principles of Planning and Target Delineation

- Intensity-modulated radiation therapy (IMRT) is becoming increasingly popular in the treatment of cervical cancer, delivered either definitively or postoperatively [1, 2].
- Multiple dosimetric and clinical outcome studies have reported reduced rates of acute [3, 4] and chronic toxicities [5] and excellent long-term outcomes [6, 7] in women with cervical cancer undergoing IMRT.
- Target delineation is an essential component of IMRT treatment in cervical cancer patients. Several international consensus studies have been published in recent years focusing on target delineation in cervical cancer patients treated definitively [8] or postoperatively [9].
- All patients should undergo a complete history and physical examination including a pelvic examination as part of initial diagnosis and staging. Standard radiographic workup in these patients includes a computed tomography (CT) scan to assess the extent of local disease involvement and sites of extrauterine spread.
- In recent years, increasing attention has been focused on the role of positron-emission tomography (PET) imaging in gynecologic cancer patients undergoing radiation therapy (RT), particularly patients with cervical cancer.
- Gynecologic cancer patients undergoing IMRT are simulated in the supine position. Immobilization of the upper and lower body is recommended. Patients should be simulated with a (comfortably) full bladder. At some centers, two scans are performed (full bladder and empty bladder) and the two scans are fused to generate an integrated target volume (ITV).
- Since the patient's vasculature serves as a surrogate for the lymph nodes, it is helpful to perform a contrast-enhanced CT simulation. PET-CT simulation is

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recommended in intact cervical cancer patients to aid in the delineation of the gross tumor volume (GTV).

- Delineated target volumes in intact cervical cancer patients include a GTV and multiple clinical target volumes (CTV): CTV_1, CTV_2, and CTV_3. See Tables 19.1 and 19.2 for detailed descriptions of these components in patients treated definitively and those undergoing postoperative IMRT.
- Planning target volumes (PTVs) are created for each CTV (see Tables 19.1 and 19.2 for CTV-PTV margins), and the final PTV used for treatment planning is generated by combining the individual PTVs. Different CTV-PTV expansions are used for each CTV component based on its degree of internal organ motion and setup uncertainty [10].
- Organs at risk (OAR) used in treatment planning include the bowel, bladder, and rectum. Some investigators also include the bilateral femoral heads. In patients undergoing chemotherapy, the pelvic bone marrow (BM) may also be included. See Table 19.3 for detailed descriptions of the OARs used in cervical cancer patient undergoing IMRT treatment planning (Figs. 19.1, 19.2, 19.3, and 19.4).

Table 19.1 Target volumes used in intact cervical cancer patients undergoing IMRT

Target volumes	Definition and description
GTV	Primary tumor defined on PET or PET-CT imaging
CTV_1	GTV + uterus + cervix (if not already encompassed in the GTV) Entire uterus should be delineated including the uterine fundus
CTV_2	Parametrial/paravaginal tissues, paratuerine fat, ovaries, and proximal vagina If there is only minimal or no vaginal tumor extension, the upper ½ of the vagina is included In patients with involvement of the upper vagina, the proximal two-thirds of the vagina should be treated If there is more extensive vaginal involvement, the entire vagina should be included in the CTV_2 Soft tissues to the medial edge of internal obturator muscle/ischial ramus should be included
CTV_3	Includes common iliac,[a] external and internal iliac nodal regions, and presacral regions The common iliac and external and internal iliac regions are defined by including the pelvic vessels plus a 7-mm expansion (excluding bone, muscle, and bowel) as well as all suspicious lymph nodes, lymphoceles, and pertinent surgical clips Soft tissues between the internal and external iliac vessels along the pelvic sidewall are included The presacral area consists of the soft tissue's anterior (minimum 1.0 cm) to the S1–S2 vertebrae Upper extent: 7 mm inferior to L4–5 interspace Lower extent: superior aspect of femoral head (lower extent of external iliacs) and paravaginal tissues at level of vaginal cuff (lower extent of internal iliacs)
PTV_1	CTV_1 + 15 mm
PTV_2	CTV_2 + 10 mm
PTV_3	CTV_3 + 7 mm

The final PTV is then generated by the union of the PTV_1, PTV_2, and PTV_3: $PTV = PTV_1 \cup PTV_2 \cup PTV_3$

IMRT intensity-modulated radiation therapy, *GTV* gross tumor volume, *PET* positron-emission tomography, *CT* computed tomography, *CTV* clinical target volume, *PTV* planning target volume

[a]To the level of L4–5 which will not include the entire common iliac nodal region in many patients

Table 19.2 Target volumes used in cervical cancer patients undergoing postoperative pelvic IMRT

Target volumes	Definition and description
GTV	Not applicable
CTV_1	Vaginal cuff
	Includes any fat and soft tissue anterior and posterior to the vaginal cuff between the bladder and rectum
CTV_2	Paravaginal/parametrial tissues, proximal vagina (excluding the cuff)
CTV_3	Includes common iliac[a] and external and internal iliac nodal regions
	The presacral region is also included and consists of the soft tissues anterior (minimum 1.0 cm) to the S1–S2 vertebrae
	The common iliac and external and internal iliac regions are defined by including the pelvic vessels plus a 7-mm expansion (excluding bone, muscle, and bowel) as well as all suspicious lymph nodes, lymphoceles, and pertinent surgical clips
	Soft tissues between the internal and external iliac vessels along the pelvic sidewall are included
	The presacral area consists of the soft tissue's anterior (minimum 1.5 cm) to the S1–S2 vertebrae
	Upper extent: 7 mm inferior to L4–5 interspace
	Lower extent: superior aspect of femoral head (lower extent of external iliacs) and paravaginal tissues at level of vaginal cuff (lower extent of internal iliacs)
PTV_1	$CTV_1 + 15$ mm
PTV_2	$CTV_2 + 10$ mm
PTV_3	$CTV_3 + 7$ mm

The final PTV is then generated by the union of the PTV_1, PTV_2, and PTV_3: $PTV = PTV_1 \cup PTV_2 \cup PTV_3$

IMRT intensity-modulated radiation therapy, *GTV* gross tumor volume, *CTV* clinical target volume, *PTV* planning target volume

[a]To the level of L4–5 which will not include the entire common iliac nodal region in many patients

Table 19.3 Organs at risk (OAR)

Organ	Definition and description
Bowel	Outermost loops of bowel from the level of the L4–5 interspace to the sigmoid flexure
	Includes the sigmoid colon and ascending/descending colon present in the pelvis
	In women with intact cervical cancer, bowel loops posterior to the uterus in the lower pelvis within the PTV are not included
Rectum	Defined by the outer rectal wall from the level of the sigmoid flexure to the anus
Bladder	Defined by the outer bladder wall
Bone marrow	The pelvic bones serve as a surrogate for the pelvic bone marrow
	Regions included are the os coxae, L5 vertebral body, entire sacrum, acetabulae, and proximal femora superior extent: superior border of L5 or the iliac crest (whichever is more superior)
	Inferior extent: ischial tuberosities
Femoral heads	Entire femoral head excluding the femoral neck

PTV planning target volume

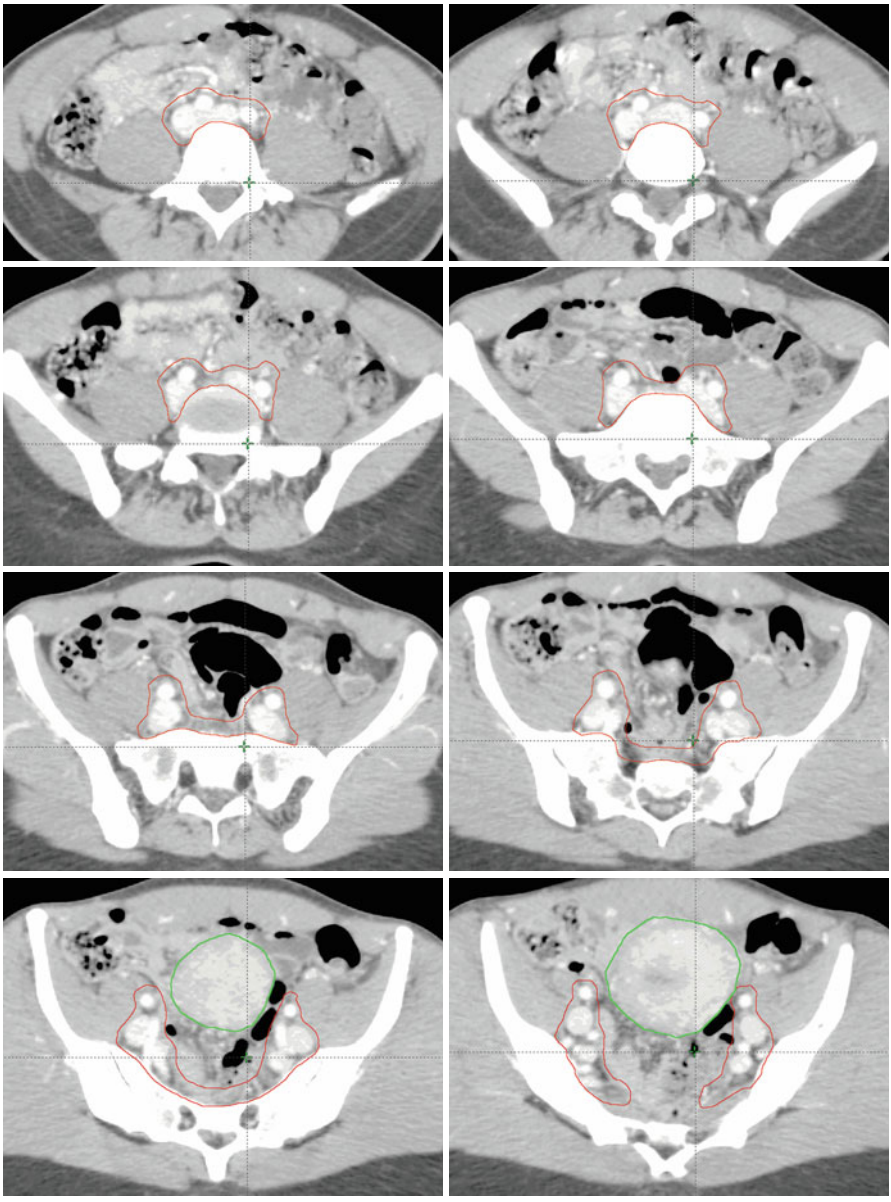


Fig. 19.1 A patient with bulky stage IIB cervical cancer undergoing definitive radiation therapy combined with concomitant chemotherapy. This patient was simulated in the supine position using a positron-emission tomography (PET)/computed tomography (CT) simulator. Target volumes shown include the gross tumor volume (GTV) (*orange*) and three clinical target volumes (CTV). CTV_1 (*green*) consists of the GTV as well as uterus and uninvolved cervix (in this patient, there was no normal cervix); CTV_2 (*blue*) includes the parametrial/paravaginal tissues, parauterine fat, ovaries, and proximal vagina; and CTV_3 (*red*) consisting of the common, internal, and external iliac lymph nodes as well as the presacral region

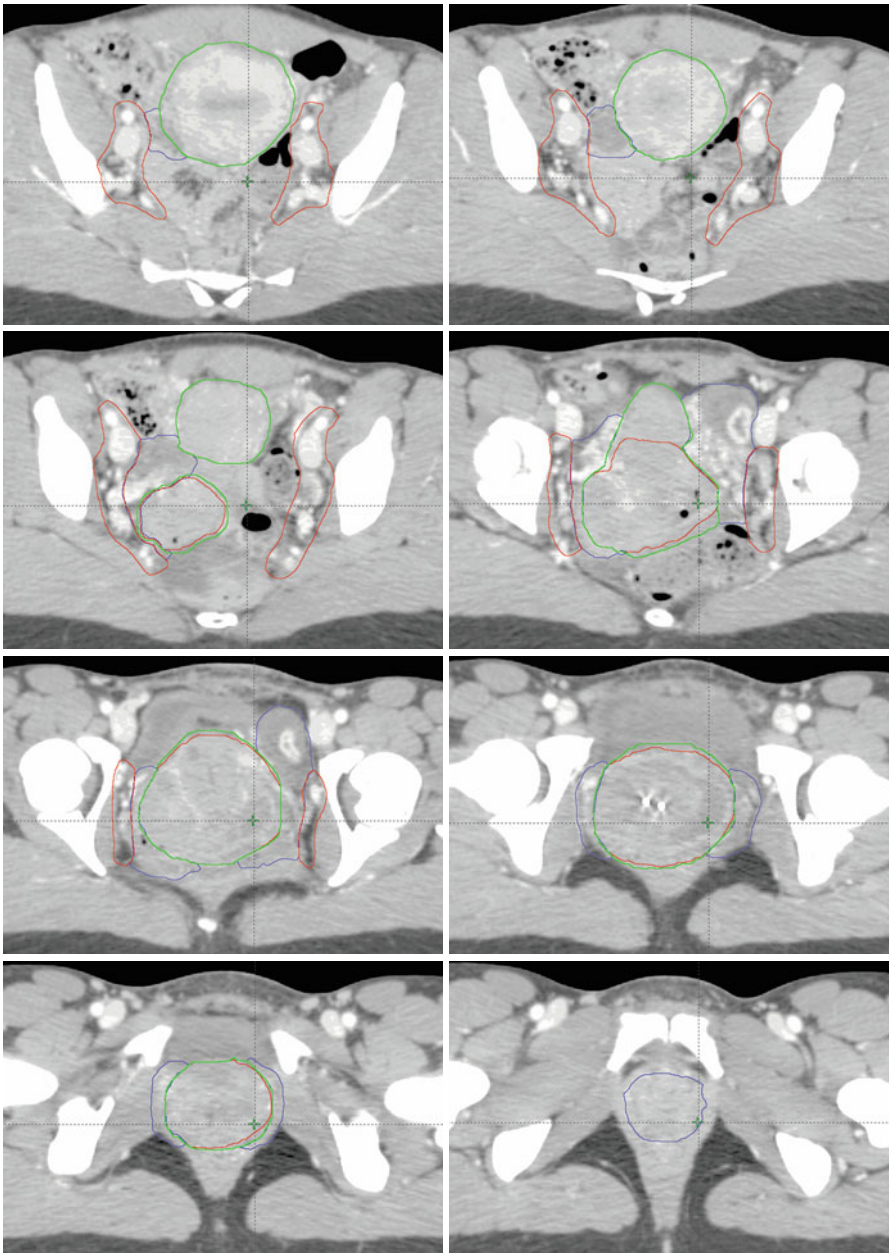


Fig. 19.1 (continued)

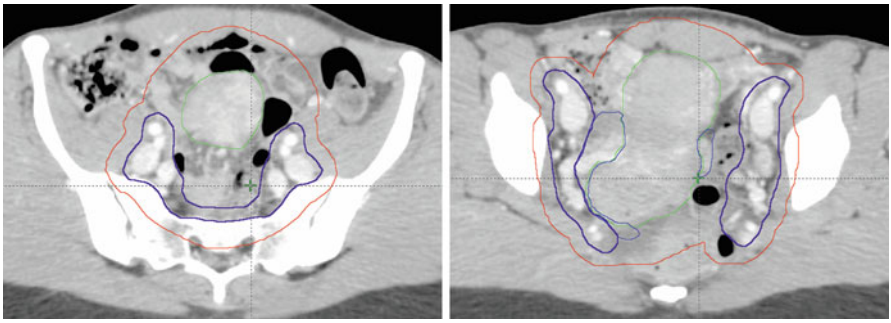


Fig. 19.2 Three separate planning target volumes (PTV) are generated in the intact cervical cancer patient described in Fig. 19.1 (see Table 19.1). The final PTV used for treatment planning is generated by combining PTV_1, PTV_2, and PTV_3. The resultant PTV (*red*) is shown in the figure encompassing CTV_1 (*green*), CTV_2 (*light blue*), and CTV_3 (*dark blue*)

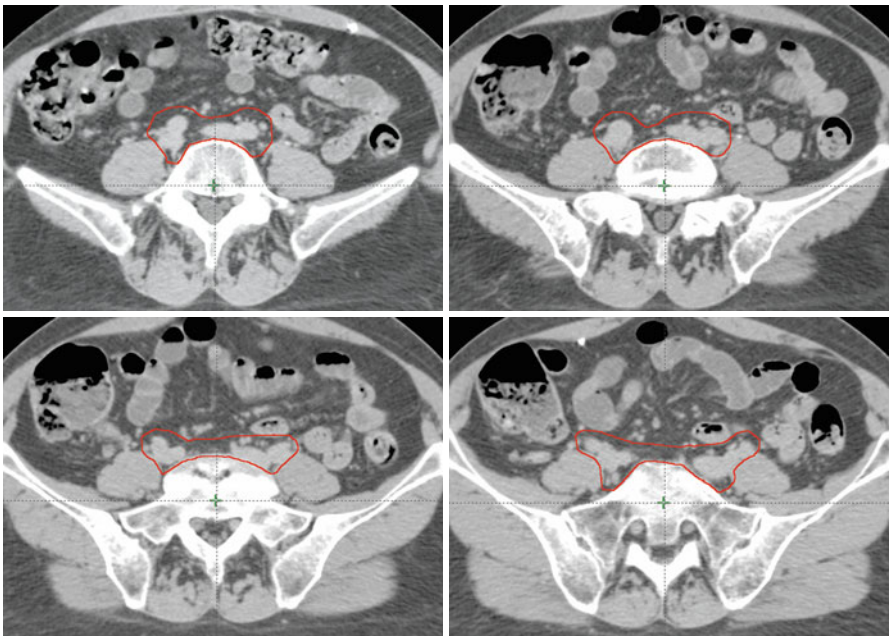


Fig. 19.3 A patient with clinical stage IB1 cervical cancer who underwent a radical hysterectomy and pelvic lymphadenectomy. Pathology revealed deep cervical stromal invasion as well as 3 of 15 positive nodes. She was treated with adjuvant intensity-modulated pelvic radiation therapy and concomitant chemotherapy. Three clinical target volumes (CTV) are shown: CTV_1 (*green*) consists of the vaginal cuff, CTV_2 (*blue*) includes the paravaginal/parametrial tissues and proximal vagina (excluding the cuff), and CTV_3 (*red*) consists of the common iliac, external and internal iliac lymph nodes, as well as presacral region

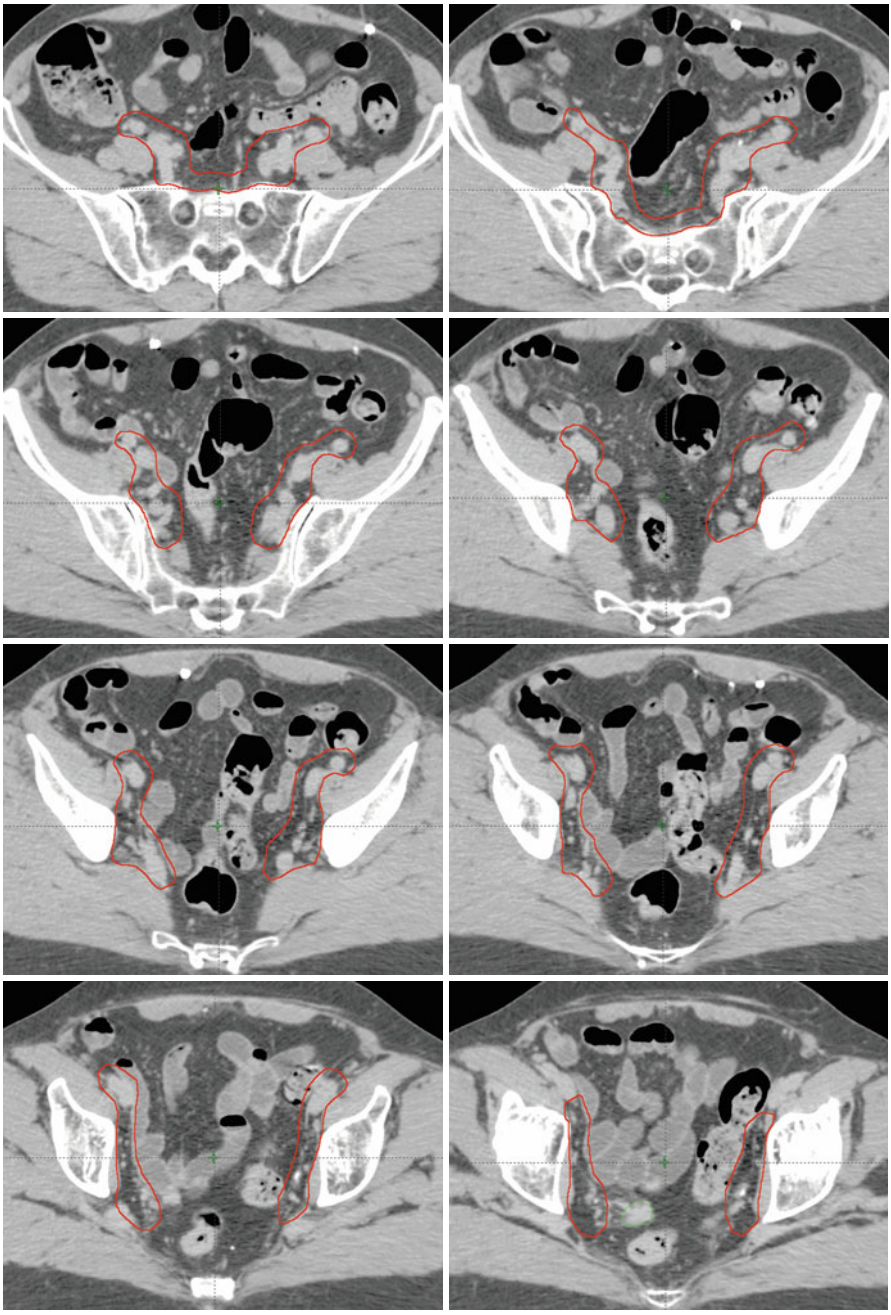
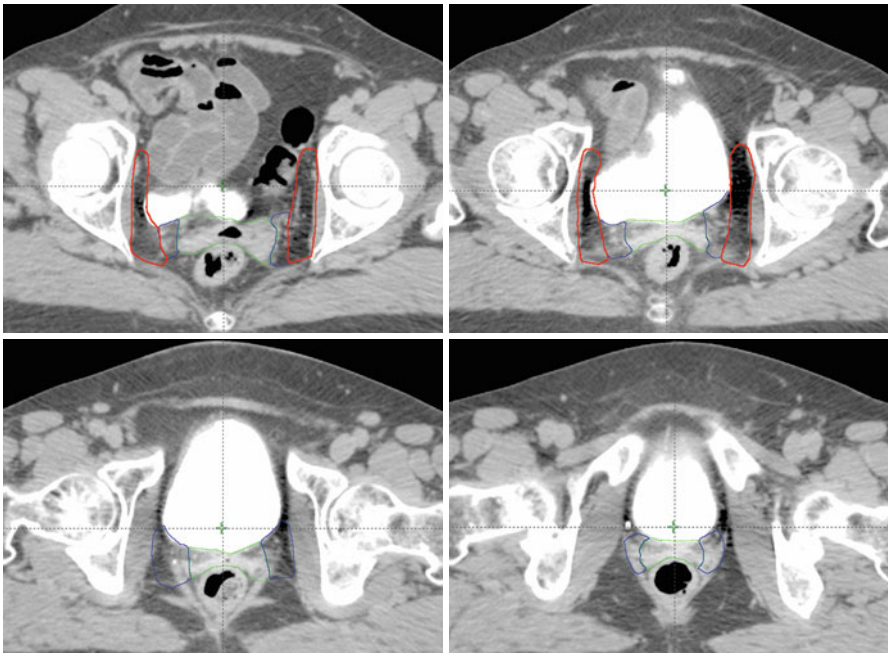


Fig. 19.3 (continued)



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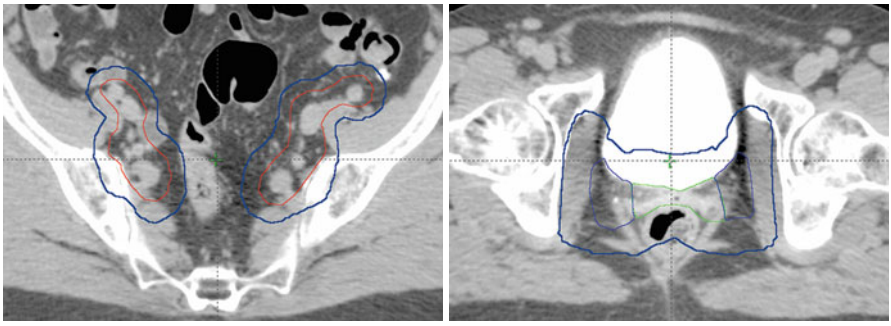

Fig. 19.4 Three separate planning target volumes (PTV) are generated in the postoperative cervical cancer patient described in Fig. 19.3 (see Table 19.1). The final PTV used for treatment planning is generated by combining PTV_1, PTV_2, and PTV_3. The resultant PTV (*dark blue*) is shown in the figure encompassing CTV_1 (*green*), CTV_2 (*light blue*), and CTV_3 (*red*)

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Endometrial Cancer

20

Arno J. Mundt, Catheryn Yashar, and Loren K. Mell

- Intensity-modulated radiation therapy (IMRT) is becoming increasingly popular in the treatment of gynecologic cancers, particularly in patients with cervical and endometrial cancers [1, 2].
- IMRT is quite appealing in endometrial cancer patients undergoing postoperative pelvic radiotherapy (RT) to reduce the volume of small bowel irradiated and thus the risk of acute and chronic toxicities [3, 4].
- Endometrial cancer patients treated with postoperative pelvic IMRT have been shown to have low rates of toxicities and high rates of pelvic control [5–7]. Long-term outcome data, however, remain limited in this setting.
- Target delineation is an essential component of IMRT treatment in endometrial cancer patients. Consensus guidelines for clinical target volume (CTV) delineation have been published [8] and have been used in the recently completed Radiation Therapy Oncology Group (RTOG) Phase II trial.
- All endometrial cancer patients should undergo a complete history and physical examination including a pelvic examination as part of initial diagnosis and staging. Standard radiographic workup in these patients includes a computed tomography (CT) scan to assess the extent of local disease involvement and sites of extrauterine spread.
- Treatment consists of upfront surgery, consisting of a total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO). Radiation therapy is delivered following surgery in women with adverse pathologic features including high-grade disease, deep myometrial invasion, cervical stromal extension, and regional lymph node involvement [9, 10].
- Traditionally, most endometrial cancer patients undergoing adjuvant RT received pelvic irradiation. However, patients undergoing surgical staging who are found to have negative nodes may undergo vaginal brachytherapy alone [11].

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DOI 10.1007/978-3-642-28860-9_20,

- Endometrial cancer patients undergoing pelvic IMRT are simulated in the supine position. Immobilization of the upper and lower body is recommended. Patients should be simulated with a (comfortably) full bladder. At some centers, two scans are performed (full bladder and empty bladder) and the two scans are fused to generate an integrated target volume (ITV).
- Since the patient's vasculature serves as a surrogate for the lymph nodes, it is helpful to perform a contrast-enhanced CT simulation.
- Delineated target volumes in uterine cancer patients undergoing adjuvant pelvic IMRT include multiple CTVs: CTV_1, CTV_2, and CTV_3. See Table 20.1 for a detailed description of these components.
- Planning target volumes (PTVs) are created for each CTV (see Table 20.1 for CTV-PTV margins), and the final PTV used for treatment planning is generated by combining the individual PTVs. Different CTV-PTV expansions are used for each CTV component based on its degree of internal organ motion and setup uncertainty.
- Organs at risk (OAR) used in treatment planning process include the bowel, bladder, and rectum. Some investigators also include the bilateral femoral heads. In patients undergoing adjuvant chemotherapy, the pelvic bone marrow (BM) may also be included and has been shown to help reduce the risk of hematologic toxicity [12]. See Table 20.2 for detailed descriptions of the OARs used in uterine cancer patient undergoing IMRT treatment planning .

Table 20.1 Target volumes used in endometrial cancer patients undergoing postoperative pelvic IMRT

Target volumes	Definition and description
GTV	Not applicable
CTV_1	Vaginal cuff Include any fat and soft tissue anterior and posterior to the vaginal cuff between the bladder and rectum
CTV_2	Paravaginal/parametrial tissues, proximal vagina (excluding the cuff)
CTV_3	Includes common iliac,[a] external and internal iliac nodal regions In patients with cervical stromal involvement, the presacral region is also included The common iliac and external and internal iliac regions are defined by including the pelvic vessels plus a 7-mm expansion (excluding bone, muscle, and bowel) as well as all suspicious lymph nodes, lymphoceles, and pertinent surgical clips Soft tissues between the internal and external iliac vessels along the pelvic sidewall are included The presacral area consists of the soft tissues anterior (minimum 1.0 cm) to the S1–S2 vertebrae Upper extent: 7 mm inferior to L4–5 interspace Lower extent: superior aspect of femoral head (lower extent of external iliacs) and paravaginal tissues at level of vaginal cuff (lower extent of internal iliacs)
PTV_1	$CTV_1 + 15$ mm
PTV_2	$CTV_2 + 10$ mm
PTV_3	$CTV_3 + 7$ mm

The final PTV is then generated by the union of the PTV_1, PTV_2, and PTV_3: $PTV = PTV_1 \cup PTV_2 \cup PTV_3$
IMRT intensity-modulated radiation therapy, *GTV* gross tumor volume, *CTV* clinical target volume, *PTV* planning target volume
[a]To the level of L4–5 which will not include the entire common iliac nodal region in many patients

Table 20.2 Organs at risk (OAR)

Organ	Definition and description
Bowel	Outermost loops of bowel from the level of the L4–5 interspace to the sigmoid flexure Includes the sigmoid colon and ascending/descending colon present in the pelvis In patients with intact cervical cancer, bowel loops posterior to the uterus in the lower pelvis within the PTV are not included
Rectum	Defined by the outer rectal wall from the level of the sigmoid flexure to the anus
Bladder	Defined by the outer bladder wall
Bone marrow	The pelvic bones serve as a surrogate for the pelvic bone marrow Regions included are the os coxae, L5 vertebral body, entire sacrum, acetabulae, and proximal femora superior extent: superior border of L5 or the iliac crest (whichever is more superior) Inferior extent: ischial tuberosities
Femoral heads	Entire femoral head excluding the femoral neck

PTV planning target volume

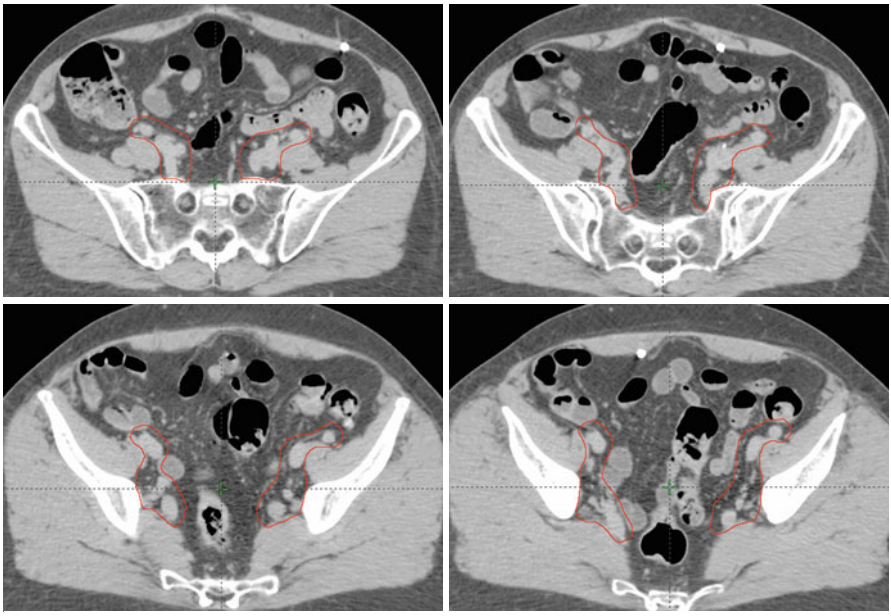

Fig. 20.1 A patient with stage IB endometrial cancer undergoing adjuvant pelvic radiation therapy. Three clinical target volumes (CTV) are shown: CTV_1 (*green*) consists of the vaginal cuff including fat and soft tissues anterior and posterior to the vaginal cuff between the bladder and rectum, CTV_2 (*blue*) includes the paravaginal/parametrial tissues and proximal, vagina (excluding the cuff) and CTV_3 (*orange*) consists of the common, external and internal iliac lymph node regions. In this patient, the pre-sacral region is not included

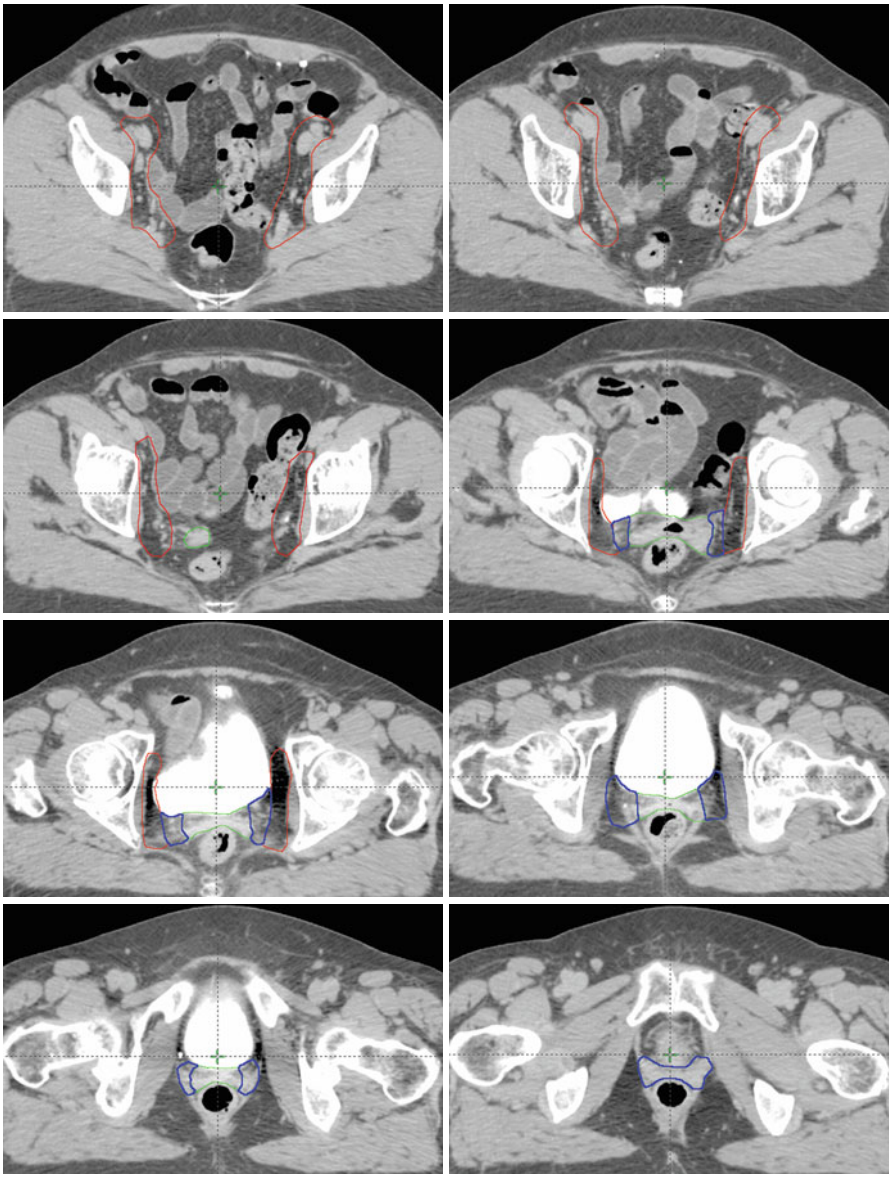

Fig. 20.1 (continued)

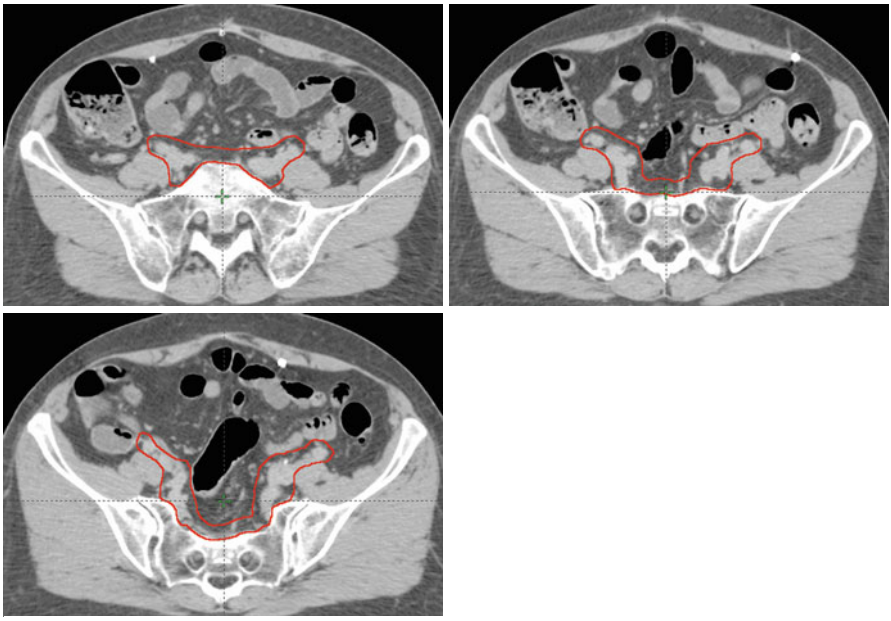

Fig. 20.2 The clinical target volume-3 (CTV_3) (*orange*) is modified in endometrial cancer patients with cervical stromal invasion to include the pre-sacral region

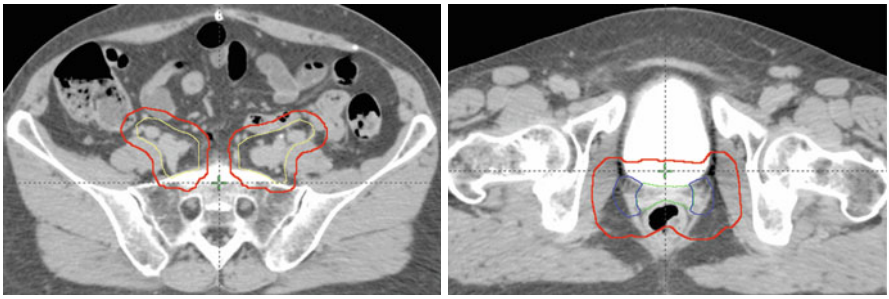

Fig. 20.3 Three separate planning target volumes (PTV) are generated in the postoperative endometrial cancer patient described in Figure 1 (see Table 1). The final PTV used for treatment planning is generated by combining PTV_1, PTV_2 and PTV_3. The resultant PTV (*red*) is shown in the figure encompassing CTV_1 (*green*), CTV_2 (*blue*) and CTV_3 (*yellow*)

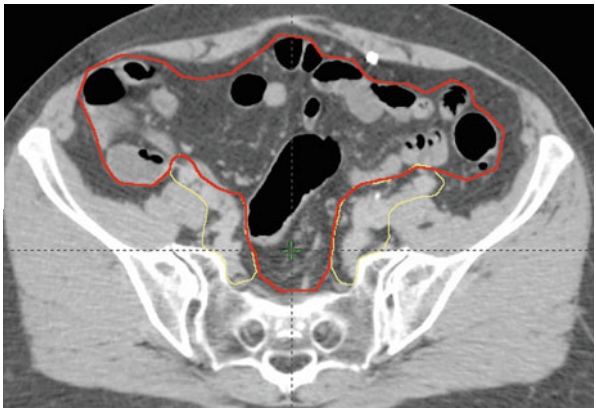

Fig. 20.4 Bowel contours (*red*) on a representative computed tomography (CT) slice in the patient described in Figure 1. The clinical target volume0-3 (CTV_3) is shown in *yellow*

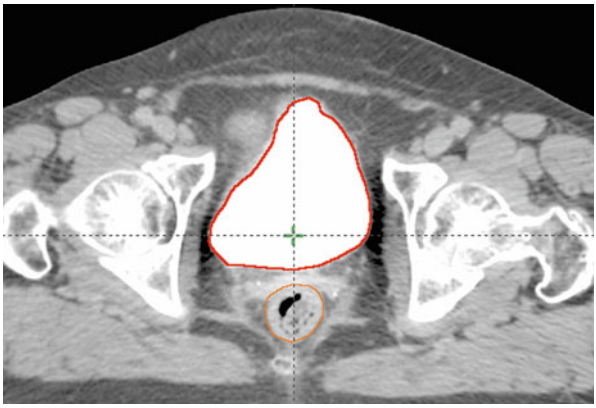

Fig. 20.5 Bladder (*red*) and rectal (*orange*) contours on a representative computed tomography (CT) slice in the patient described in Figure 1

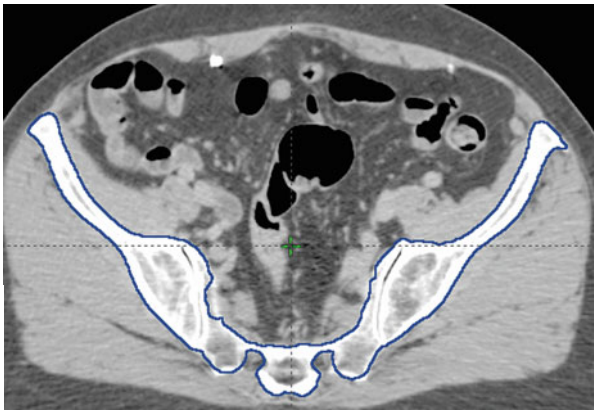

Fig. 20.6 Pelvic bone marrow (*dark blue*) contours ina patiet with endometrial cancer undergoing concomitant chemoradiotheraphy

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Ovarian Cancer

21

Arno J. Mundt, Catheryn Yashar, and Loren K. Mell

- Radiation therapy (RT) has long occupied a role in the treatment of ovarian cancer and is typically delivered following upfront surgery consisting of omentectomy, total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO), peritoneal sampling, and cytoreduction of gross peritoneal disease and often pelvic and para-aortic lymph node dissection.
- The predominant RT approach in these patients is whole abdominal RT (WART) (also known as abdominopelvic RT). Long-term outcomes were highly favorable in ovarian cancer patients treated with adjuvant WART, especially in women with microscopic or no residual disease [1, 2].
- Despite favorable treatment results and even a prospective phase III randomized trial demonstrating identical survival rates following WART or chemotherapy [3], WART has been largely abandoned at many centers at least those in the USA.
- The question remains whether there is a role for adjuvant WART in conjunction with chemotherapy and surgery. Multiple prospective clinical trials have reported favorable results using surgery and chemotherapy plus WART in locally advanced patients [4, 5].
- Given the large volumes irradiated and multiple organs at risk (OAR), intensity-modulated WART (IM-WART) has been proposed as an alternative to conventional RT techniques in patients with ovarian cancer. Multiple dosimetric studies have reported significant sparing of OAR using IMRT planning, including the kidneys, liver, and pelvic bones [6–8]. Clinical outcome data, however, remain limited in patients treated with IM-WART [9–11].

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- Patients undergoing IM-WART should be simulated in the supine position, with customized immobilization of the upper and lower body. Since the patient's vasculature serves as a surrogate for the lymph node regions, it may be helpful to perform a contrast-enhanced CT simulation.
- A gross tumor volume (GTV) is not typically contoured since these patients are treated adjuvantly; however, a GTV should be specified in patients with enlarged unresected lymph nodes or other gross disease sites.
- A clinical target volume (CTV) is contoured on each axial computed tomography (CT) slice and consists of the entire peritoneal cavity including the pelvic and para-aortic lymph node regions and liver surface. If a "pelvic boost" is planned, a second CTV (CTV_{pelvis}) should be contoured. Moreover, if the pelvic and/or para-aortic lymph nodes are to be taken to a higher dose, a CTV_{nodal} should also be contoured.
- No consensus guidelines currently exist regarding target delineation or treatment planning in ovarian cancer patients undergoing IM-WART. Given the declining use of WART in this setting, it is unlikely such guidelines will ever be produced.
- A planning target volume (PTVs) should be created for the CTV (or CTVs). The optimal CTV-PTV margin in patients undergoing IM-WART (Table 21.1) remains unclear; our recommendation is 1 cm.
- At many centers, the PTV is taken to a total dose of 30 Gy in 1.5 Gy daily fractions. If a pelvic boost is delivered, the total pelvic dose should be approximately 45–50.4 Gy. Additional nodal boosts (if delivered) should be based on the size of involved lymph nodes.
- OARs used in treatment planning include the bilateral kidneys, liver (except 1 cm of the outer surface), vertebral bodies, and pelvic bones (as a surrogate for bone marrow). Some investigators include the heart and bilateral femoral heads. A planning margin (0.5 cm) may be added around the bilateral kidneys to account for internal organ motion of the kidneys. See Table 21.2 for a description of the OARs used in patients undergoing IM-WART (Fig. 21.1).

Table 21.1 Target volumes used in ovarian cancer patients undergoing adjuvant IM-WART

Target volumes	Definition and description
GTV	Not applicable
CTV	Entire peritoneal cavity Upper extent: top of the diaphragms Lower extent: bottom of the obturator foramina Liver surface (outer 1 cm of liver) Pelvic and para-aortic lymph nodes
CTV_{pelvis}	Peritoneal cavity within the pelvis Pelvic lymph nodes Upper extent: 7 mm inferior to the L4–5 interspace Lower extent: bottom of the obturator foramina
CTV_{nodal}	Select pelvic and/or para-aortic lymph nodes
PTV	CTV + 1.0 cm
PTV_{pelvis}	CTV_{pelvis} + 1.0 cm
PTV_{nodal}	CTV_{nodal} + 0.7 cm

IM-WART intensity-modulated whole abdominal radiotherapy, *GTV* gross tumor volume, *CTV* clinical target volume, *PTV* planning target volume
[a]Some investigators contour the lymph node regions separately

Table 21.2 Organs at risk (OAR)

Organ	Definition and description
Kidneys	Entire kidney parenchyma[a]
Liver	Entire liver excluding a 1-cm outer border
Heart	Entire heart
Bone marrow	Vertebral bodies and pelvic bones serve as a surrogate for the bone marrow Regions included are the vertebral bodies (within the PTV), os coxae, entire sacrum, acetabulae, and proximal femora Superior extent: superior border of the PTV Inferior extent: ischial tuberosities
Femoral heads	Entire femoral head excluding the femoral neck

[a]An additional 0.5-cm planning margin may be added to account for internal organ motion

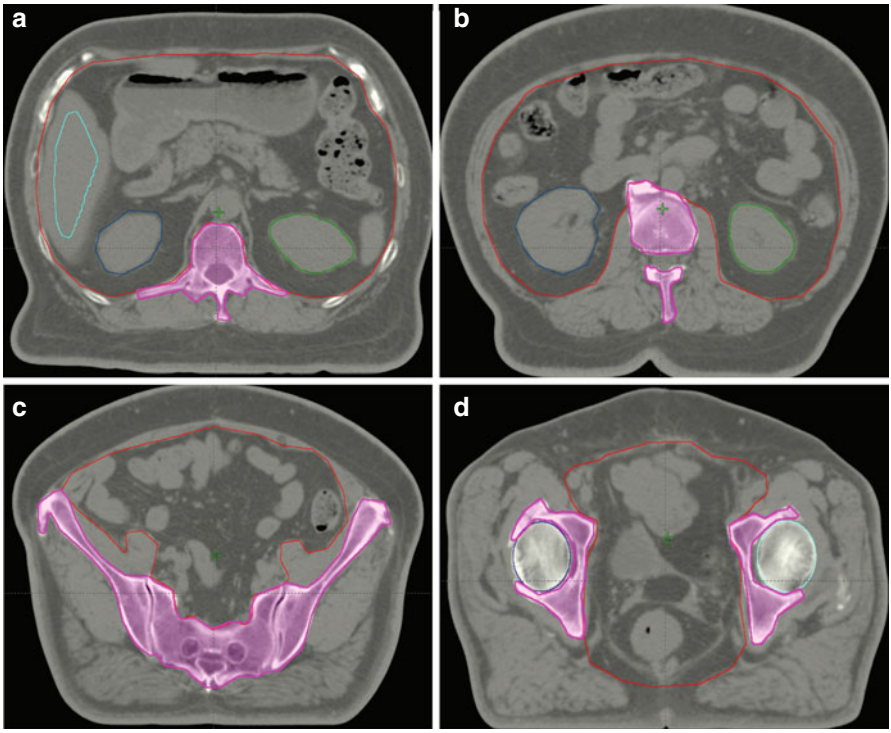

Fig. 21.1 A patient with stage IIIC grade 3 ovarian cancer who underwent upfront surgery and optimal cytoreduction. (**a**) Upper abdomen. Clinical target volume (CTV) (*red*), liver (*light blue*), right kidney (*dark blue*), left kidney (*green*), and vertebral body (*purple*). Not that a 1-cm rim of the outer edge of the liver is included in the CTV. (**b**) Mid abdomen. Clinical target volume (CTV) (*red*), right kidney (*dark blue*), left kidney (*green*), and bone (*purple*). (**c**) Upper pelvis. Clinical target volume (CTV) (*red*) and bone (*purple*). (**d**) Mid pelvis. Clinical target volume (CTV) (*red*), bone (*purple*), right (*dark blue*), and left (*light blue*) femoral heads

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Vaginal Cancer

22

Arno J. Mundt, Catheryn Yashar, and Loren K. Mell

- Radiation therapy (RT) is the treatment of choice of most patients with vaginal cancer. Select early-stage patients with small volume disease limited to the upper vagina, however, can be treated with either a partial or radical vaginectomy [1].
- Early-stage vaginal cancer patients typically receive brachytherapy alone or combined with external beam RT in cases with invasion into the paravaginal tissues. At some centers, external beam RT is added even in early-stage patients [2]. Overall, high rates of local control and survival are achieved, particularly in women with stage I disease [2, 3].
- All patients with locally advanced disease should receive a combination of external beam RT and brachytherapy. The type of brachytherapy is dependent on disease extent, with intracavitary brachytherapy used for superficially invasive disease (<0.5 cm invasion) and interstitial brachytherapy for all other tumors. Chemotherapy is administered concomitantly at many centers in an attempt to augment patient outcomes (extrapolating from the experience in cervical cancer).
- Various external beam approaches are used in vaginal cancer patients depending on tumor location and disease extent. In women with disease limited to the upper two-thirds of the vagina, pelvic RT is delivered. Those with involvement of the lower one-third of the vagina are treated with pelvic-inguinal RT.
- Given the large volumes irradiated and the growing experience using intensity-modulated RT (IMRT) in gynecologic cancer patients [4, 5], IMRT is often used in the treatment of patients with vaginal cancer. To date, no dosimetric or clinical studies have been published supporting this approach.

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- All vaginal cancer patients undergoing IMRT should be simulated in the supine position, with customized immobilization of the upper and lower body. Since the patient's vasculature serves as a surrogate for the lymph nodes, it may be helpful to perform a contrast-enhanced CT simulation. PET-CT simulation is helpful in the delineation of the gross tumor volume (GTV).
- Patients should be simulated with a (comfortably) full bladder. At some centers, two scans are performed (full bladder and empty bladder) analogous to cervical cancer patients and the two scans are fused to generate an integrated target volume (ITV). This is particularly appealing in the treatment of tumors in the upper vagina which may be more susceptible to displacement by the bladder and rectum.
- Unlike cervical and endometrial cancer [6, 7], no consensus guidelines currently exist regarding target delineation or treatment planning in vaginal cancer patients undergoing IMRT. Given the rarity of this disease, it is unlikely such guidelines will ever be produced.
- Delineated target volumes are GTV and two clinical target volumes (CTV). The CTV_1 should include the GTV plus adjacent uninvolved vagina. The CTV_2 should encompass the paravaginal/parametrial tissue pelvic lymph nodes. In women with involvement of the lower one-third of the vagina, the CTV_2 should also include the bilateral inguinofemoral lymph nodes. See Table 22.1 for a detailed description of the target volumes in these patients.
- Planning target volumes (PTVs) are created for each CTV (Table 22.1), and the final PTV used for treatment planning is generated by combining the individual PTVs. Since optimal CTV-PTV expansions are not known in vaginal cancer, it is recommended to use the similar expansions used in patients with cervical cancer [8].
- Organs at risk (OAR) used in treatment planning include the bowel, bladder, and rectum. In patients with involvement of the lower one-third of the vagina undergoing pelvic-inguinal IMRT, the bilateral femoral heads and anus should also be included. In women undergoing chemotherapy, the pelvic bone marrow (BM) may also be included. See Table 22.2 for detailed descriptions of the OARs used in vaginal cancer (Fig. 22.1).

Table 22.1 Target volumes used in vaginal cancer patients undergoing IMRT

Target volumes	Definition and description
GTV	Primary tumor defined on CT or PET-CT imaging
CTV_1	GTV plus a minimum of 3 cm of vagina superiorly and inferiorly
CTV_2	Paravaginal/parametrial tissues adjacent to CTV_1 In patients with disease limited to the upper two-thirds of the vagina, the pelvic lymph nodes (common iliac,[a] external and internal iliac nodal regions, and presacral regions) should be included. The common iliac and external and internal iliac regions are defined by including the pelvic vessels plus a 7-mm expansion The presacral area consists of the soft tissues anterior (minimum 1.0 cm) to the S1–S2 vertebrae In patients with disease involving the lower one-third of the vagina, the bilateral inguinofemoral lymph nodes should also be included Bilateral inguinofemoral lymph nodes are defined by including generous margins (1–1.5 cm)[b] around the vessels (excluding bone and muscle and skin) as well as any visualized lymph nodes in adjacent fat/soft tissues
PTV_1	$CTV_1 + 15$ mm[c]
PTV_2	$CTV_2 + 7$ mm

The final PTV is then generated by the union of the PTV_1 and PTV_2: $PTV = PTV_1 \cup PTV_2$ and may be needed to be trimmed back from the skin surface in the inguinal regions (in patients with lower vaginal tumors/extension)

IMRT intensity-modulated radiation therapy, *GTV* gross tumor volume, *PET* positron-emission tomography, *CT* computed tomography, *CTV* clinical target volume, *PTV* planning target volume

[a]To the level of L4–5 which will not include the entire common iliac nodal region in many patients. At some centers, patients with negative pelvic lymph nodes are treated with a reduced pelvic field with an upper border at the level of the sacroiliac joints

[b]The margin needed around the inguinofemoral vessels remains controversial

[c]This margin can be reduced to 1 cm for tumors confined to the vagina

Table 22.2 Organs at risk (OAR)

Organ	Definition and description
Bowel	Outermost loops of bowel from the level of the L4–5 interspace to the sigmoid flexure Includes the sigmoid colon and ascending/descending colon present in the pelvis In women with intact cervical cancer, bowel loops posterior to the uterus in the lower pelvis within the PTV are not included
Rectum	Defined by the outer rectal wall from the level of the sigmoid flexure to the anus
Anus	Defined by the outer wall of the anus
Bladder	Defined by the outer bladder wall
Bone marrow	The pelvic bones serve as a surrogate for the pelvic bone marrow Regions included are the os coxae, L5 vertebral body, entire sacrum, acetabulae, and proximal femora superior extent: superior border of L5 or the iliac crest (whichever is more superior) Inferior extent: ischial tuberosities (in patients with upper vaginal lesions) and the lower extent of the PTV (in patients with lower vagina tumors)
Femoral heads	Entire femoral head excluding the femoral neck

PTV planning target volume

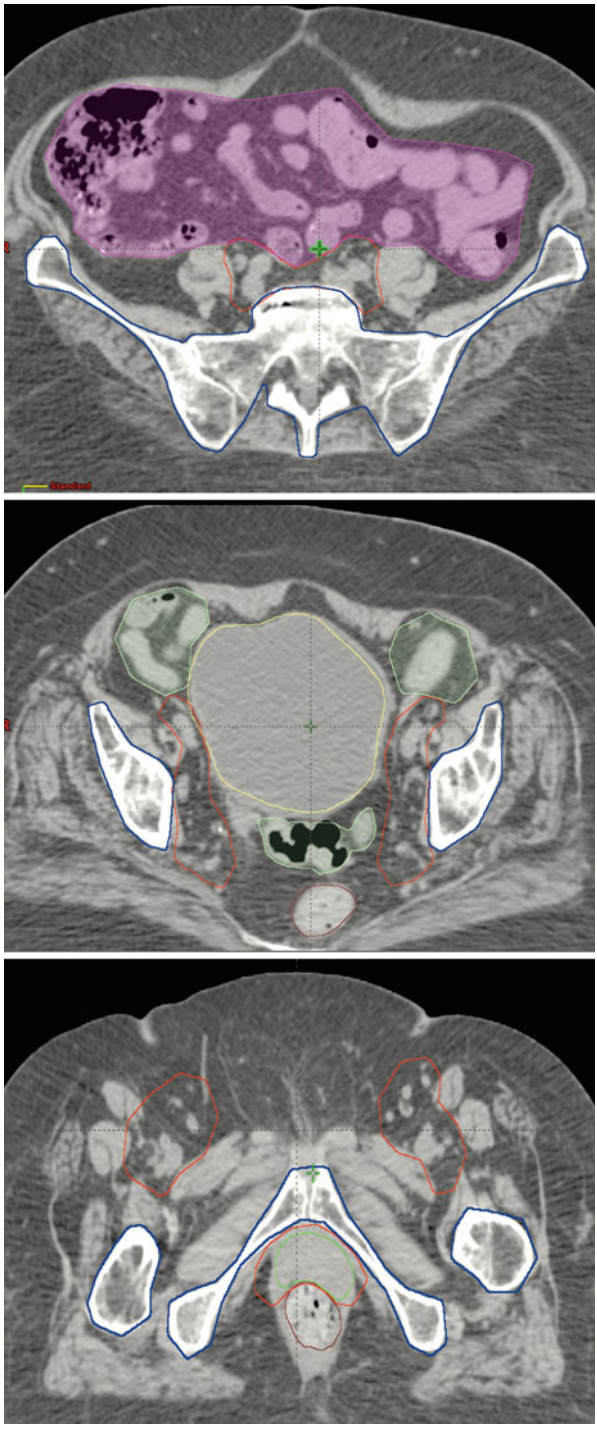

Fig. 22.1 A patient with stage IIB vaginal cancer treated with external beam radiation therapy (RT) and concomitant chemotherapy followed by interstitial brachytherapy. (**a**) Upper pelvis. Clinical target volume-2 (CTV_2) (*red*), pelvic bones (*dark blue*), and bowel (*purple*). (**b**) Mid pelvis. CTV_2 (*red*), bowel (*green*), rectum (*brown*), and bones (*dark blue*). (**c**) Lower pelvis. CTV_2 (*red*), gross tumor volume (*green*), pelvic bones (*dark blue*), and rectum (*brown*)

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Vulvar Cancer

23

Arno J. Mundt, Catheryn Yashar, and Loren K. Mell

- The treatment of vulvar cancer consists of upfront surgery, typically radical vulvectomy or wide local excision in select patients with small well-lateralized tumors. Most patients undergo bilateral inguinofemoral dissections, particularly those found to have tumor invasion >3 mm, lymphovascular invasion (LVI) and/or high-grade disease.
- Radiation therapy (RT) is typically delivered following surgery in women with high-risk features including LVI, tumor invasion >5 mm, surgical margins <8 mm, grade 3 disease, positive lymph nodes, and/or microscopic positive margins [1–3].
- Women presenting with unresectable disease are candidates for preoperative RT [4, 5]. At many centers, such patients also receive concomitant chemotherapy [6–8].
- The standard RT approach in vulvar cancer patients consists of pelvic-inguinal irradiation. Brachytherapy has a limited role in vulvar cancer patients, apart from women with a positive vaginal margin or those with medically inoperable disease.
- Given the large volumes irradiated and the growing experience using intensity-modulated RT (IMRT) in gynecologic cancer patients [9, 10], IMRT is receiving increasing attention in the treatment of vulvar cancer.
- Dosimetric and preliminary clinical studies have reported superior normal tissue sparing and lower rates of acute and chronic toxicities in vulvar cancer patients receiving IMRT compared to those undergoing conventional approaches [11–14]. Long-term outcome in these patients, however, remains limited.

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- Vulvar cancer patients undergoing IMRT are simulated supine in a modest frog-leg position, with customized immobilization of the upper and lower body. Since the patient's vasculature serves as a surrogate for the lymph nodes, it may be helpful to perform a contrast-enhanced computed tomography (CT) simulation. It is advisable to simulate all patients with bolus placed over the vulva, particularly in patients treated preoperatively.
- Positron-emission tomography (PET)-CT simulation may be helpful in the delineation of the gross tumor volume (GTV) in patients undergoing preoperative IMRT.
- Unlike cervical and endometrial cancer [15, 16], no consensus guidelines currently exist guiding target delineation or treatment planning in vulvar cancer patients undergoing IMRT. Fortunately, consensus guidelines are expected in the near future.
- Delineated target volumes in vaginal cancer patients include a GTV (in preoperative patients) and two clinical target volumes (CTV). CTV_1 encompasses the GTV, uninvolved vulvar tissue, and adjacent soft tissues. CTV_2 includes the pelvic and inguinofemoral lymph nodes bilaterally. Each CTV is then expanded to create planning target volumes (PTVs). See Table 23.1 for a description of these volumes.
- Organs at risk (OAR) used in treatment planning process typically include the bowel, bladder, rectum, anus, and bilateral femoral heads. In women undergoing chemotherapy, the pelvic bone marrow (BM) may also be included. See Table 23.2 for detailed descriptions of the OARs used in vulvar cancer (Fig. 23.1).

Table 23.1 Target volumes used in vulvar cancer patients undergoing IMRT

Target volumes	Definition and description
GTV	Primary tumor defined on CT or PET/CT imaging (preoperative patients only)
CTV_1	GTV plus remaining uninvolved vulva and adjacent soft tissues
CTV_2	Pelvic and bilateral inguinofemoral lymph node regions
	The pelvic lymph nodes (common iliac,[a] external and internal iliac nodal regions) are defined by including the pelvic vessels plus a 7 mm expansion
	The presacral area should be included in patients with vaginal involvement and consists of the soft tissues anterior (minimum 1.0 cm) to the S1–S2 vertebrae
	In patients with anal/rectal involvement, the perirectal lymph nodes should also be included
	Inguinofemoral lymph nodes are defined by including generous margins (1–1.5 cm)[b] around the vessels (excluding bone and muscle and skin) as well as any visualized lymph nodes in adjacent fat/soft tissues
PTV_1	$CTV_1 + 10$ mm
PTV_2	$CTV_2 + 7$ mm

The final PTV is then generated by the union of the PTV_1 and PTV_2: $PTV = PTV_1 \cup PTV_2$ and may be needed to be trimmed back from the skin surface in the inguinal nodal region

IMRT intensity-modulated radiation therapy, *GTV* gross tumor volume, *PET* positron-emission tomography, *CT* computed tomography, *CTV* clinical target volume, *PTV* planning target volume

[a]To the level of L4–5 which will not include the entire common iliac nodal region in many patients. At some centers in patients with negative pelvic lymph nodes, the common iliacs are not included, and the upper extent of the treatment volume is limited to the bottom of the sacroiliac joints

[b]The margin needed around the inguinofemoral vessels remains controversial

Table 23.2 Organs at risk (OAR)

Organ	Definition and description
Bowel	Outermost loops of bowel from the level of the L4–5 interspace to the sigmoid flexure
	Includes the sigmoid colon and ascending/descending colon present in the pelvis
	In women with intact cervical cancer, bowel loops posterior to the uterus in the lower pelvis within the PTV are not included
Rectum	Defined by the outer rectal wall from the level of the sigmoid flexure to the anus
Anus	Defined by the outer wall of the anus
Bladder	Defined by the outer bladder wall
Bone marrow	The pelvic bones serve as a surrogate for the pelvic bone marrow
	Regions included are the os coxae, L5 vertebral body, entire sacrum, acetabulae, and proximal femora
Femoral heads	Entire femoral head excluding the femoral neck

PTV planning target volume

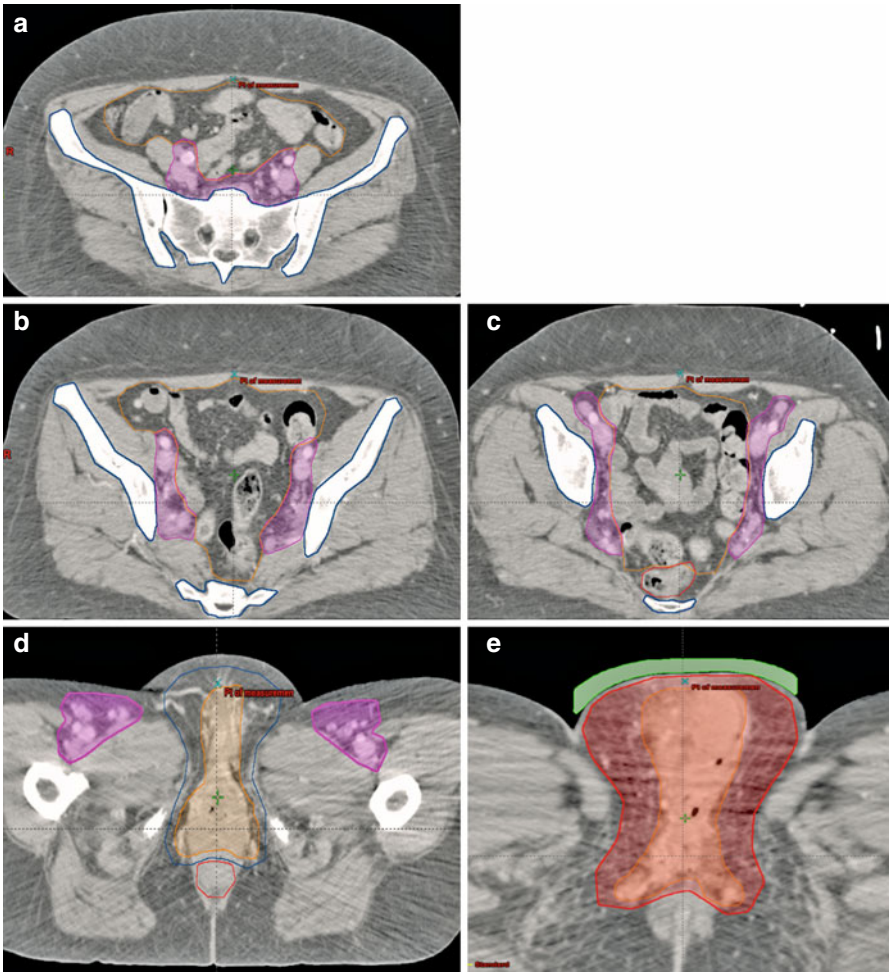

Fig. 23.1 A patient with unresectable vulvar cancer undergoing preoperative intensity modulated radiation therapy (IMRT) and concomitant chemotherapy. (**a**) Upper pelvis. Clinical target volume-2 (CTV_2) (*purple*), pelvic bones (*dark blue*), and bowel (*orange*). (**b**) Mid upper pelvis. CTV_2 (*purple*), bowel (*orange*), and pelvic bones (*dark blue*). (**c**) Mid lower pelvis. CTV_2 (*purple*), pelvic bones (*dark blue*), rectum (*red*), and bowel (*orange*). (**d**) Lower pelvis. CTV_2 (*purple*), gross tumor volume (*orange*), CTV_1 (*blue*), and rectum (*red*) (**e**) Vulvar region. GTV (*orange*) CTV_1 (*blue*) and overlying bolus (*green*) placed on the vulva

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Prostate Adenocarcinoma

24

Neil Desai and Michael Zelefksy

General Principles of Planning and Target Delineation

- Intensity-modulated radiation therapy (IMRT) is the standard technique for external beam radiation therapy (EBRT) of prostate adenocarcinoma. Various fractionation schemes exist, and EBRT is used in both the definitive and post-operative settings. However, all approaches rely on accurate target delineation to realize safely the benefits of dose escalation. This chapter will describe the approach at MSKCC and provide walk-throughs of typical scenarios.
- Initial case workup includes digital rectal examination, urinary and erectile function scores, and relevant labs. MRI with endorectal coil is recommended for evaluation for extracapsular extension, seminal vesicle invasion, intravesicular extension, BPH, and evidence of gross disease requiring dose painting post-operatively.
- CT simulation is performed at MSKCC with 2-mm slice thickness:
  - Image guidance: gold fiducials or Calypso® beacons should be placed at least 5 days prior.
  - Preparation: bowel prep night prior, PO contrast 90 min before sim.
  - Immobilization: mold such as Aquaplast® in supine position.
  - Regimen specific protocols: full bladder, foley catheter for urethral delineation, and MRI fusion for dose painting.
- Clinical target volume (CTV) should be delineated on every slice of the planning CT. A general description of target volumes and margins are indicated in Table 24.1.

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Table 24.1 Suggested target volumes for EBRT and contouring concepts

Treatment setting	Protocol	Dose (cGy)*	PTV margin	CTV description
Definitive	Conventional	8,000–8,600	6 mm	Prostate and seminal vesicles (Fig. 24.1)
	Hypo-fractionated (full bladder, foley)	700 or higher × 5	5 mm except at rectum (3 mm)	• Begin contours mid-gland where prostate borders are most easily identifiable • Caudally, identify apex relative to GUD based on landmarks noted in the figure that identify the convergence of the levator ani (i.e., "slit" of McLaughlin et al.) • Lateral boundary = levator ani • Anterior = anterior fibromuscular stroma (AFS) • Posteriorly, rectum is opposed at mid-gland but falls away caudally, so trace rectum from anal canal to avoid error • Superiorly, incorporate SV but not the associated vasculature above into the final CTV. The SV can be contoured separately, but using one structure smoothens transition aids consistent interpretation of the adjacent bladder • Check 3D structure to assess for symmetry and interpretation errors. See Fig. 24.2
Adjuvant/salvage	(Full bladder)	7,200 ± dose painting boost to gross residual disease	10 mm except at rectum (6 mm)	• Within RTOG guidelines (Figs. 24.3 and 24.4): • Caudally begin just above GUD. Identify vesicourethral anastomosis (VUA) as slice below last with urine and begin contouring 8–12 mm below. MRI fusion may aid • At superior border of pubic symphysis, pull back anterior border gradually over 3–4 slices to the 3-mm margin allowed on bladder, forming classic "dumbbell" shape noted in the figure • Cranial border should extend approximately 2 cm above the pubic symphysis, but it is not necessary to encompass all hemostatic clips • Laterally bound by obturator internus • Dose paint gross residual disease on MRI (Fig. 24.7b)

Either	Pelvic nodes	4,500	10 mm	• Non-RTOG (see Fig. 24.5): • Target vessels: common iliac below L5–S1 interspace, external iliac, internal iliac into pudendal, and obturator vessels • Posterior boundary of PTV (internal iliac branches) is most prone to over-contouring which would increase dose to rectum • Stopping points: end external iliac at top of femoral head, end inferior node contours (obturator/pudendal) at superior aspect of pubic symphysis

*Doses provided here are specific to to current practices at MSKCC. Prescriptions for definitive treatment of intact prostate in particular should be specified based on doses validated for efficacy and safety with the treatment planning and setup allowances specific to each institution's practice

- Volume walk-throughs: see Figs. 24.1, 24.2, 24.3, 24.4, and 24.5 for examples of treatment of the prostate and seminal vesicles (SV), pelvic nodes, and post-operative fossa. Special cases are highlighted in Figs. 24.6 and 24.7. General concepts of target delineation and quality assessment are highlighted:
  - Key anatomic boundaries and landmarks to guide interpretation
  - Quality assessment via 3D projection

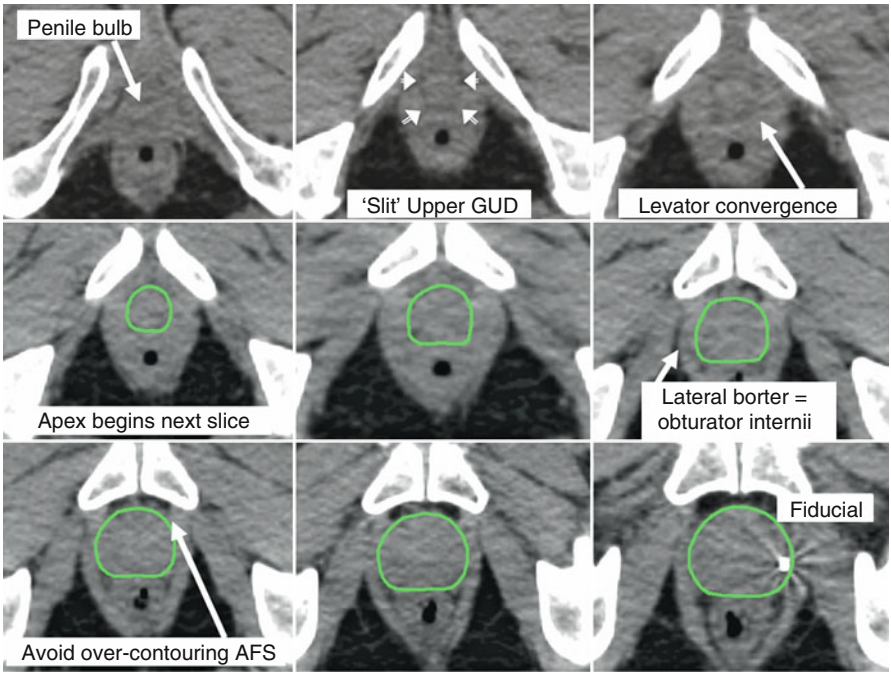

Fig. 24.1 A patient with low-risk NCCN criteria disease with suggestion on MRI of possible seminal vesicle (SV) invasion treated definitively to the prostate and SV. This series of representative images from a 2-mm slice thickness CT simulation demonstrates general boundary discrimination and CTV delineation. They begin at the apex and proceed caudally. Not all slices are shown

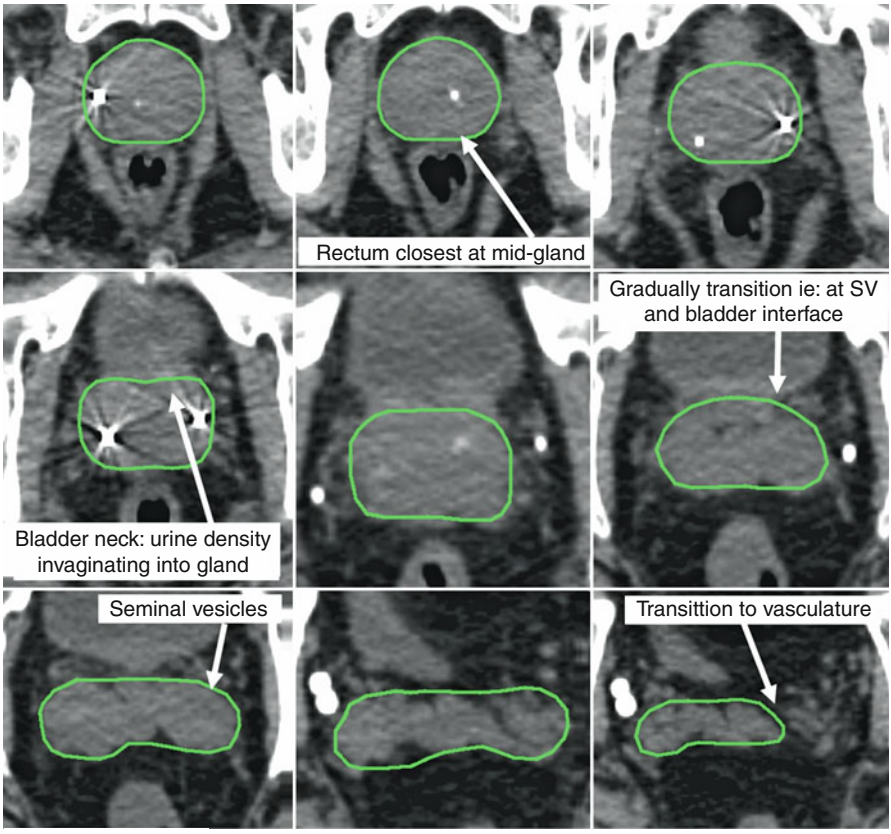

Fig. 24.1 (continued)

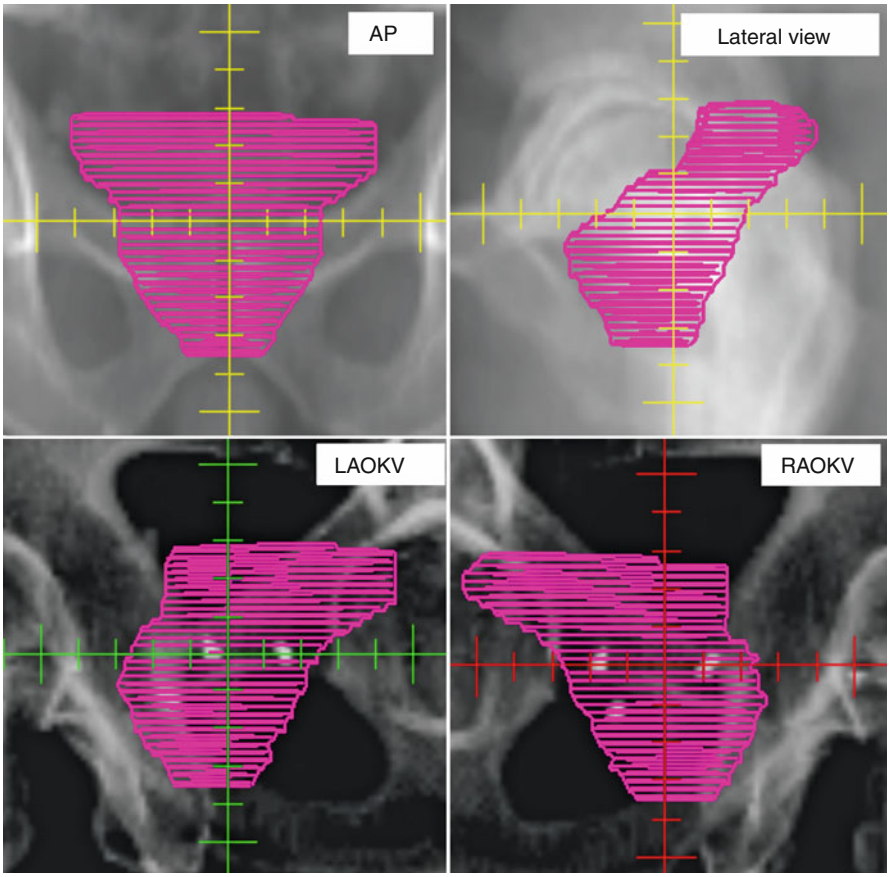

Fig. 24.2 Three-dimensional projection of CTV in various views for quality assessment. Note the appearance of a relatively globular gland underneath a winged structure representing the seminal vesicles superiorly. Cross-referencing of these projections to axial contours allows for detection of common misinterpretations of anatomy, i.e., extending too far into the GUD will produce extension of the pedestal structure inferiorly. Moreover, gross irregularities in the overall structure may reflect overcorrection from slice to slice that is not anatomically faithful, especially when averaging organ deformation and motion during treatment

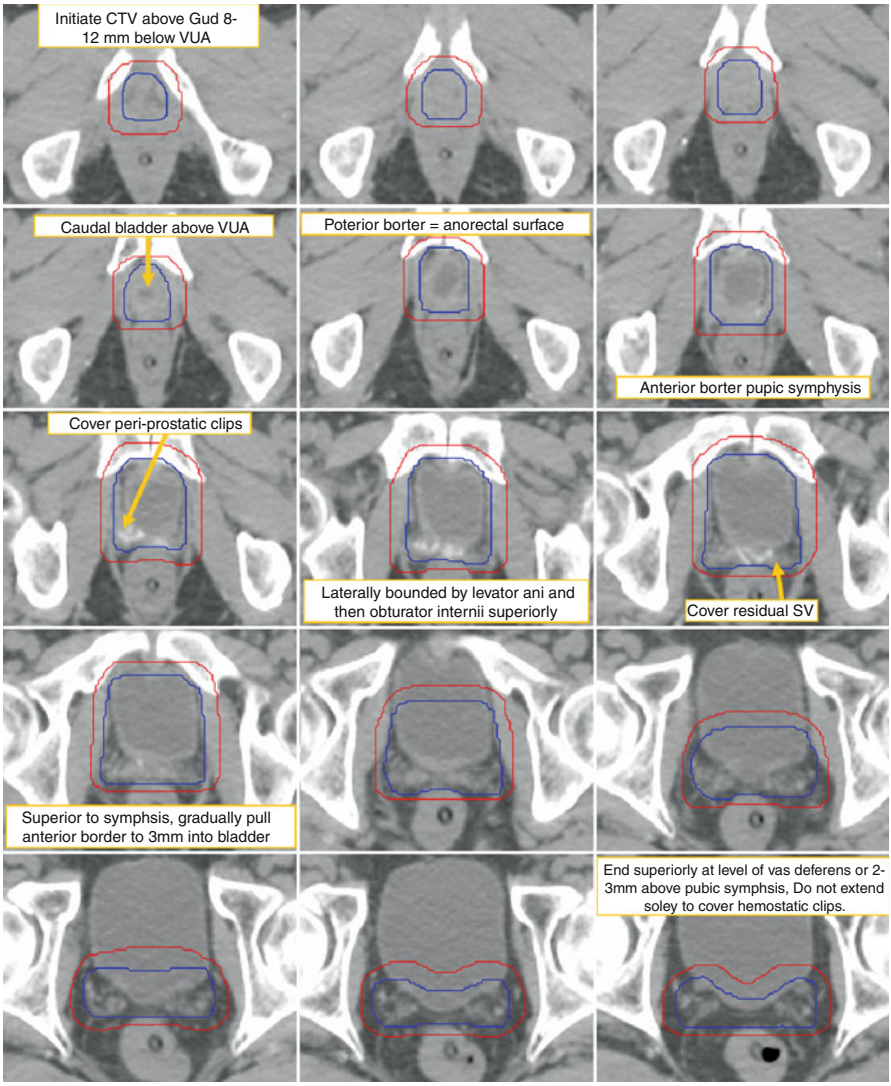

Fig. 24.3 Post-robotic prostatectomy target delineation for salvage intent. A 60-year-old with high-risk pT3a GS7 PSA 6.8 disease with focal ECE and steadily rising PSA. Representative images from 2-mm slice thickness simulation CT with full bladder protocol begin caudally and proceed cranially. Note that manual modification of the PTV after expansion is shown alongside the initial CTV. This helps avoid overdosing the rectum by excessive draping of the "dumbbell" shape cranially at the anterolateral rectum

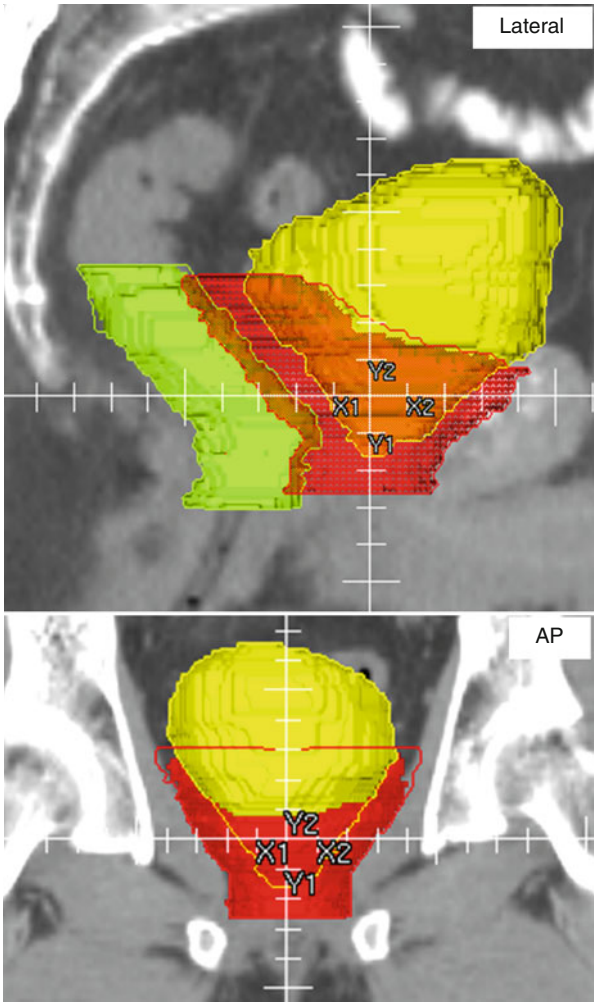

Fig. 24.4 Three-dimensional projection of PTV in orthogonal views for quality assessment. As opposed to an intact prostate treatment plan, the contours for a postoperative plan will necessarily approximate the bladder and rectum in order to cover areas of potential seeding. These areas include the anterior perirectal space, the vesicoureteral anastomosis (VUA) and the new spaces created at the posterior bladder interface with the pelvic floor and VUA. The overlap of PTV margin with rectum (*green*) and bladder (*yellow*) are highlighted here. In particular, a gradual tapering of the anterior PTV boundary superior to the pubic symphysis is ensured by inspection of the 3D projection. Smoothing out this transition avoids abrupt changes in dose distribution that are susceptible to errant targeting based on day-to-day changes in bladder volume despite a full bladder protocol

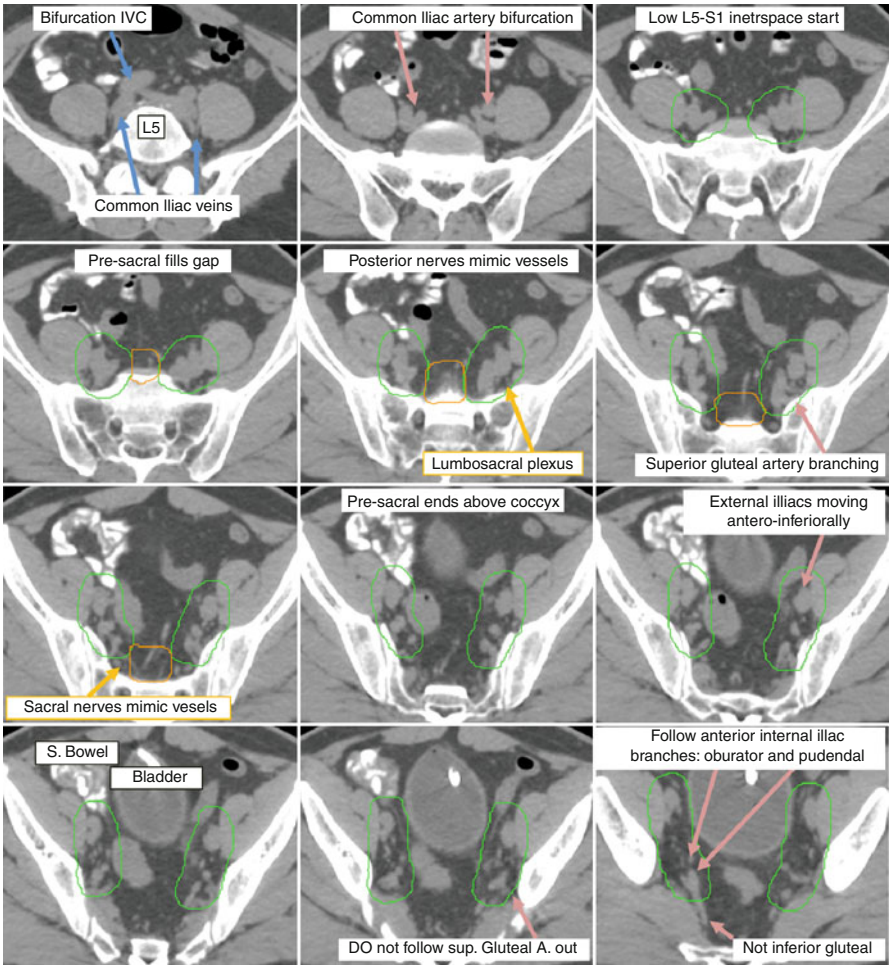

Fig. 24.5 Pelvic lymph node CTV delineation. A 71-year-old male with NCCN intermediate-risk disease with MRI suggestion of SV invasion undergoing combination HDR brachytherapy followed by EBRT. Again, representative images from a 2-mm slice thickness CT simulation scan are provided beginning cranially and proceeding caudally

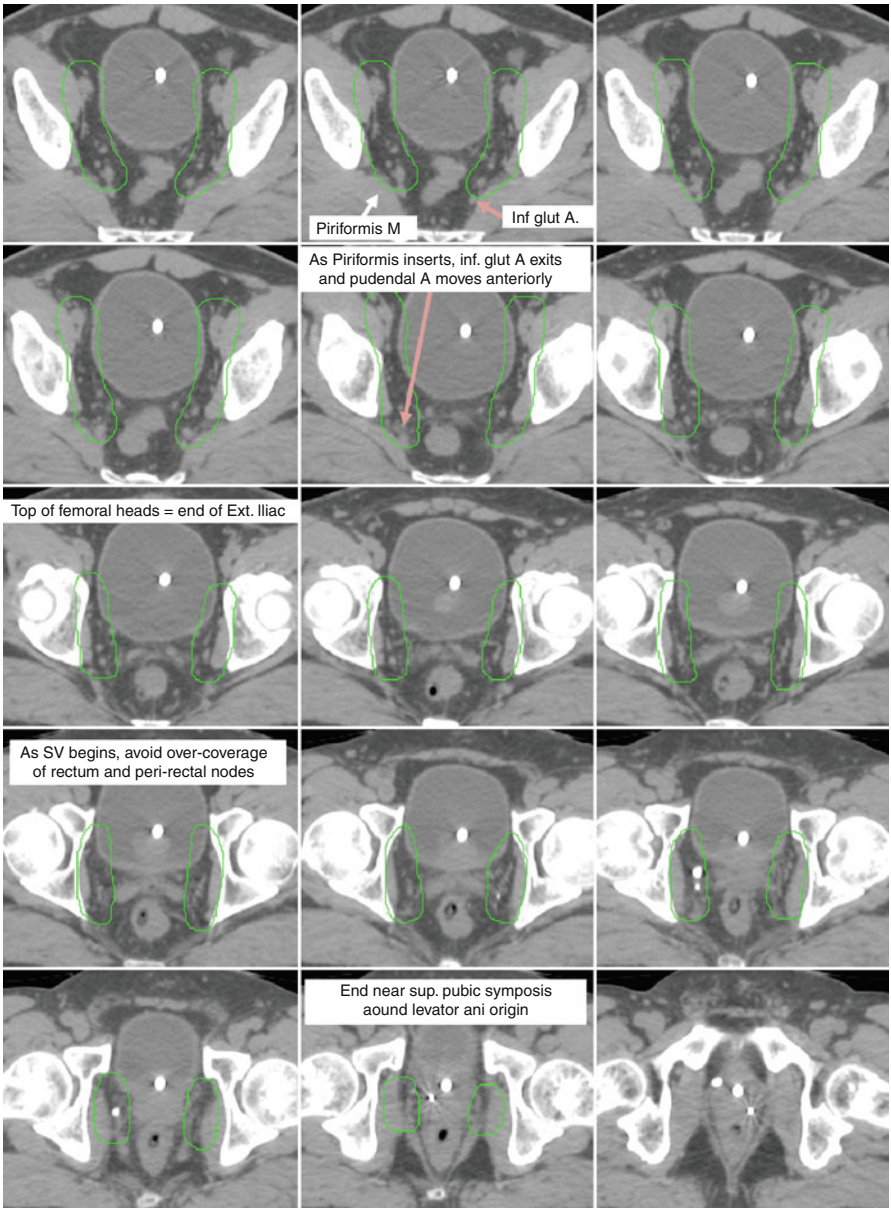

Fig. 24.5 (continued)

Special Cases

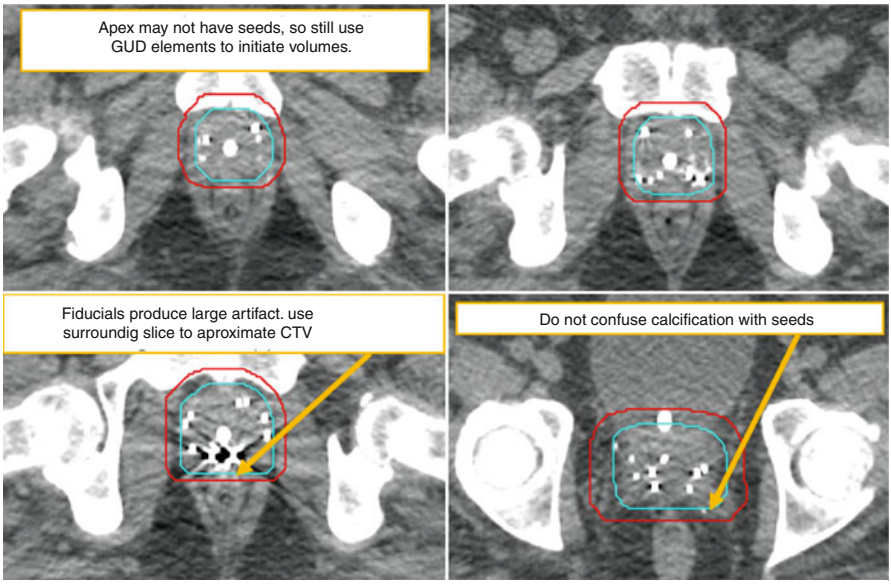

Fig. 24.6 Combination therapy with EBRT following brachytherapy. General concepts: include seeds, do not assume seed coverage peripherally delineates boundaries, interpolate smoothened boundaries at areas of fiducial/seed scatter, contour urethra via Foley for dosimetry. *CTV* Cyan blue; *PTV* Red

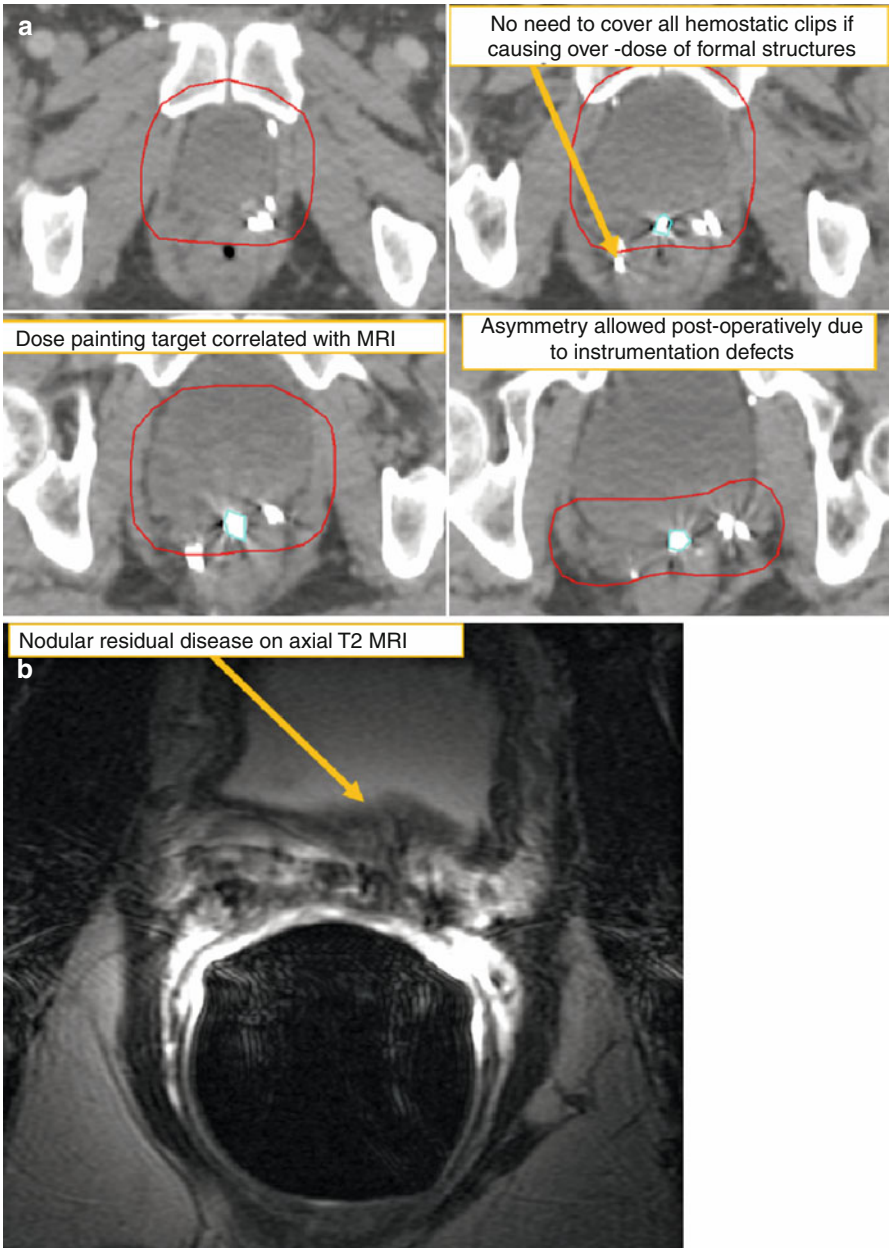

Fig. 24.7 Dose painting PTV in the post-prostatectomy treatment with gross residual disease (**a**). Patient is a 49-year-old with pT3aN0 GS 8 disease who underwent retropubic prostatectomy with multifocal ECE, positive margins, and gross residual disease on follow-up MRI (**b**). The focus was marked for image-guided dose painting with ultrasound-guided placement of Calypso beacons. Note that a degree of asymmetry is allowable in postoperative PTV given the instrumentation. Also note that in contrast to the prior example of a post-robotic prostatectomy, a retropubic open approach usually leaves more hemostatic clips, which do not all need to be covered. *PTV – red, gross disease dose painted boost – cyan blue*

Further Reading

Boehmer D et al (2006) Guidelines for primary radiotherapy of patients with prostate cancer. Radiother Oncol 79(3):259–269, EORTC guidelines for definitive therapy CTV delineation, which are not particularly used in this manual

McLaughlin PW et al (2010) Radiographic and anatomic basis for prostate contouring errors and methods to improve prostate contouring accuracy. Int J Radiat Oncol Biol Phys 76(2):369–378, Excellent demonstration of the anatomic features useful in determining boundaries to the CTV and demonstrating common errors in anatomic interpretation. Particularly useful are the comparisons of MRI to CT scan images

Pollack A et al (2010) RTOG 0534 protocol information: a phase III trial of short-term androgen deprivation with pelvic lymph node or prostate bed only radiotherapy (SPPORT) in prostate cancer patients with a rising PSA after radical prostatectomy. See Section 6.0 Radiation Therapy. Available online at RTOG website: http://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?action=openFile&FileID=4642. General approach to both the postoperative fossa and pelvic lymph nodes are demonstrated in this protocol

Poortmans P et al (2007) Guidelines for target volume definition in post-operative radiotherapy for prostate cancer, on behalf of the EORTC Radiation Oncology Group. Radiother Oncol 84(2):121–127, EORT guidelines for postoperative target delineation. Note that here, we more closely approximate RTOG guidelines for therapy

Bladder Cancer

25

Dayssy A. Diaz, Alan Pollack,
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General Principles of Planning and Target Delineation

- Bladder preservation therapy multimodal with concurrent chemotherapy and radiotherapy. Bladder preservation is a treatment option primarily for patients with clinical T2 or T3a disease, no ureteral obstruction, complete transurethral resection of bladder tumor (TURBT), and regionally localized tumor [1–4].
- CT simulation and three-dimensional conformal radiation therapy (3D-CRT) are necessary for the adequate planning of treatment.
- For simulation and treatment using 3D-CRT, the patient is supine and the bladder is emptied to ensure reproducibility. A sequential boost to the GTV is also delivered typically with an empty bladder for reproducibility (Table 25.1). If cone beam CT is available, a second simulation with the bladder partially full will allow for some sparing of the uninvolved bladder.
- IMRT is not standard for the delivery of radiotherapy for bladder cancer; however, it has many advantages and will eventually become the standard of care.
- During simulation and treatment using IMRT, the patient is supine and the bladder is semi-full to allow for dose painting to the GTV daily. Daily cone beam CT should be used to ensure adequate bladder filling and that rectal filling mimics simulation. Target volumes and radiation dose in IMRT are detailed in Table 25.2.
- Arc-based treatment is ideal to reduce the length of treatment and minimize changes in bladder volume during treatment delivery.

Critical Structures: femoral heads: maximum dose: 45 Gy; anorectum: 50 % of the volume should receive less than 55 Gy; bowel: <300 cc's receiving a dose greater than 45 Gy

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Table 25.1 Field setup and target volumes in using the treatment of bladder cancer using 3D-CRT Figs. 25.1–25.3

Target volumes	Field margins
Small pelvic fields (include CTV_1) (45 Gy)	*AP/PA* *Superior-inferior:* mid-sacroiliac region to just below the obturator foramen *Anterior posterior:* 1.5–2.0 cm laterally beyond the medial aspect of the pelvic bone Customized blocks should be used to reduce the exposure of the femoral heads
	Lateral *Superior-inferior:* as AP/PA *Anterior:* 2.5 cm anterior to the bladder but avoiding flashing the skin *Posterior:* 2.5 cm posterior to the bladder or any visible tumor Customized block to protect bowel anterior to external iliac lymph nodes
Whole bladder field (CTV_2) (54 Gy)	$PTV_2 = CTV_2 + 2$ cm
Tumor boost field (CTV_3) (64 Gy)	$PTV_3 = CTV_3 + 2$ cm

Table 25.2 Target volumes of IMRT for bladder cancer

Target volumes	Field margins
GTV	Tumor region seen on cystoscopy and imaging studies
CTV1	Encompasses the entire bladder, prostate, and the regional lymph nodes
CTV2	Encompasses the entire bladder plus any bladder associated masses visible on CT
CTV3	Encompasses the GTV for final boost

Intensity-Modulated Radiation Therapy (IMRT)

Image-guided radiation therapy allows for adjustments due to target motion prior to treatment delivery. This reduces uncertainty and, consequently, PTV margins. Although not standard, IMRT is a reasonable option to minimize dose to bowel as well as to spare uninvolved bladder from high doses of radiation. The dose fractionation that is shown below is one option that takes advantage of data supporting accelerated fractionation to reduce repopulation [5].

Simulation and Planning

The use of image guidance allows for reproducible treatment with a full bladder, facilitating improved bladder sparing and acceleration of treatment (Table 25.3).

Table 25.3 Planned tumor volumes and radiation dose in IMRT for bladder cancer

Target volumes	Structures	Total dose and fractionations
Small pelvic fields (include PTV_1)	Internal and external iliac vessels plus 7-mm margin	51 Gy/30 fractions at 1.7 Gy/Fx
Whole bladder field (PTV_2)	Include the entire bladder and prostate plus 1 cm	54 Gy/30 fractions at 1.8 Gy/Fx
Tumor boost field (CTV_3)	Area of bladder involver by tumor based on TURBT or palpable disease plus 7 mm	64.5 Gy/30 fractions at 2.15 Gy/Fx

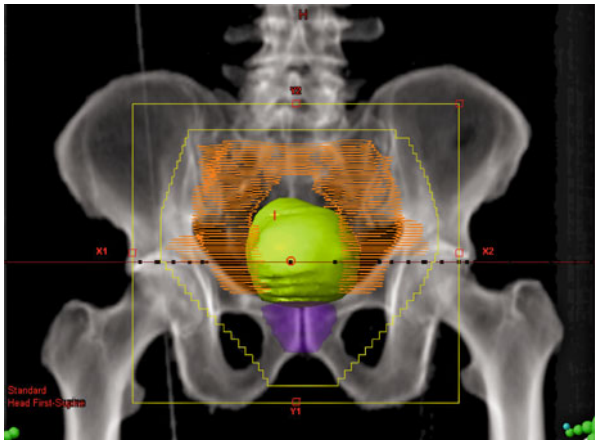

Fig. 25.1 AP portal image for 3D bladder field

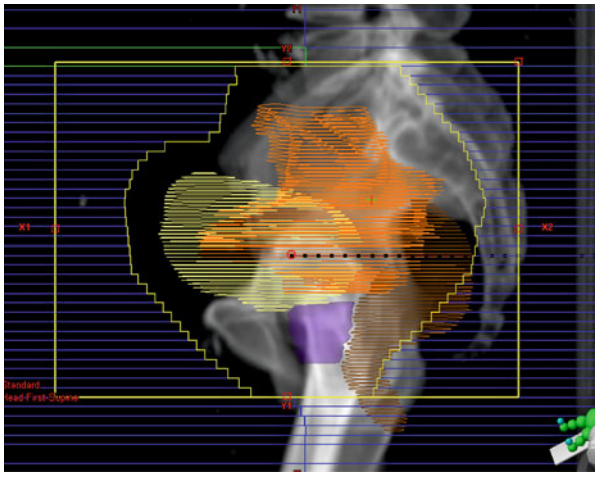

Fig. 25.2 Lateral portal image for 3D bladder field

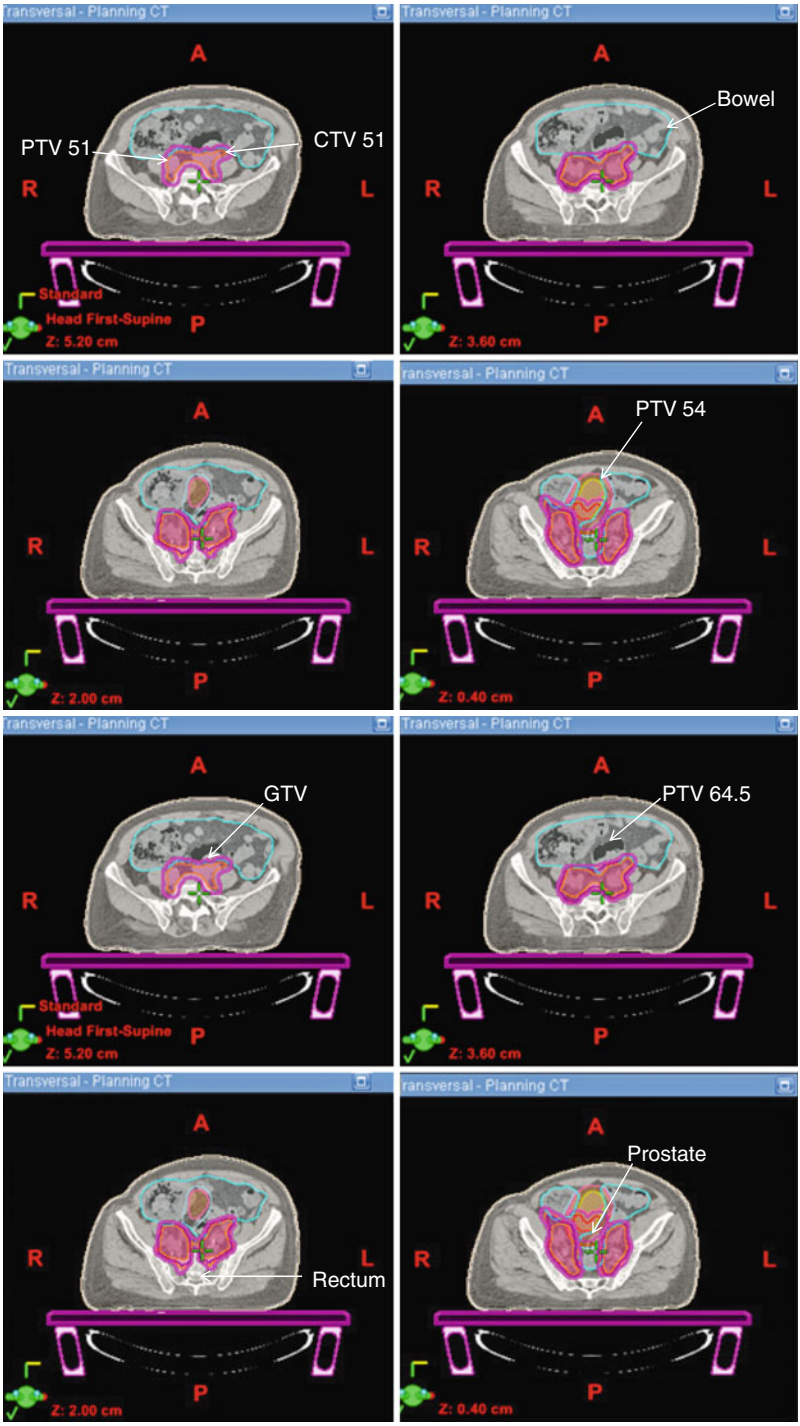

Fig. 25.3 Axial CT slices with targets and critical structures contoured

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Seminoma

26

Dayssy A. Diaz, Alan Pollack,
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General Principles of Planning and Target Delineation

- Prior to treatment, an adequate staging workup should be performed. Complete H&P including scrotal and testicular examination, serum tumor markers (α-feto-protein, β-human chorionic gonadotropin, and LDH), scrotal ultrasound, CT of the abdomen and pelvis, and CXR [1].
- Prior to simulation, fertility assessment with possible sperm banking.
- Patients are CT simulated in the supine position; contrast is not required for the scan. Testicular shielding of the uninvolved testicle is preferred (particularly for patients who will receive radiotherapy with dogleg field) (Fig. 26.1).
- Based on results from MRC TE 10 [2] (which showed reduced toxicity in patients who received radiotherapy to a para-aortic field only (Fig. 26.2) vs. a dogleg field) (Table 26.1), patients with stage I seminoma should receive adjuvant radiotherapy confined to para-aortic lymph nodes unless there is prior inguinal or scrotal violation (lymphatic alteration). However, in patients with stage I and poor compliance, pelvic lymph nodes should be included in the field (dogleg field) given increased risk of pelvic recurrence (<4 %). Patients with stage II should, in general, receive radiation using a dogleg.
- If prior inguinal surgery, ipsilateral inguinal and iliac regions should be included in the field; If there is history of scrotum violation or tunica albuginea penetration, electron boost of scrotum should be considered.
- Para-aortic lymph nodes and vessels pertinent to field setup and target volume selection and delineation are presented in Fig. 26.3.

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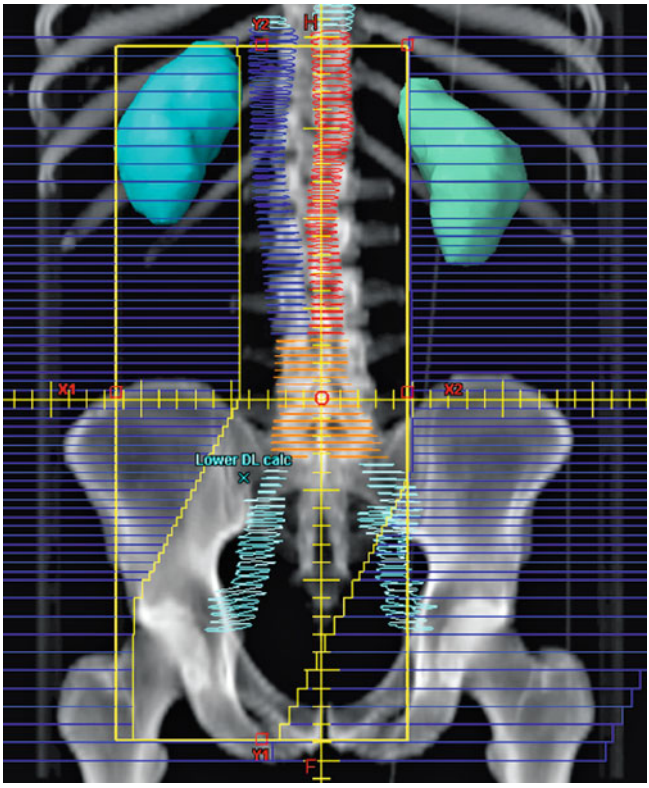

Fig. 26.1 Radiation treatment portal for a dogleg field

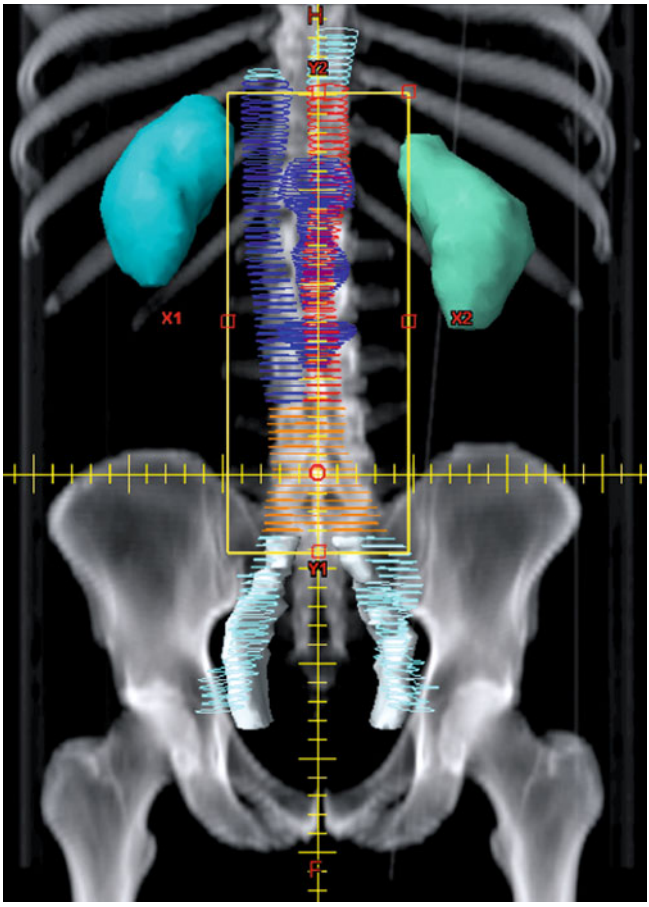

Fig. 26.2 Radiation treatment portal for a para-aortic only field

Table 26.1 Treatment fields used in radiotherapy for seminoma: dogleg versus para-aortic fields

Treatment field and target	Definition of field borders and target volumes
Dogleg field	Superior: disk space between T10 and T11 Inferior: mid obturator foramen Lateral: tips of transverse processes of lumbar vertebra (typically L3 with consideration of kidney location) and 2-cm margin on all visible nodes, extending inferiorly to cover the lateral edge of the acetabulum down to the mid obturator level
Para-aortic field	Superior: disk space between T10 and T11 Inferior: disk space between L5 and S1 Lateral: tips of transverse processes of lumbar vertebra (typically L3 with consideration of kidney location) and 2-cm margin on all visible nodes; para-aortic nodal CTV includes vessel contours (aorta and IVC) + 7 mm, excluding bones
nCTV (positive nodal CTV and PTV)	Gross tumor volume plus 1.5 cm, excluding bones. PTV = CTV + 3–5 mm margin

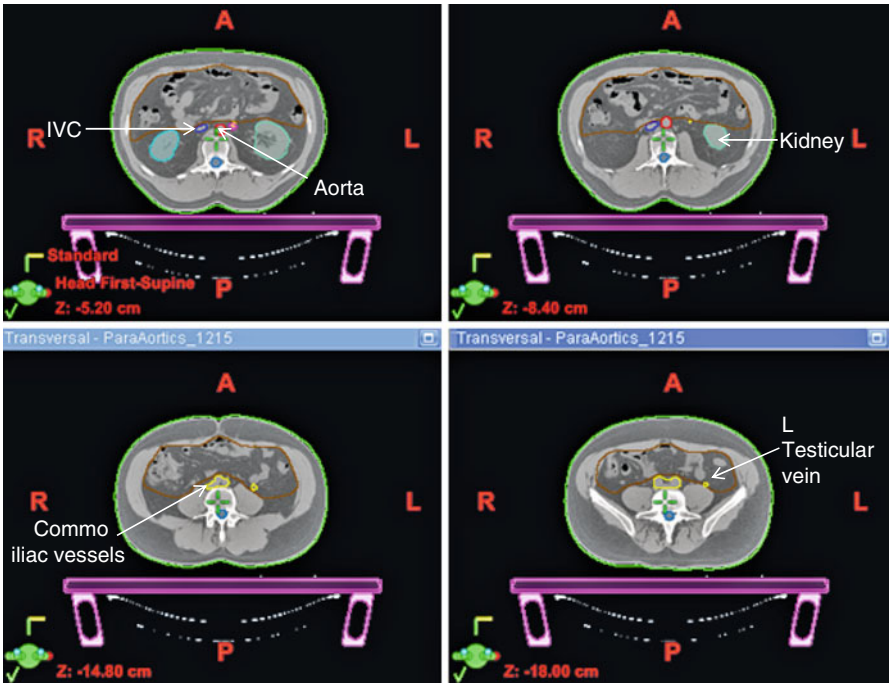

Fig. 26.3 Representative CT slices with important structures identified

Standard radiation dose for stage I seminoma is 20 Gy in 10 daily fractions [3]; for stage II, radiation dose to the uninvolved nodal regions can be 25.05 Gy in 15 fractions plus 5 Gy boost to the gross lymphadenopathy as in-field failures at this dose are extremely rare. However, the ICUD consensus [1] is that the boost is 10 Gy and the EUA recommendations are 30 Gy for stage IIA and 36 Gy for stage IIB patients [4].

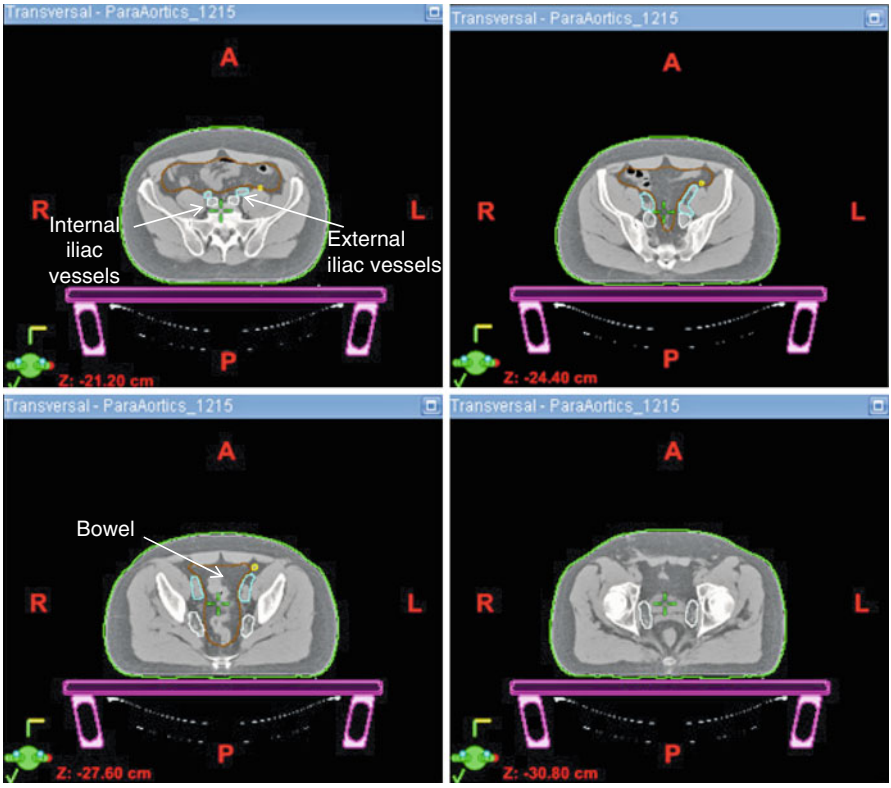

Fig. 26.3 (continued)

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Palliative Radiation for Brain Metastases

27

David C. Weksberg, Jiade J. Lu, and Eric L. Chang

- The brain is one of the most common sites of cancer metastasis, and radiation, in conjunction with surgery and steroid therapy, is a cornerstone of management of brain metastases. Whole brain radiation therapy (WBRT) using conventional external beam radiation is most commonly employed. Stereotactic radiosurgery (SRS) can be used in the adjuvant or upfront settings for patients with limited number of intracranial metastatic foci, sufficient extracranial disease control, and appropriate performance status.
- A detailed history and physical examination with emphasis on the neurological examination, as well as appropriate laboratory tests, should be performed to investigate the extent of the disease. Imaging of the brain should be acquired, preferably MRI with gadolinium contrast.
- The use of WBRT is well established for patients with symptomatic brain metastasis (Fig. 27.1). WBRT is also employed in the setting of prophylactic cranial irradiation (PCI) to prevent the development of brain metastasis in small-cell lung cancer (SCLC).
- A wide variety of dose and fractionation schemes are used for WBRT, with 30 Gy in 10 fractions being the most common. For patients with a relatively long life expectancy

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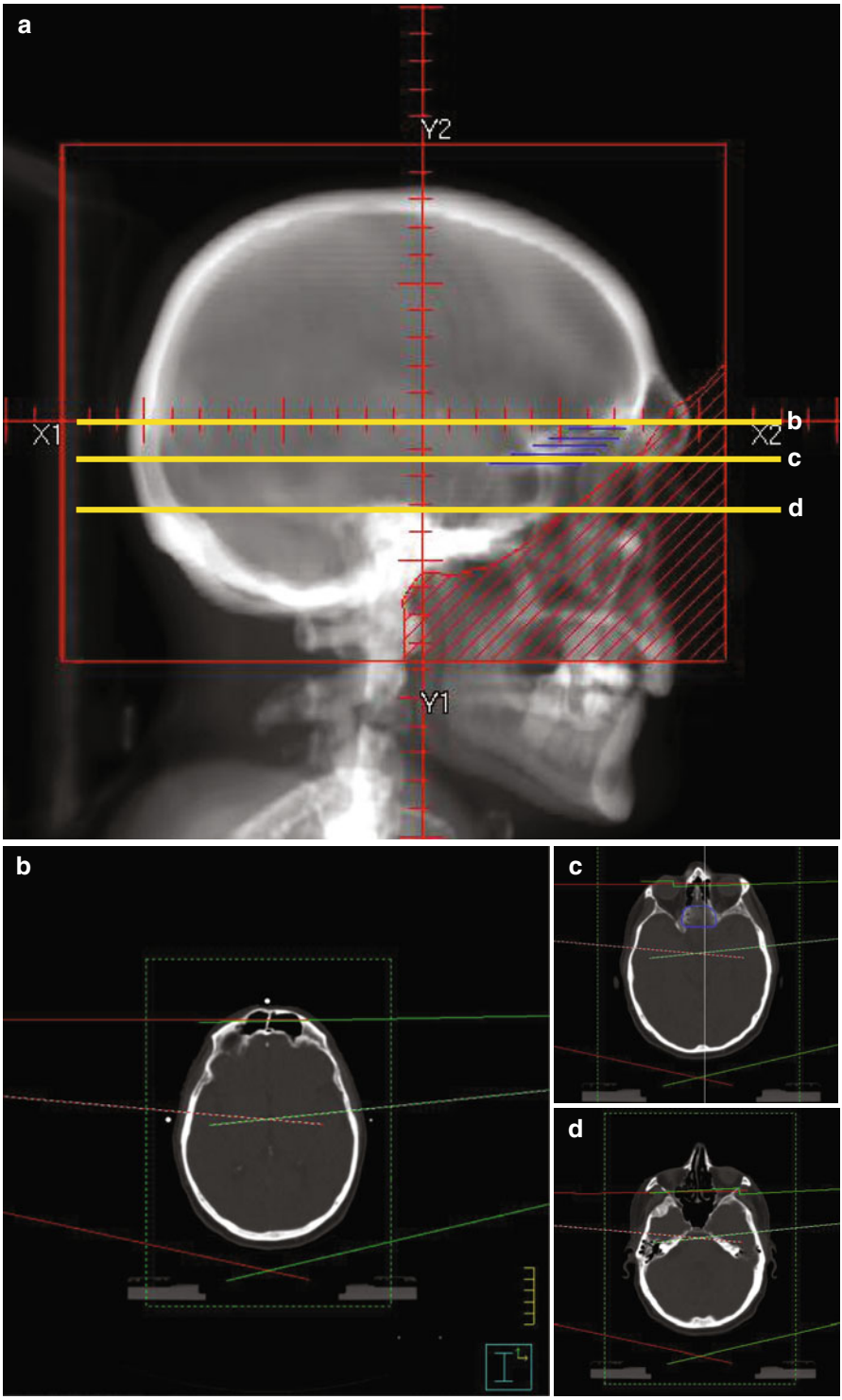
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d
Y1
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(and greater concern for neurocognitive sequelae) more protracted fractionation schemes (30 Gy in 12 fractions, 37.5 in 15 fractions) can be considered. The most commonly recommended dose for PCI in SCLC is 25 Gy in 10 daily fractions.

- The optimal use of SRS in conjunction with WBRT or as stand-alone treatment remains controversial. Randomized data supports the addition of SRS before or after WBRT for patients with 1–3 metastases [1]. SRS alone may also be offered to patients with 1–3 lesions [2, 3], provided that close imaging follow-up can be obtained to monitor for additional disease.
- SRS is generally appropriate for lesions less than 4 cm in largest diameter. Independent of size, neurosurgical management may be preferred for lesions causing mass effect. SRS of the surgical cavity following resection remains investigational.
- For WBRT simulation, the patient should be imaged in the supine position, using a head holder and an immobilizing mask in supine position. Non-contrast CT imaging with 3–5-mm slice thickness is preferred for treatment planning; however, clinical patient setup can be required in the emergent setting. Axial images from the vertex through the upper cervical spine should be obtained.
- The typical treatment technique consists of opposed lateral photon beams. Field design is demonstrated in Fig. 27.1 and should take care to provide adequate coverage of the cribriform plate and temporal lobes. Figure 27.2 illustrates variations of the standard WBRT fields to account for differing clinical situations.
- For frame-based SRS, a stereotactic head frame should be placed by a neurosurgeon. Optimally, a volumetric (1-mm slices), contrast-enhanced MRI is used for target delineation and treatment planning. In multi-isocenter, cobalt-based SRS systems (Gamma Knife), this MRI can be directly used for treatment planning. However, for linear accelerator (LINAC)-based SRS, a thin-slice CT must be acquired for dose calculation and additional scans (i.e., volumetric MRI) can be co-registered for treatment planning.
- For frame-based SRS, the gross tumor volume (GTV) is contoured as the visualized lesion on contrast-enhanced MRI (Fig. 27.3). No CTV or PTV expansions are used (in frameless systems, a 1–2-mm PTV expansion should be created). Dose is typically prescribed to the 50 % isodose line for Gamma Knife and 80–95 % for linac-based SRS, with the choice of prescription dose determined by lesion size (Table 27.1). SRS can create a highly conformal dose distribution, allowing for treatment of lesions in close proximity to critical structures (Fig. 27.4); however, care must be paid to normal tissue tolerance (Table 27.2).
- Additional references for further reading are provided below [4–13].

Fig. 27.1 Standard WBRT fields. Conventional opposed lateral fields are rotated slightly off-axis (RAO/LAO) to create coplanar anterior field edges which do not diverge into the lenses. (**a**) Beam's eye view (RAO) and blocking. The inferior field edge is set at C1 with at least 2 cm of flash posteriorly and superiorly. The block begins at the anterior aspect of the C1 vertebral body and is designed to spare nontarget tissues, while taking care to provide adequate margin on the temporal lobes and cribriform plate (*blue*). (**b**) Central axis view showing coplanar anterior field edges. (**c**) Axial slices demonstrating adequate margin on the cribriform plate (*blue*) and avoidance of divergent dose through the lenses. (**d**) Axial slice demonstrating adequate margin on the temporal lobes.

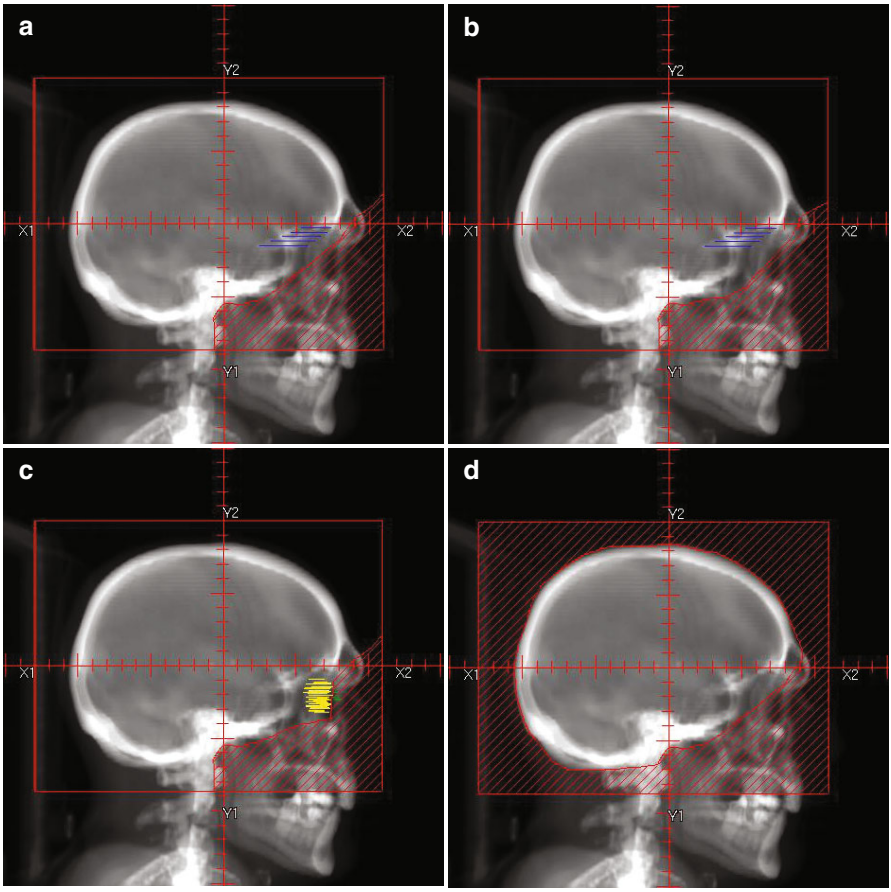

Fig. 27.2 Variations on WBRT fields. (**a**) Conventional fields (RAO/LAO) as described in (**b**) More generous WBRT fields used in the setting of leptomeningeal disease – these fields provide additional margin on the cribriform plate (*blue*). (**c**) Conventional fields (RAO/LAO) covering the traditional WBRT target with the addition of coverage of the bilateral retinas (*yellow*) in the setting of proven retinal involvement (e.g., CNS lymphoma, CNS prophylaxis for leukemia, leukemic infiltrate to the retina) with blocking of the lens (*green*) and anterior chamber. (**d**) Scalp-sparing WBRT fields – the block edge is set at the outer table of the calvarium to minimize alopecia in patients for whom cosmesis is of particular concern.

Fig. 27.3 SRS treatment of three metastatic lesions. A Leksell Gamma Knife was used for treatment of a patient with three metastatic lesions from non-small-cell lung cancer. Contrast-enhanced volumetric MRI (1-mm cuts) demonstrated three enhancing lesions in the right parietal lobe (lesion 1), right cerebellar hemisphere (lesion 2), and right occipital lobe (lesion 3). All three lesions were prescribed 20 Gy based on size criteria (Table 27.1). Axial, coronal, and sagittal images from the planning MRI are depicted, as well as representative slices from the treatment plan showing the prescription isodose line in *yellow*, with additional isodose lines shown in *green*.

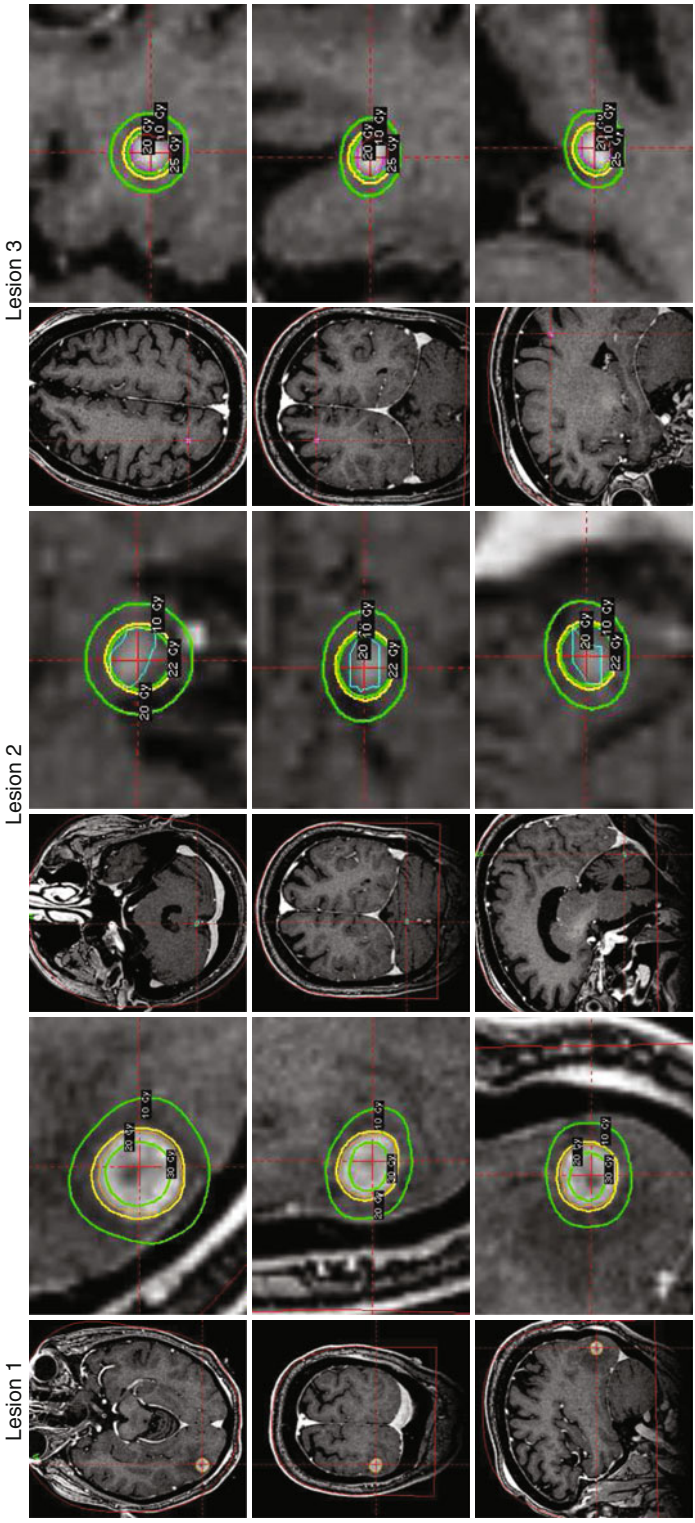
Lesion 3
Lesion 2
Lesion 1

Table 27.1 SRS dose prescriptions by lesion size [14]

Tumor size (cm)	Prescription dose (Gy)
<2	20–24
2–3	18
3–4	15

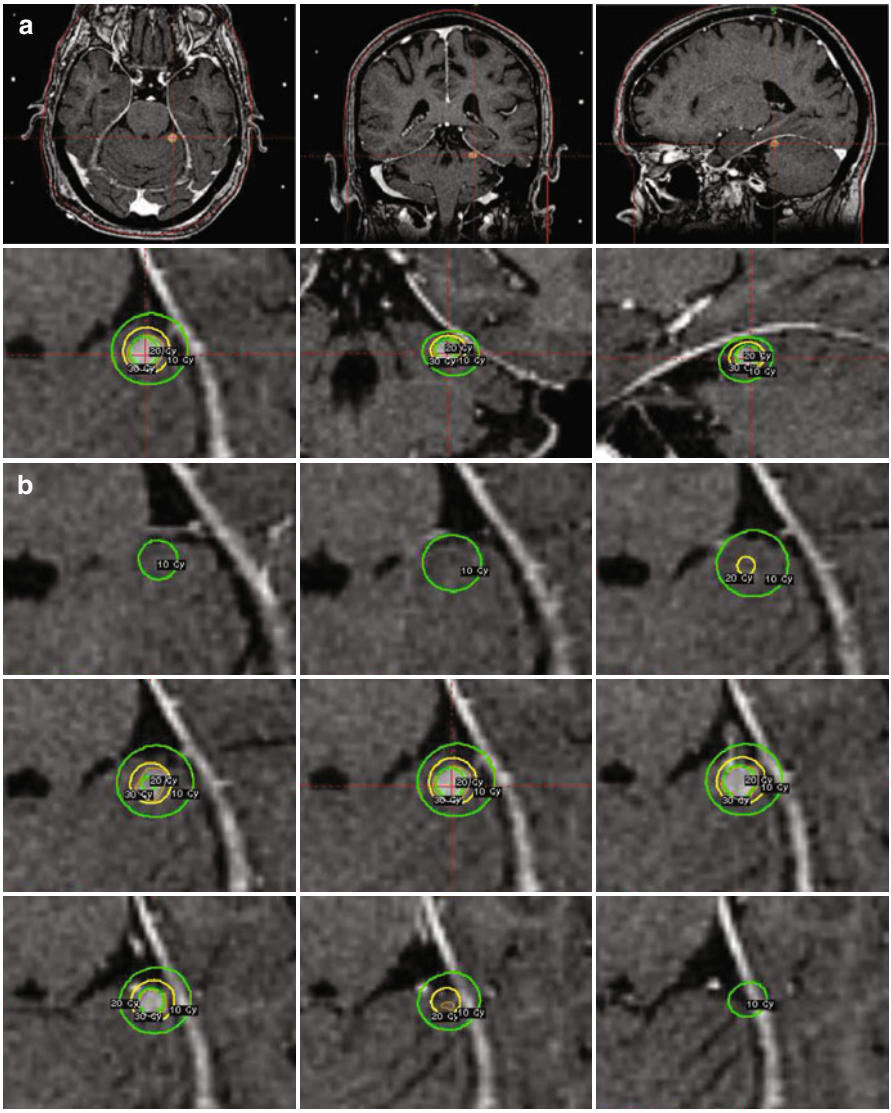

Fig. 27.4 SRS treatment of a cerebellar lesion in close proximity to the brainstem. (**a**) Axial, coronal, and sagittal slices from a volumetric (1 mm) contrast-enhanced MRI through the center of the metastatic lesion, contoured in orange. The 20-Gy prescription isodose line is shown in *yellow*, with 30 Gy and 10 Gy lines in *green*. (**b**) Serial axial images delineating the entire volume receiving 10 Gy. The sharp dose falloff allows treatment of this lesion adjacent to the brainstem (see Table 27.2 for dose constraints).

Table 27.2 Critical structure dose constraints

Organ at risk	Dose constraint (Gy)
Brain stem	12
Optic structures	8

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Benign Tumors of the Central Nervous System

28

Sheen Cherian, Samuel T. Chao, Erin S. Murphy, and John H. Suh

General Principles of Radiotherapy Planning and Target Volume Delineation

- The commonly encountered benign tumors of the CNS include low-grade glioma, meningioma, vestibular schwannoma, and pituitary adenoma. Intensity-modulated radiotherapy (IMRT), 3D-conformal radiotherapy (3D-CRT), fractionated stereotactic radiotherapy (FSRT), and stereotactic radiosurgery (SRS) are standard techniques used for definitive radiotherapy of these tumors. In treating CNS tumors, accurate delineation of GTV is crucial due to close proximity of organs at risk (OAR).
- A detailed clinical history, physical examination with emphasis on the neurological examination, appropriate laboratory investigation, pretreatment visual acuity and visual field charting, audiometric assessment, and performance status evaluation should be done as a prerequisite for definitive radiation therapy. Adequate imaging is needed for diagnosis, staging, and planning.
- If feasible, surgery remains the primary treatment modality. For all benign tumors, gross tumor resection (GTR) remains the surgical goal, if it can be done without added morbidity.
- For simulation, the patient is scanned supine with arms by the side. For SRS, a stereotactic head frame should be used while a rigid thermoplastic mask is sufficient for 3D-CRT and IMRT. Spiral CT with 2- to 3-mm slice acquisition from vertex to mid-cervical spine is used for planning. IV contrast for enhancing lesions may be used to improve delineation of target volumes. Typically, diagnostic MRI scans will be co-registered to planning CT for delineating gross tumor volume (GTV).

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- GTV should be delineated on every CT slice. For low-grade glioma, the GTV should be delineated as the extent of visible abnormality demonstrated on the T2-weighted MRI sequence. For the other benign tumors, GTV should be delineated as the outer edge of the gadolinium enhancement seen on T1-weighted MRI sequence. OAR need to be outlined and dose constraints need to be defined according to tumor dose and fractionation (Table 28.1, Figs. 28.1, 28.2, 28.3, 28.4, 28.5, 28.6, 28.7, 28.8, 28.9, 28.10, and 28.11).

Table 28.1 Target volumes

Disease	Target volume definitions and descriptions	Dose and fractionation
Glioma	GTV_{54}: extent of visible abnormality demonstrated on T2-weighted MRI sequence is the GTV CTV = GTV + 1.5–2 cm: GTV is grown three-dimensionally into a CTV by a margin of 1.5–2 cm with respect for natural boundaries (tentorium, bone, etc.) PTV = CTV + 0.3 cm: the CTV to PTV margin is 0.3–0.5 cm	54 Gy/30 fractions [1]
Meningioma	GTV_{54}: the outer edge of the gadolinium enhancement seen on T1-weighted MRI sequence forms the GTV CTV = GTV: there is no CTV margin for benign meningioma PTV = CTV + 0.3–0.5 cm: CTV to PTV margin is 0.3–0.5 cm For SRS, GTV is treated without any margins	54 Gy/30 fractions [2] SRS dose: 12–14 Gy in a single fraction, prescribed to the 50 % isodose line (IDL) [3]
Pituitary adenoma	GTV_{45}: the outer edge of the gadolinium enhancement seen on T1-weighted MRI sequence forms the GTV CTV = GTV: there is essentially no CTV margin for pituitary adenoma PTV = CTV + 0.3–0.5 cm: CTV to PTV margin is 0.3–0.5 cm For SRS, GTV is treated without any margins	45 Gy/25 fractions for nonfunctional tumors, 50.4–54 Gy for functional tumors [4] SRS dose: 15–16 Gy for nonfunctional tumors, 18–25 Gy for functional tumors [4]
Vestibular schwannoma	GTV_{45}: the outer edge of the gadolinium enhancement seen on T1-weighted MRI sequence forms the GTV CTV = GTV: there is no CTV margin for vestibular schwannoma PTV = CTV + 0.3–0.5 cm: CTV to PTV margin is 0.3–0.5 cm For SRS, GTV is treated without any margins	45–54 Gy/25–30 fractions [5] SRS dose: 13 Gy to 50 % IDL [5]

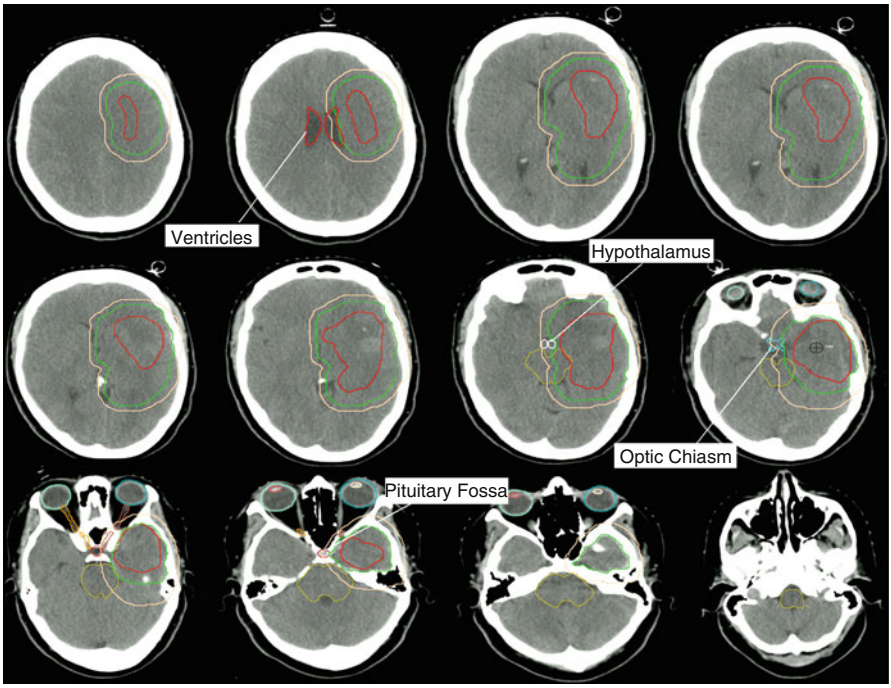

Fig. 28.1 Low-grade glioma, outlined on planning CT according to visible abnormality seen on T2-weighted MRI sequence

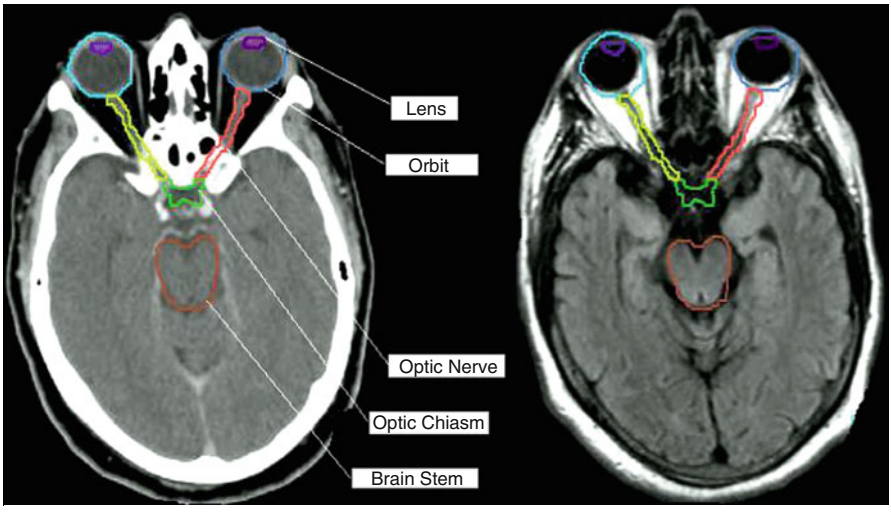

Fig. 28.2 Organs at risk outlined on planning CT scan and co-registered MRI

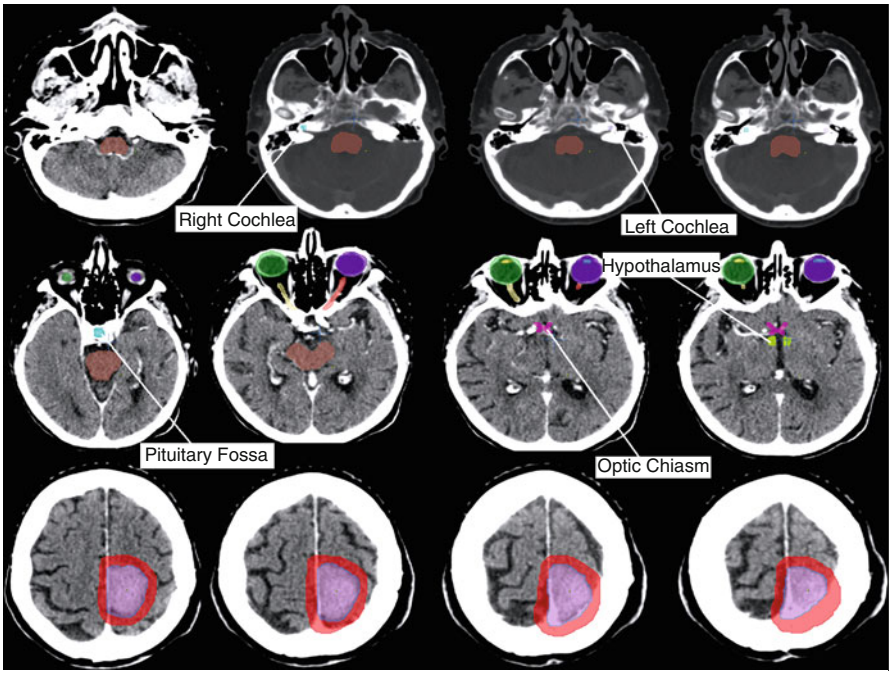

Fig. 28.3 Parasagittal meningioma and critical structures contoured on planning CT

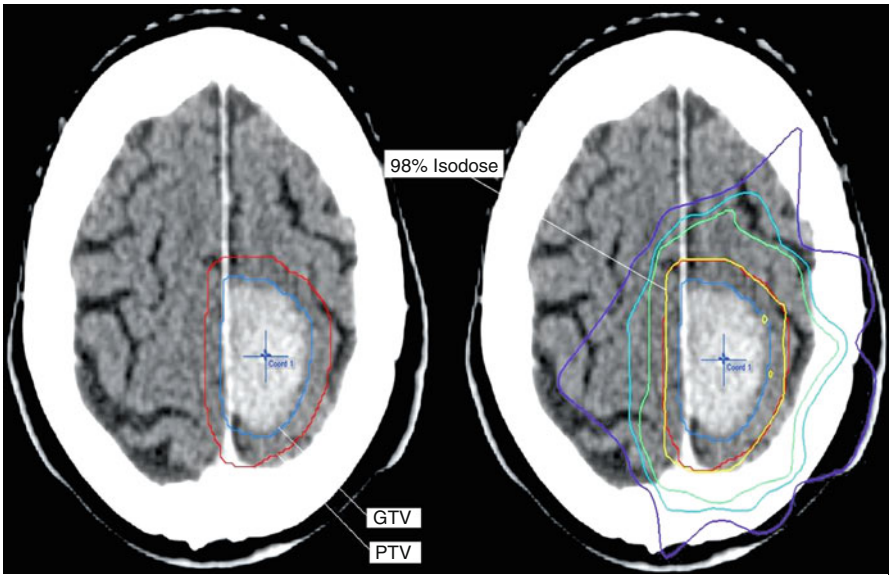

Fig. 28.4 Parasagittal meningioma with dural attachment and isodose lines on axial CT views

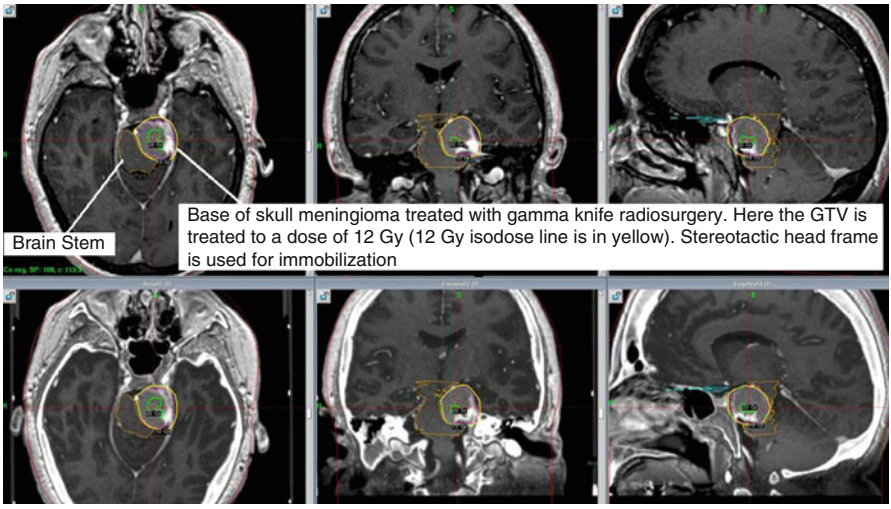

Fig. 28.5 Base of skull meningioma shown in the axial, coronal, and sagittal plane treated with SRS (CT/MRI fusion); the 12 Gy isodose line is conformally covering the PTV

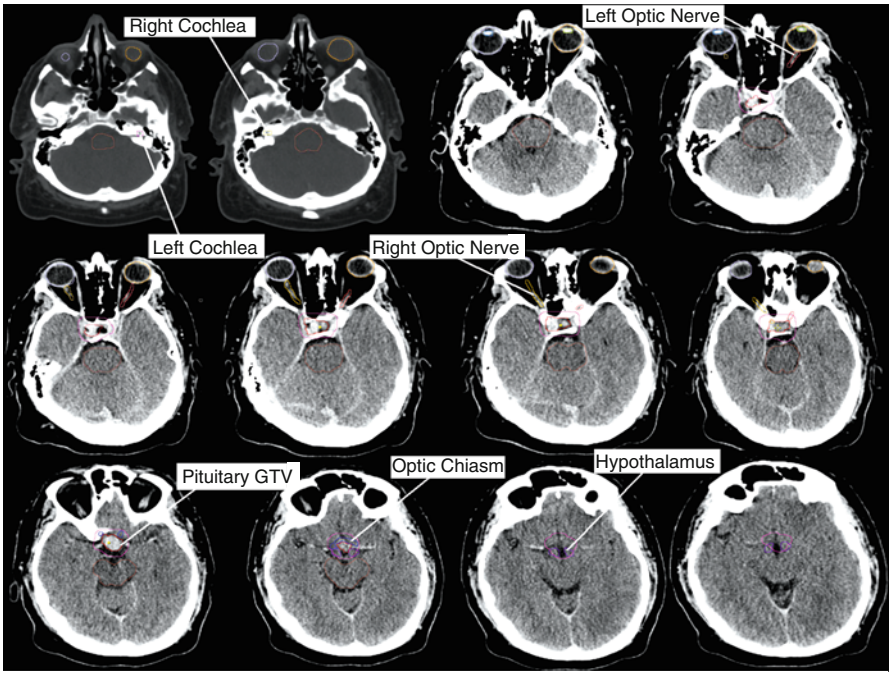

Fig. 28.6 Pituitary adenoma with critical structure contoured on planning CT scan

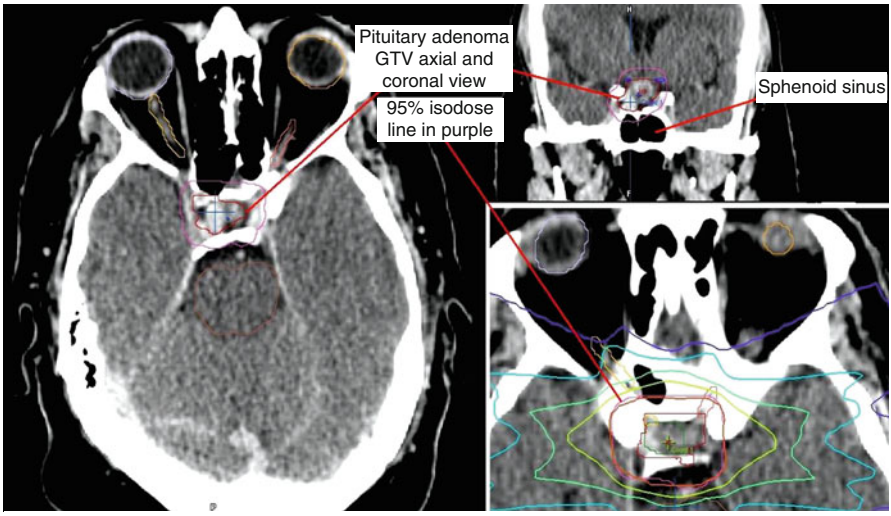

Fig. 28.7 Pituitary adenoma (axial and coronal CT views), with 95 % isodose line conformally covering the PTV

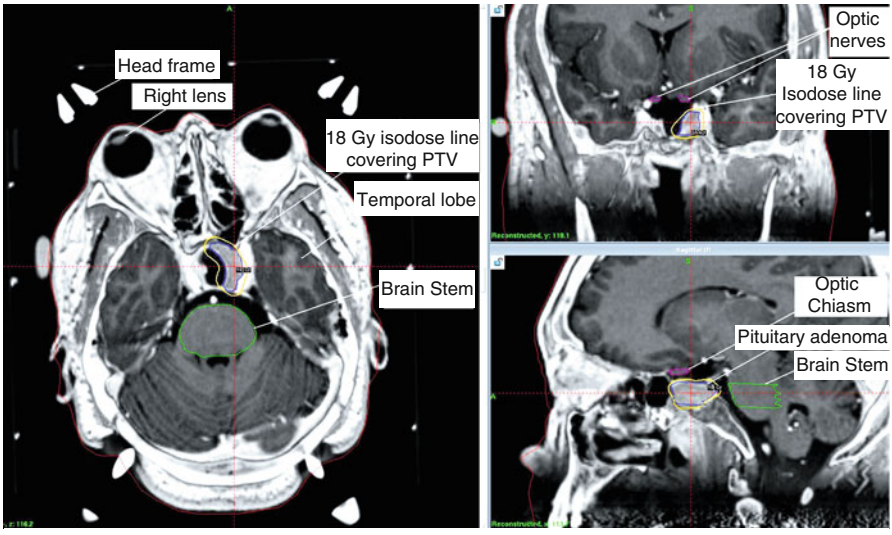

Fig. 28.8 Pituitary adenoma on axial, coronal, and sagittal CT/MRI fusion (gadolinium-enhanced T1 sequence fused with contrast-enhanced planning CT) treated with SRS

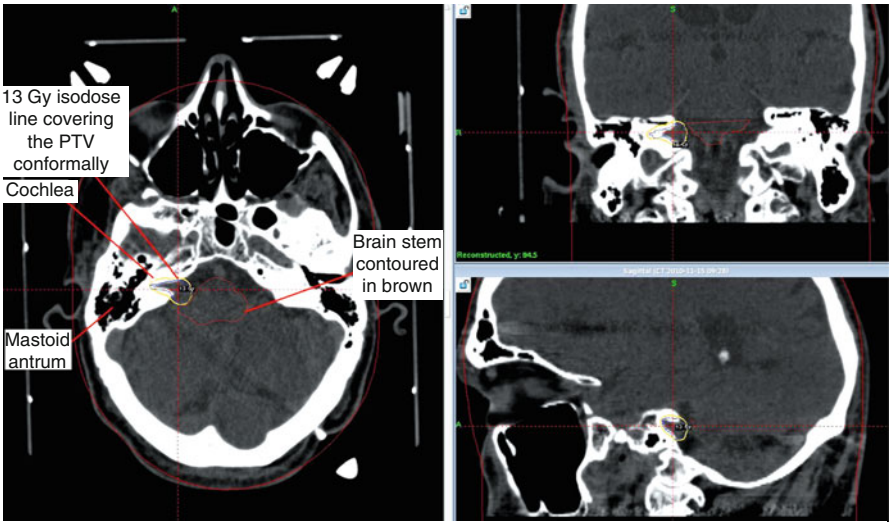

Fig. 28.9 Vestibular schwannoma treated with SRS (axial, coronal, and sagittal CT bone window views)

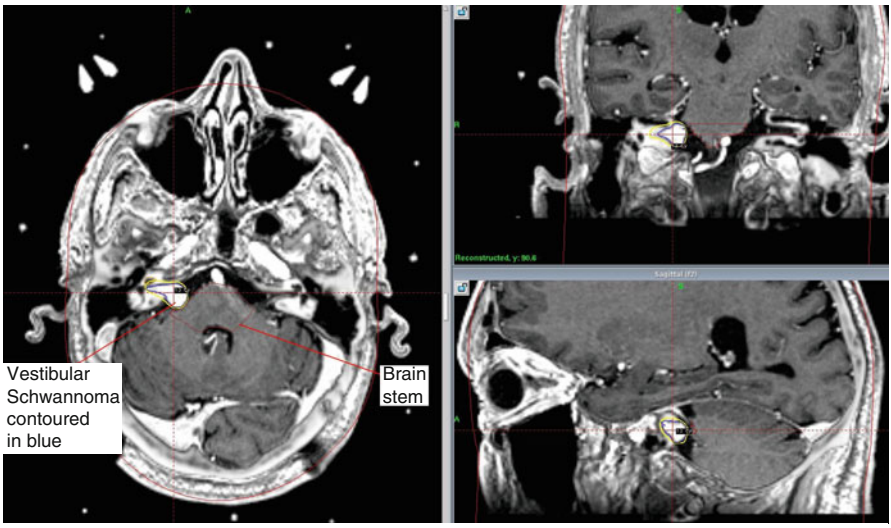

Fig. 28.10 Vestibular schwannoma GTV outlined on CT/MRI fusion for SRS, typically gadolinium-enhanced T1-weighted MRI sequence is fused with contrast-enhanced planning CT scan

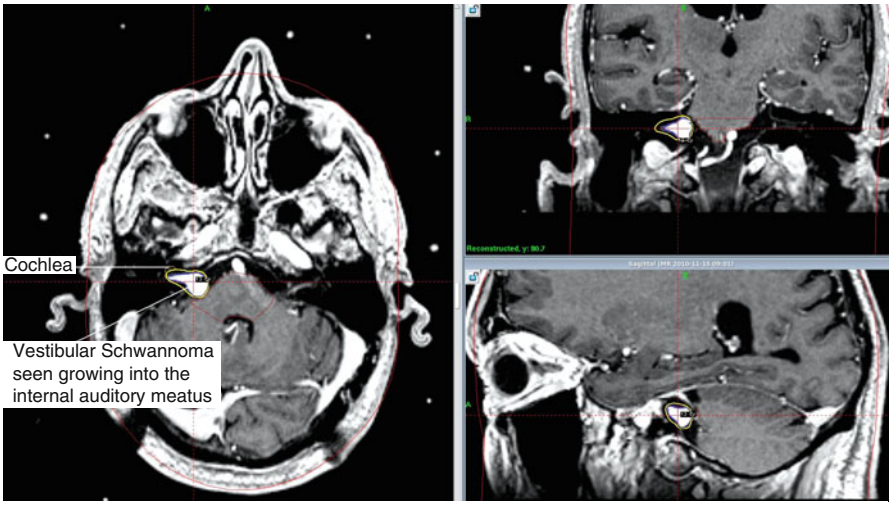

Fig. 28.11 Vestibular schwannoma contoured on T1 gadolinium-enhanced MRI sequence

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Hodgkin's and Non-Hodgkin's Lymphoma

29

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General Principles of Tumor Volume Delineation and Field Setup

- Delineation and field setup for radiation therapy for both Hodgkin's and non-Hodgkin's lymphoma depend on the origin of the disease, the use and response to systemic chemotherapy, as well as the extent of disease.
- Extended-field radiation therapy (EFRT) was historically used as definitive management without chemotherapy. Combined modality therapy has allowed reduction of treatment field size (Fig. 29.1a, Table 29.1).
- Involved-field radiation therapy (IFRT) is now used as standard therapy to treat smaller fields resulting in lower doses delivered to normal tissues compared to EFRT (Fig. 29.1b).
- Involved-node radiation therapy (INRT) is currently being used in select clinical trials to further reduce field size and dose to normal structures in an effort to reduce late effects (Fig. 29.1c).
- Treatment dose to various subtypes of Hodgkin's and non-Hodgkin's lymphoma differ based on their histology, stage, and response to chemotherapy and is therefore out of the scope of this chapter on target volume selection/delineation and field setup.

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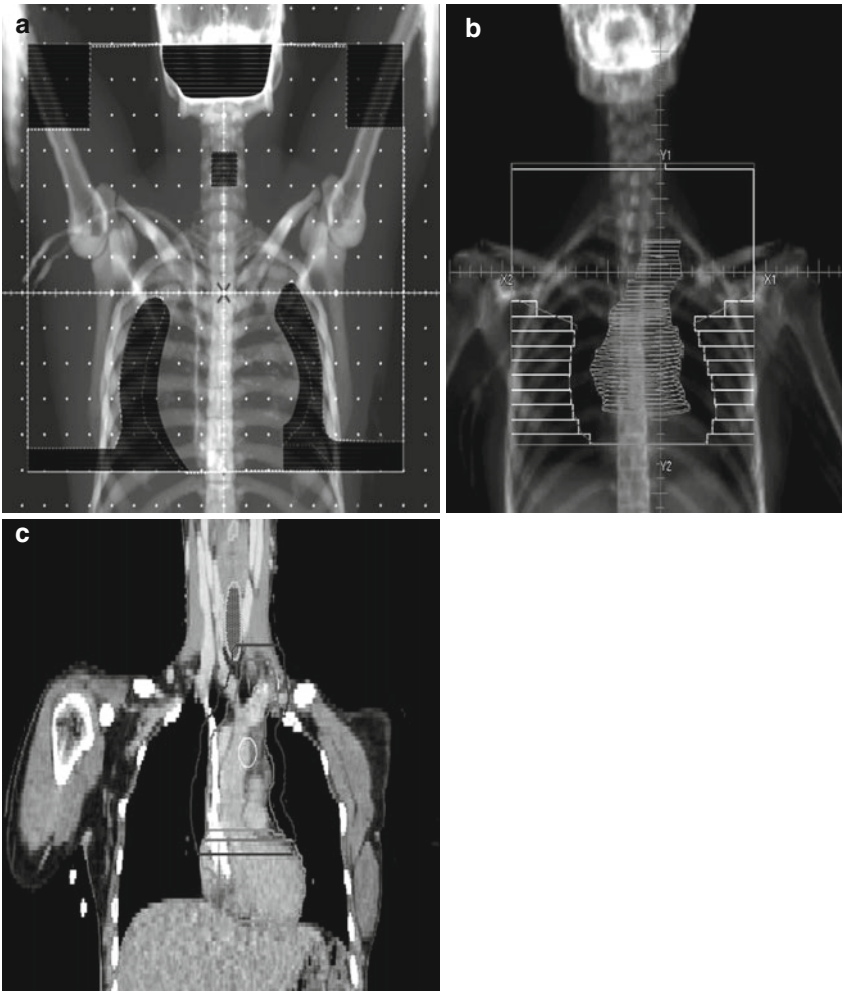

Fig. 29.1 Evolution of radiation treatment fields. (**a**) Extended-field (**b**) Involved-field (**c**) Involved-node

Table 29.1 Extended-field radiation treatment fields and definitions

Extended fields	Definition
Mantle	Bilateral cervical, supraclavicular, axillae, mediastinal, and hilar nodes (Fig. 29.2a)
Mini-mantle	Mantle excluding the mediastinum
Modified mantle	Mantle excluding the axillae
Inverted-Y	Para-aortic, bilateral pelvic nodes, ± spleen (Fig. 29.2b)
Total lymphoid irradiation (TLI)	Mantle and inverted-Y fields
Subtotal lymphoid irradiation (SLI)	TLI excluding the pelvis

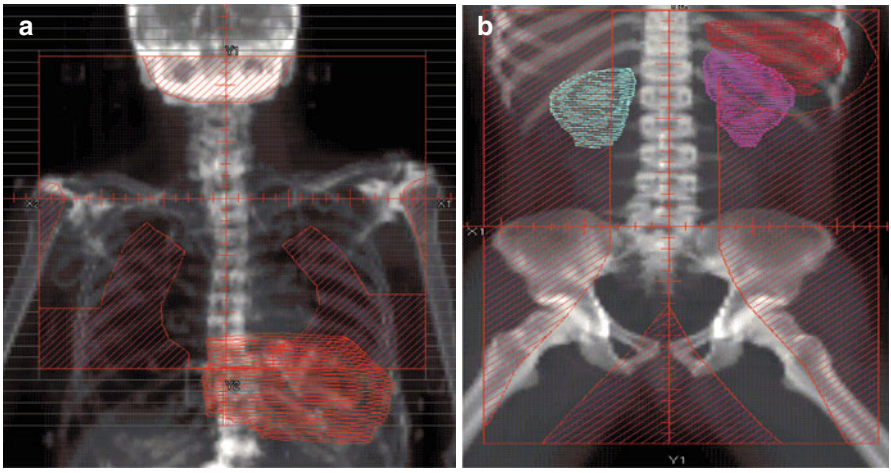

Fig. 29.2 (**a**) DRR of a mantle field (**b**) DRR of an inverted-Y field

Table 29.2 Suggested involved-field borders for cervical/supraclavicular region using standard IFRT [1]

Superior border	1–2 cm above the lower tip of the mastoid process
Inferior border	2 cm below the clavicle
Medial border	If the supraclavicular nodes are not involved, the medial border should be placed at the ipsilateral transverse processes as long as the coverage of nodal involvement is not compromised as a result of medially involved lymph nodes (Fig. 29.3a) If the supraclavicular nodes are involved or there are medial nodes close to the vertebral bodies seen on initial staging neck CT scan, the medial border should be placed at the contralateral transverse processes (Fig. 29.3b)
Lateral border	Includes the medial 2/3 of the clavicle

Involved-Field Radiation Therapy

General Principles of Planning for the Cervical/Supraclavicular Region

- Treatment of the entire cervical region includes the unilateral or bilateral neck and supraclavicular lymph nodes extending from the base of the skull to the clavicles. The field borders of this region are listed in Table 29.2.
- IV contrast should be used for accurate identification of the vessels.
- The patient is simulated in the supine position with the neck hyperextended and immobilized using a thermoplastic mask extending over the head, neck, and shoulder region.
- If treating AP/PA, a posterior mouth block should be used if the patient is treated supine to block divergence through the mouth.

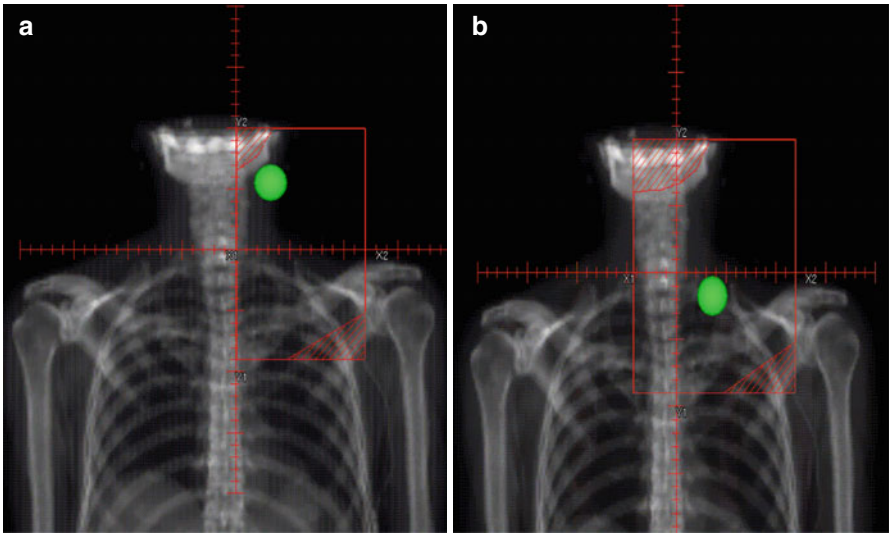

Fig. 29.3 (**a**) DRR of IFRT for a patient with a unilateral cervical lymph node (**b**) DRR of IFRT for a patient with a unilateral supraclavicular lymph node

- If using conformal therapy, keep cord and larynx to as low as reasonably achievable (ALARA). If treating AP/PA, a posterior cervical cord block can be placed if the maximum cord dose exceeds 36 Gy; a larynx block can be added at 18 Gy unless an adequate margin cannot be achieved due to medial cervical lymph nodes present in the location. In addition, a 50 % partial transmission larynx block can be used for the full duration of treatment.
- To aid in rational block design and/or use of conformal therapy, Table 29.3 since this is not related to RTOG contouring guidelines for the neck lymph node levels can be used for anatomic delineation of the initially involved lymph node levels.

Unilateral Cervical/Supraclavicular Region (Fig. 29.3a and 29.3b)

Bilateral Cervical/Supraclavicular Region (Fig. 29.4)

General Principles of Planning for the Axillary Region

- Treatment of the axillary region using standard IFRT includes the ipsilateral axillary, infraclavicular, and supraclavicular lymph nodes. The field boarders of this region is listed in Table 29.4. Reduction in the standard IFRT field may be considered in an effort to spare normal tissues if clinically permissible.
- In adults, the arms should be preferentially placed above the head and immobilized using a custom mold to enhance reproducibility (Fig. 29.5b). This pulls the axillary lymph nodes from the chest to allow for additional lung blocking.

Table 29.3 RTOG contouring borders of levels I–V [2]

Level	Site	Superior	Inferior	Anterior	Posterior	Lateral	Medial
IA	Submental gland	Geniohyoid muscle (m.), plane tangent to basilar edge of mandible	Plane tangent to body of hyoid bone	Symphysis menti, platysma m.	Body of hyoid bone	Medial edge of anterior belly of digastric m.	n/a
IB	Submandibular gland	Mylohyoid m., cranial edge of submandibular gland	Plane through central part of hyoid bone	Symphysis menti, platysma m.	Posterior edge of submandibular gland	Basilar edge/inner side of mandible, platysma m., skin	Lateral edge of ant. belly of digastric m.
IIA	Upper jugular (anterior to the spinal accessory nerve)	Caudal edge of lateral process of C1	Caudal edge of the body of the hyoid bone	Posterior edge of submandibular gland; anterior edge of internal carotid artery; posterior edge of posterior belly of digastric m.	Posterior border of internal jugular vein	Medial edge of sternocleidomastoid (SCM) m.	Medial edge of internal carotid artery, paraspinal (levator scapulae) m.
IIB	Upper jugular (posterior to the spinal accessory nerve)	Caudal edge of lateral process of C1	Caudal edge of the body of the hyoid bone	Posterior border of the internal jugular vein	Posterior border of the SCM m.	Medial edge of the SCM m.	Medial edge of the internal carotid artery, paraspinal (levator scapulae) m.

(continued)

Table 29.3 (continued)

Level	Site	Superior	Inferior	Anterior	Posterior	Lateral	Medial
III	Middle jugular	Caudal edge of the hyoid bone	Caudal edge of the cricoid cartilage	Posterolateral edge of the sternohyoid m.; anterior edge of the SCM m.	Posterior edge of the SCM m.	Medial edge of the SCM m.	Medial edge of the internal carotid artery, paraspinal (scalenus) m.
IV	Lower jugular	Caudal edge of the cricoid cartilage	2 cm cranial to the sternoclavicular joint	Anteromedial edge of the SCM m.	Posterior edge of the SCM m.	Medial edge of the SCM m.	Medial edge of the internal carotid artery, paraspinal (scalenus) m.
V	Posterior triangle spinal accessory nodes	Cranial edge of the hyoid bone	The clavicle after the posterior border of the trapezius m. is no longer present	Posterior edge of the SCM m.	Anterior border of the trapezius m.	Platysma m., skin	Paraspinal (levator scapulae, splenius capitis) m.

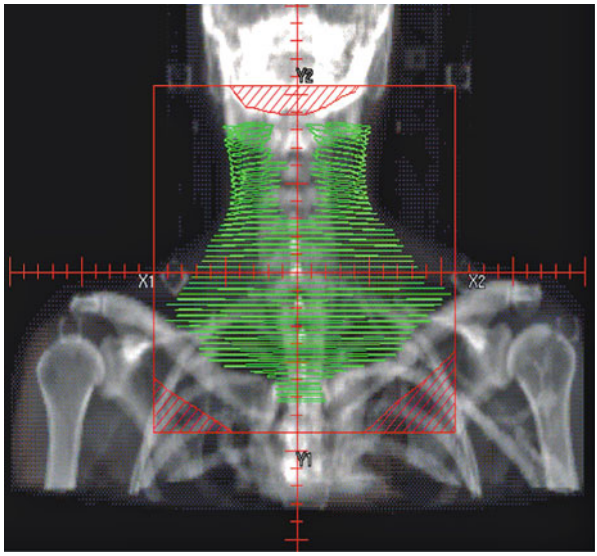

Fig. 29.4 DRR of IFRT for a patient with bilateral cervical/supraclavicular lymph nodes and a thyroid mass. Treat both cervical and supraclavicular regions with the same superior, inferior, and lateral borders as described in Table 1.2 if using standard IFRT

Table 29.4 Suggested involved-field borders for the axillary region using standard IFRT [1]

Superior border	C5–C6 or 2 cm above the pre-chemotherapy extent of disease
Inferior border	The tip of the scapula or 2 cm below the lowest axillary lymph node
Medial border	Ipsilateral cervical transverse process. If supraclavicular lymph nodes are involved, include the vertebral bodies
Lateral border	Flash the axilla

- Humeral head blocking should be avoided in adults simulated with their arms above their heads to avoid blocking axillary lymph nodes.
- In young children, the arms should be placed akimbo to allow humeral head shielding to protect the epiphyseal plate for bone growth (Fig. 29.5a).
- CT simulation allows for accurate delineation of the axillary lymph node region and appropriate blocking [3]. IV contrast should be used for delineation of vasculature to aid in contouring if conformal therapy is planned.
- To aid in rational block design and/or use of conformal therapy, the RTOG contouring guidelines for the axillary lymph node levels can be used for anatomic delineation of the initially involved lymph node levels and potential reduction in field size compared to standard IFRT (Table 29.5).

General Principles of Planning for the Mediastinal Region

- Treatment of the mediastinal region includes the mediastinum, bilateral hila, and bilateral supraclavicular lymph nodes (Fig. 29.6, Table 29.6).
- CT simulation with IV contrast allows for precise localization of vasculature and normal structures such as the heart to aid in conformal therapy.

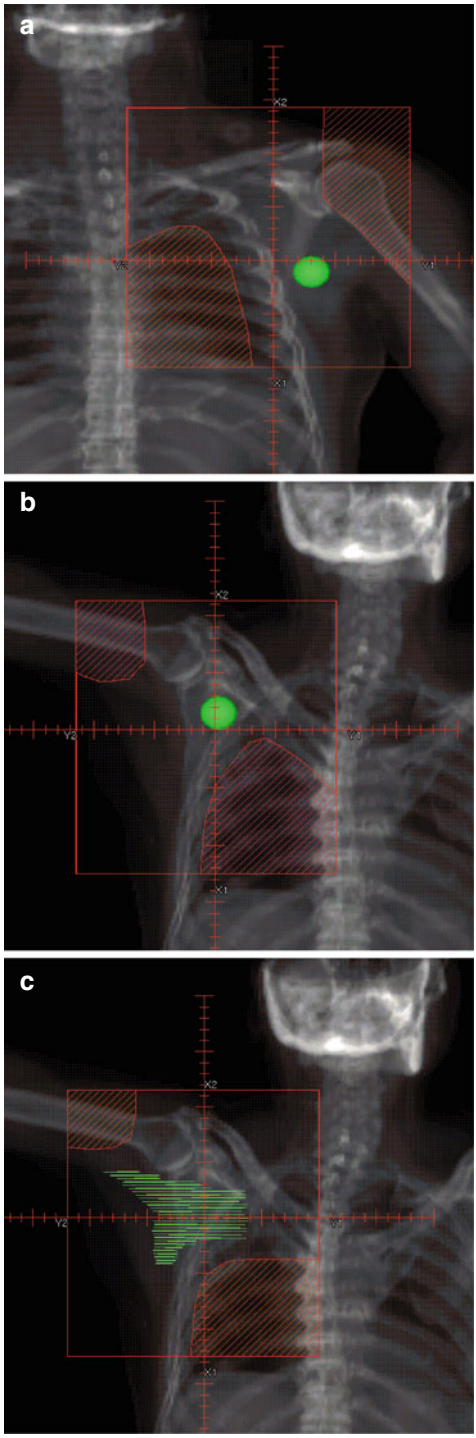

Fig. 29.5 (**a**) DRR of axillary field with patient simulated with arms akimbo (**b**) DRR of axillary field with patient simulated with arms above head. Note that the humeral heads should not be blocked when arms are placed in this position (**c**) DRR of axilla clinical target volume contoured according to RTOG guidelines using standard IFRT

Table 29.5 RTOG contouring borders for supraclavicular and axillary regions

Level	Superior	Inferior	Anterior	Posterior	Lateral	Medial
Supraclavicular	Caudal to the cricoid cartilage	Junction of brachiochephalic-axillary veins/caudal edge of the clavicular head	Sternocleidomastoid (SCM) m.	Anterior aspect of the scalene m.	*Superior*: lateral edge of SCM m. *Inferior*: junction 1st rib-clavicle	Excludes thyroid and trachea
Level I axilla	Axillary vessels cross lateral edge of pectoralis (pec.) minor m.	Pec. major m. inserts into ribs	Plane defined by the anterior surface of pec. major m. and latissimus (Lat.) dorsi m.	Anterior surface of subscapularis m.	Medial border of lat dorsi m.	Lateral border of pec. minor m.
Level II axilla	Axillary vessels cross medial edge of pec. minor m.	Axillary vessels cross lateral edge of pec. minor m.	Anterior surface pec. minor m.	Ribs and intercostal muscles	Lateral border of pec. minor m.	Medial border of pec. minor m.
Level III axilla	Pec. minor m. insert on cricoid	Axillary vessels cross medial edge of pec. minor m.	Posterior surface pec. major m.	Ribs and intercostal muscles	Medial border of pec. minor m.	Thoracic inlet

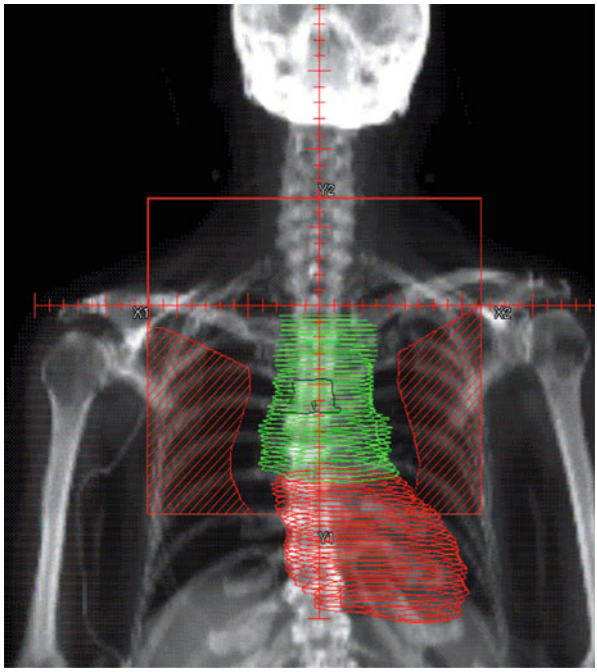

Fig. 29.6 DRR of IFRT for a patient with mediastinal lymph node involvement

Table 29.6 Suggested involved-field borders for the mediastinal region using standard IFRT

Superior border	C5–C6 interspace or the top of the larynx if the supraclavicular lymph nodes are involved. The superior border should be at least 2 cm above the pre-chemotherapy extent of disease
Inferior border	5 cm below the carina or 2 cm below the pre-chemotherapy inferior extent of disease
Lateral border	1.5-cm margin on the post-chemotherapy transverse extent of the volume
Hilar region	1-cm margin if not initially involved, otherwise 1.5-cm margin

- The patient is simulated with the arms akimbo or at the sides. If the axillary lymph nodes are involved, the patient is simulated with their arms placed above the head.
- Due to the risk of secondary breast cancer from mediastinal radiation, the breast should be positioned laterally away from the field and taped for immobilization. The breast can also be outlined with a wire during simulation for better visualization and avoidance during treatment planning.
- To contour normal breasts for the purpose of conformal therapy and organ at risk (OAR) avoidance, the RTOG breast contouring atlas can be used (not presented here) [4]. To aid in rational block design and/or use of conformal therapy, the Mountain and Dressler contouring borders [5] can be referenced on (Table 29.7).

Table 29.7 Mountain and Dressler contouring borders for mediastinal contouring

Level	Site	Superior	Inferior	Anterior	Posterior	Lateral	Medial
1R, 1L 2R, 2L	Highest mediastinal and upper paratracheal nodes	Upper limit of the sternal notch	Superior to the aortic arch	Posterior to the vessels (right subclavian vein, left brachiocephalic vein, etc.)	Posterior wall of the trachea	Pleural envelope	Midline trachea
3A	Prevascular nodes	Upper limit of the sternal notch	Carina	Sternum, clavicular heads, and ribs	*Superior*: anterior border of stations 1–2 excluding great arteries *Inferior*: station 6 on the left and the anterior border of the superior vena cava (SVC) on the right	Pleural envelope	n/a
3P	Retrotracheal nodes	Upper limit of the sternal notch	Carina	Posterior to the trachea *Superior*: posterior aspect of Stations 1–2 *Inferior*: stations 4R and 4L inferiorly	1 cm posterior to the anterior and lateral borders of the vertebral body	*Right*: air-tissue interface *Left superior*: air-tissue interface *Left inferior*: aorta	n/a

(continued)

Table 29.7 (continued)

Level	Site	Superior	Inferior	Anterior	Posterior	Lateral	Medial
4R	Right lower paratracheal nodes	Top of the aortic arch	Right upper lobe bronchus (or where the right pulmonary artery crosses the middle of the mediastinum)	Right brachiocephalic vein followed by the SVC and the arch or ascending aorta	*Superior*: posterior wall of the trachea *Inferior*: anterior to the right main stem bronchus	*Superior*: pleural envelope *Intermediate*: medial to SVC and arch of the azygos vein *Inferior*: right upper lobe pulmonary vein	Midline trachea
4L	Left lower paratracheal nodes	Top of the aortic arch	Left upper lobe bronchus	The great vessels or the aorta	Posterior wall of the trachea or the anterior aspect of the left main bronchus	*Superior*: aortic arch *Intermediate*: between the ascending and descending aorta *Inferior*: pulmonary trunk and/or left pulmonary artery	Midline trachea *Inferior*: right pulmonary artery and station 7
5	Subaortic (aortic-pulmonary window)	Most inferior aspect of the aortic arch	Lowest image that the right pulmonary artery is maximally visualized	Midpoint of the ascending aorta or visible soft tissue	Anterior aspect of the descending aorta, the lateral aspect of the pulmonary trunk, and the upper lobe pulmonary veins and the left lateral aspect of the pulmonary trunk	Pleural envelope	Station 4L, the pulmonary trunk, and the left pulmonary artery

6	Para-aortic nodes	Top of the aortic arch	Same as Station 5	1 cm around the ascending aorta and the aortic arch	Anterior and lateral walls of the ascending aorta, aortic arch, and the anterior aspect of the medial wall of the pulmonary trunk until station 5	1 cm around the ascending aorta and the aortic arch	n/a
7	Subcarinal nodes	Carina	Origin of the right middle lobe bronchus	Station 4R, Station 4L, the right pulmonary artery, and/or the left superior pulmonary vein	Station 8 and does not extend past the posterior wall of the main bronchi	Space between the right main and left main bronchi	n/a
8	Paraesophageal nodes	Carina	Gastroesophageal junction	Station 7 *Superior*: left main stem bronchus *Inferior*: heart	Abuts the descending aorta and 1 cm posterior to the anterior aspect of the vertebral body	Within the pleural envelope and abuts the descending aorta on the left	n/a

(continued)

Table 29.7 (continued)

Level	Site	Superior	Inferior	Anterior	Posterior	Lateral	Medial
10R, 11R	Right hilar and interlobar nodes	Point of division of the right upper lobe bronchus into segmental branches	Origin of the superior segmental bronchus of the right lower lobe	Air-tissue interface (when CT slice is displayed in mediastinal window) with inclusion of the main bronchus, lobar bronchi, and vessels in the hilum	Air-tissue interface (when CT slice is displayed in mediastinal window) with inclusion of the main bronchus, lobar bronchi, and vessels in the hilum	Air-tissue interface (when CT slice is displayed in mediastinal window)	Lateral border of the SVC and the middle of the vertebral body
10L, 11L	Left hilar nodes and interlobar nodes	Bifurcation of the upper lobar bronchus into the segmental bronchi	Point at which the left lower lobe bronchus branches into segments	Posterior border of the left pulmonary artery	Posterior border of the lower pulmonary artery	Air-tissue interface (when CT slice is displayed in mediastinal window) with exclusion of the segmental bronchi	Between the lateral border of the pulmonary trunk and the lateral border of the descending aorta

General Principles of Planning for the Para-Aortic Region

- Treatment of the para-aortic region includes the para-aortic lymph nodes with or without the spleen (Fig. 29.7, Table 29.8).
- CT simulation should be utilized to aid in contouring the aorta and inferior vena cava (IVC) where the para-aortic lymph nodes lie. With contrast, the bilateral kidneys can also be readily identified for avoidance. The kidneys should be outlined and considered when designing the blocks for treatment planning.
- The patient may be immobilized with a custom mold, particularly if a three-dimensional conformal treatment is planned.
- Shield testicles in men with a clamshell and consider the position of the ovaries for reproductive age women.

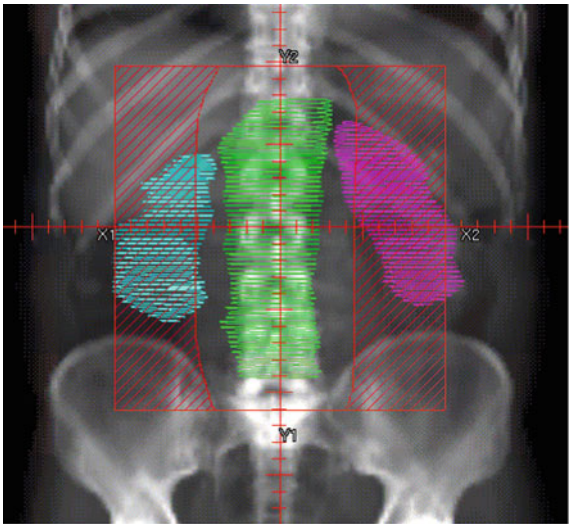

Fig. 29.7 DRR of IFRT for a patient with para-aortic lymph node involvement

Table 29.8 Suggested involved-field borders for the para-aortic region using standard IFRT [1]

Borders	Setups
Superior border	Top of T11 and at least 2 cm above the pre-chemotherapy volume
Inferior border	Bottom of L4 and at least 2 cm below the pre-chemotherapy volume
Lateral borders	Include the edge of the transverse processes and at least 2 cm lateral to the post-chemotherapy volume
Spleen	Treated only if initial imaging is suggestive of disease involvement The post-chemotherapy volume is treated with 1.5-cm margins Motion assessment of the spleen can be performed using 4D CT scan to confirm movement with respiration for rational margin placement. If the patient has undergone splenectomy, the field can be extended to include the splenic hilar region. This region may be marked by radiopaque clips placed at the time of surgery. If no clips were placed, the field can be extended at T12–L1, where the splenic hilar lymph nodes are located along the splenic vasculature
Porta hepatis	This region should only be included if originally involved with disease

General Principles of Planning for the Pelvic Region

- The patient may be simulated in a "frog-leg" position to separate the leg from the external genitalia and flatten any inguinal skin folds to minimize a potential skin reaction.
- Treatment of the pelvic region includes the external iliac, femoral, and inguinal lymph nodes (Fig. 29.8, Table 29.9). Reduction in field size may be considered depending on the clinical scenario in an effort to reduce dose to normal structures.
- Shield testicles in men with a clamshell and consider position of the ovaries for reproductive age women.

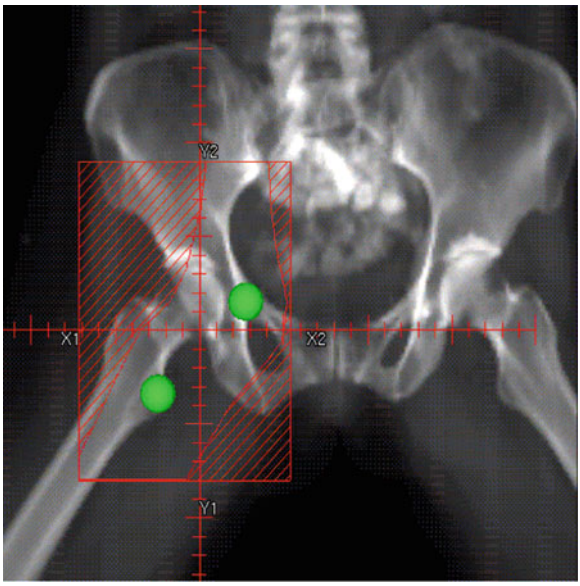

Fig. 29.8 DRR of IFRT for a patient with pelvic lymph node involvement

Table 29.9 Suggested involved-field radiation borders for the pelvic region using standard IFRT [1]

Borders	Setups
Superior border	Middle of the sacroiliac joint or 2 cm above the pre-chemotherapy extent of disease
Inferior border	At least 2 cm below the pre-chemotherapy lymph nodes or 5 cm below the lesser trochanter
Medial border	At least 2 cm medial to the pre-chemotherapy lymph nodes or may extend to include the medial border of the obturator foramen
Lateral border	At least 2 cm lateral to the pre-chemotherapy lymph nodes or may extend to include the greater trochanter
Common iliacs	If there is evidence of common iliac lymph node involvement, the superior border is extended to the L4–L5 interspace with at least a 2-cm margin above the pre-chemotherapy lymph node volume

Involved-Node Radiation Therapy (INRT)

General Principles for the Target Definition and Selection for INRT

- INRT is best performed on a clinical protocol using standardized guidelines. The EORTC-GELA guidelines are detailed in Tables 29.10, 29.11, 29.12, and 29.13, and the German Hodgkin's Study Group Guidelines are detailed in Tables 29.14 and 29.15.
- All patients should be examined by a radiation oncologist prior to initiating chemotherapy.
- CT scans should be performed before and after chemotherapy and when possible, in the treatment position. PET/CT scans are recommended to be performed in the treatment position for proper identification of all initially involved lymph node sites.
- An online EORTC-GELA contouring atlas is available at http://groups.eortc.be/lymphoma/final_eortc-gela_notebook.pdf

EORTC-GELA Guidelines [6–8]

Table 29.10 Target volumes for the cervical/axillary region in complete remission (CR) or unconfirmed CR (CRu)

Target volumes	Suggested target volume selection and delineation
GTV	Does not exist since initially involved lymph nodes are either no longer visible, of normal size, or are in CRu
CTV	Includes the initial lymph node volume *before* chemotherapy
	Incorporates the initial location and extent of disease and takes into account the displacement of normal tissues
	In the case of a CRu, the lymph node remnants should be included in the CTV
PTV	The PTV is the CTV with an additional margin to account for organ movement and setup variation
	The margin should be 1 cm isotropically which is sufficient in the majority of cases

Table 29.11 Target volumes for the mediastinal region *complete remission (CR) or unconfirmed CR (CRu).* The target definition for the mediastinum is different in order to minimize lung and cardiac toxicity

Target volumes	Suggested target volume selection and delineation
GTV	Does not exist since initially involved lymph nodes are either no longer visible, of normal size, or are in CRu
CTV	Length corresponds to the length of the mediastinal mass or lymph node(s) *before* chemotherapy Width corresponds to the width of the mediastinal mass or lymph node(s) *after* chemotherapy In the case of a CRu, the lymph node remnants should be included in the CTV In the case of a CR or a CRu, the normal mediastinum is contoured and the CTV should not exceed the lateral mediastinal boundaries except where lymph node remnants persist Whenever possible, avoid blood vessels and the heart and limit lung toxicity
PTV	The margin should be 1 cm isotropically which is sufficient in the majority of cases (see Fig. 29.9b, d)

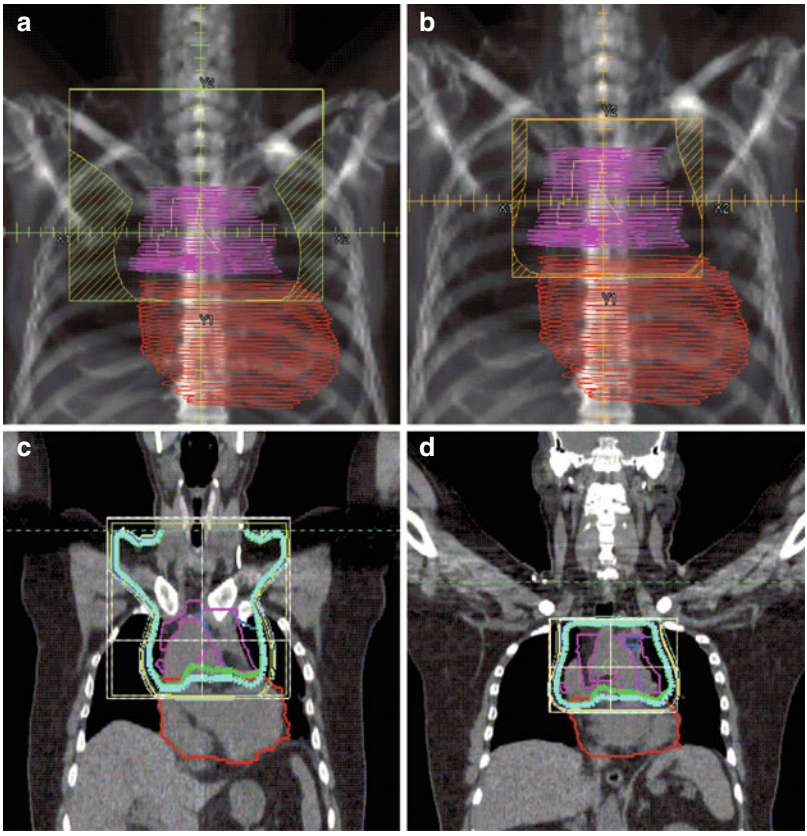

Fig. 29.9 (**a**) IFRT DRR of the mediastinum (**b**) INRT DRR of the mediastinum (**c**) IFRT treatment plan of the mediastinum (**d**) INRT treatment plan of the mediastinum

Table 29.12 Target volumes for the cervical/axillary region in partial remission (PR)

Target volumes	Suggested target volume selection and delineation
GTV	Represents the lymph node remnant(s)
CTV	Includes the initial lymph node volume *before* chemotherapy
	Incorporates the initial location and extent of disease and takes into account the displacement of normal tissues
PTV	Initial PTV (PTV1): CTV including the GTV with a 1-cm isotropic margin
	Boost PTV (PTV2): GTV alone with a 1-cm isotropic margin

Table 29.13 Target volumes for the mediastinal region in partial remission (PR)

Target volumes	Suggested target volume selection and delineation
GTV	Represents the lymph node remnant(s) or the remaining mass alone
CTV	The length of the CTV corresponds to the length of the mediastinal mass or lymph node(s) *before* chemotherapy
	CTV width corresponds to the width of the mediastinal mass or lymph node(s) *after* chemotherapy
	The normal mediastinum is contoured and the CTV should not exceed the lateral mediastinal boundaries except where lymph node or mass remnant(s) persist
	Whenever possible, avoid blood vessels and the heart and limit lung toxicity
PTV	Initial PTV (PTV1): CTV including the GTV with a 1-cm isotropic margin
	Boost PTV (PTV2): GTV alone with a 1-cm isotropic margin

German Hodgkin's Study Group Guidelines [9]

Table 29.14 Target volumes *excluding the mediastinal region* suggested by the German Hodgkin's Lymphoma Group

Target volume	Suggested target volume selection and delineation
CTV	Includes the initial lymph node volume *before* chemotherapy
	Incorporates the initial location and extent of disease and takes into account the displacement of normal tissues
	In the case of a CR or a CRu with visible lymph node remnant(s), the initial location and extent of the disease should be included in the CTV
PTV[a]	The margin should be 2 cm in the axial and 3 cm in the craniocaudal direction However, it may be reduced to 1–1.5 cm to avoid nearby at risk organs (e.g., spinal cord, kidney)
	The traditional involved-field borders should be respected. For example, the superior border of a high cervical lymph node should be the mastoid tip

[a]A minimum target volume of 5 × 5 cm is recommended

Table 29.15 Target volumes for the *mediastinal region* suggested by the German Hodgkin's Lymphoma Group

Target volume	Suggested target volume selection and delineation
CTV	The length of the CTV corresponds to the length of the mediastinal mass or lymph node(s) *before* chemotherapy The width of the CTV corresponds to the width of the mediastinal mass or lymph node(s) *after* chemotherapy In the case of a CR or a CRu with visible lymph node remnant(s) that do not exceed the lateral mediastinal boundaries, the CTV should encompass the normal mediastinum In the case of a PR that exceeds the lateral mediastinal boundaries, the width of the CTV is the width of the mediastinal mass or lymph node(s) *after* chemotherapy as described above
PTV[a]	The margin should be 1 cm in the axial and 3 cm in the craniocaudal direction

[a]A minimum target volume of 5 × 5 cm is recommended

Table 29.16 Suggested target volume delineation for gastric, orbital, and sinonasal lymphoma

Origin	Suggested target volume selection and delineation
Gastric (Fig. 29.10)	GTV = gross disease CTV = GTV + stomach from gastroesophageal to gastroduodenal junction PTV = CTV + 2 cm margin using 4D CT assessment of respiratory motion[a]
Orbital (Fig. 29.11)	GTV = gross disease CTV = GTV + whole orbit PTV = CTV + 5-mm margin
Sinonasal	GTV = gross disease CTV = GTV + entire involved sinus(es) PTV = CTV + 3–5-mm margin depending upon setup technique

[a]The PTV margin should be adjusted accordingly based on the results of 4D assessment. In some cases, 2 cm may not be adequate given the degree of stomach motion

Contouring for Select Extranodal Sites

General Principles of Patient Setup and TV Delineation for Gastric Lymphoma

- Patients should fast 2 h prior to simulation and treatment in order to decrease gastric motility. Oral contrast should be used in all cases and IV contrast is recommended if there are involved lymph nodes.
- Patients should be simulated with arms up if using conformal radiation therapy and immobilized using a custom mold. Respiratory motion should be assessed using a 4D CT scan.
- Modern radiation techniques, including 3DCRT and IMRT, are recommended to spare dose to the kidney and liver. Suggested target volumes for gastric lymphoma radiation therapy are presented in Table 29.16.

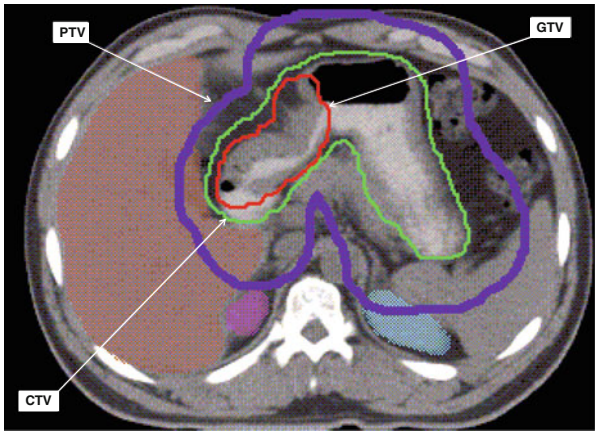

Fig. 29.10 Target volume delineation in a patient with a gastric lymphoma

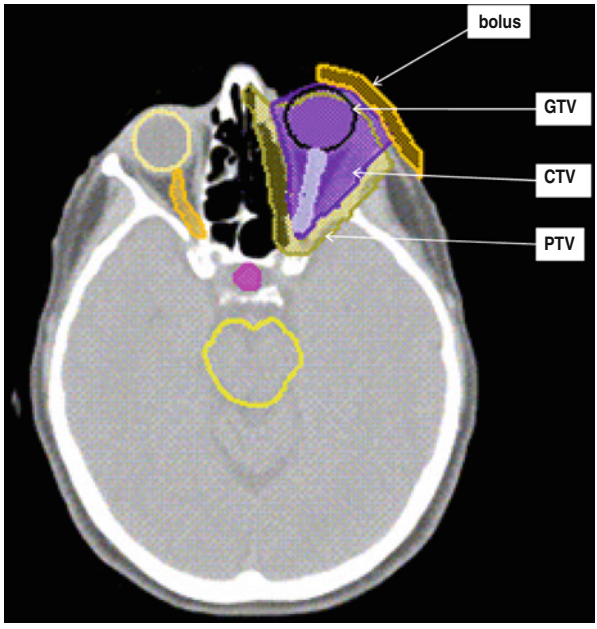

Fig. 29.11 Target volume delineation in a patient with an orbital lymphoma

General Principles of Patient Setup and TV Delineation for Orbital and Sinonasal Lymphoma

- The patient is simulated in the supine position with arms down and head immobilized using a thermoplastic mask.
- For orbital lymphoma, treat with superior-inferior wedge pair technique, 3DCRT, or IMRT. May add bolus to increase superficial dose to localized soft tissue disease and consider lacrimal gland shield if prescribed dose ≥30 Gy.

- For limited indolent disease of the conjunctivae, treat with anterior electron beam setup or may consider electron/photon mixed energy; consider lens shield if tumor located in the periphery.
- For sinonasal lymphomas, treatment with 3DCRT or IMRT is recommended given the higher doses delivered in the treatment of this disease and the number of surrounding critical structures.
- Suggested target volumes for orbital and sinonasal lymphoma radiation therapy are presented in Table 29.16.

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Soft Tissue Sarcoma

30

Colleen Dickie and Brian O'Sullivan

General Principles of Planning and Target Delineation

- Anatomic location, size, depth (with respect to the superficial fascia), and pathological features dictate the management of soft tissue sarcoma (STS).
- Invasion is typically in the longitudinal direction within muscle and confined to the compartment of origin. Suspicious peritumoral changes, henceforth referred to as edema, may harbor microscopic disease. Edema is most often pronounced in the cranio-caudal dimension and should ordinarily be encompassed in the radiotherapy target volume.
- STS generally respect barriers to tumor spread such as bone, interosseous membrane, and major fascial planes, and this concept should be exploited in tissue/function preserving radiotherapy planning, especially in extremity lesions.
- Retroperitoneal tumors commonly grow to a large size and initially displace but eventually invade adjacent organs and tissues.
- In the event of an "unplanned" surgical resection with positive margins (surgical error), the RT target volume needs to generously include all disturbed muscle compartments in addition to any other tissues considered to be directly involved (see Figs. 30.1 and 30.2).
- For preoperative planning target volume definition, CT simulation imaging fused with MR imaging should be performed, ideally with the patient in the treatment position, to help guide delineation of the gross tumor volume (GTV) and clinical target volume (CTV). (see Figs. 30.1 and 30.2).
- For postoperative planning target volume definition after assumed complete surgical resection, there is no GTV to delineate. The location of the original GTV following the operation ($_{postop}$GTV) should be recreated in the planning CT dataset using preoperative CT/MRI imaging if available (see Figs. 30.3, 30.4, and 30.5).

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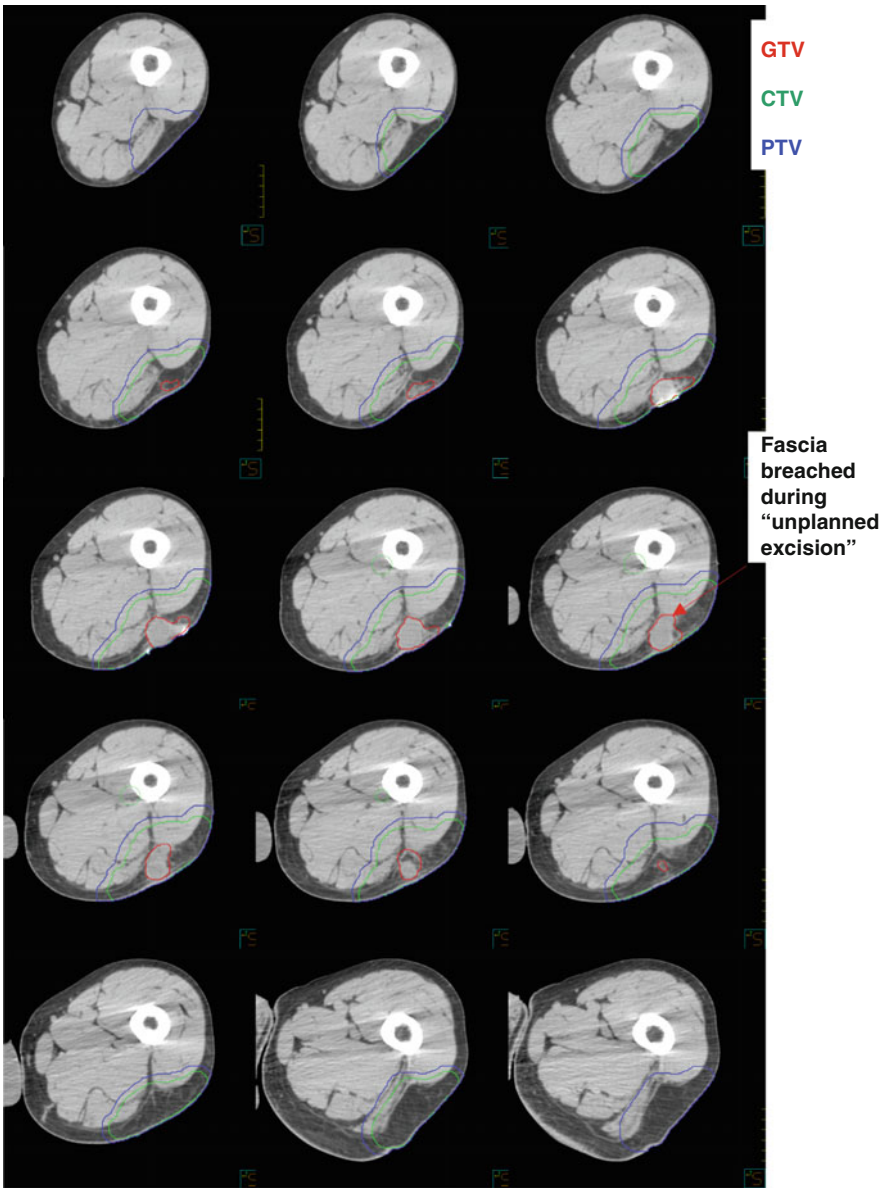

Fig. 30.1 A patient with a T2bN0M0 grade 3 dedifferentiated liposarcoma in the posterolateral thigh. This patient presented having had a previous unplanned excision of a superficial lesion where the fascia of the vastus lateralis was breached but did not involve the deeper compartment originally. CT simulation used 2.0-mm slice thickness. Notice the area of violated fascia due to previous surgical error. Shown are representative slices

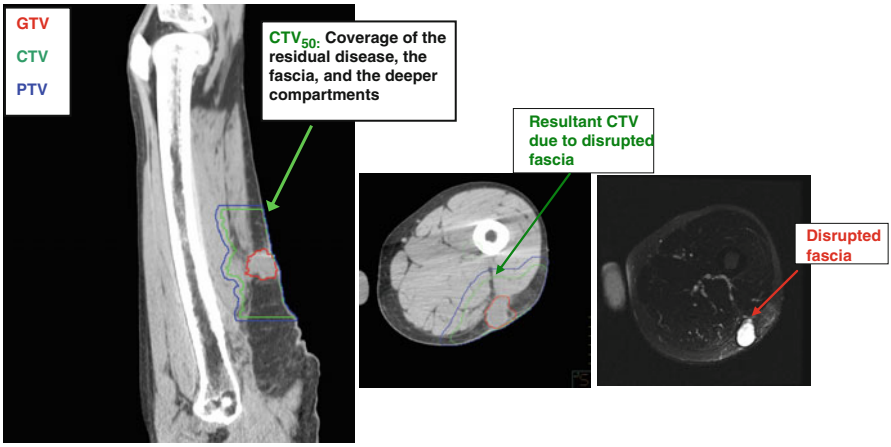

Fig. 30.2 Example of GTV, CTV, and PTV displayed in the sagittal view as well as an axial view of the disrupted fascia as a result of an unplanned excision with the corresponding planning CT target volumes

- For preoperative cases, 50 Gy is ordinarily used and target volumes include the GTV and the CTV_{50} and should be delineated on every slice on the planning CT (see Figs. 30.1 and 30.2).
- For postoperative RT delivery, 66 Gy is ordinarily used (60 Gy can be used in margin clear, low-grade cases) with an additional peripheral CTV volume for tissues with a lower risk of tumor infestation (see Figs. 30.3, 30.4 and 30.5).
- For unresectable residual gross disease, 70 Gy in 2 Gy/fraction or equivalent dose fractionation is ordinarily used depending on the tolerance of the anatomic region.
- Suggested GTV and CTV_{50} for preoperative IMRT of extremity STS are detailed in Tables 30.1.
- Suggested $_{postop}$GTV and CTV_{66} for postoperative IMRT of extremity STS are detailed in Tables 30.2.
- Suggested GTV and CTV (dose 50–50.4 Gy) for preoperative IMRT of retroperitoneal STS are detailed in Tables 30.3 (Figs. 30.6 and 30.7).

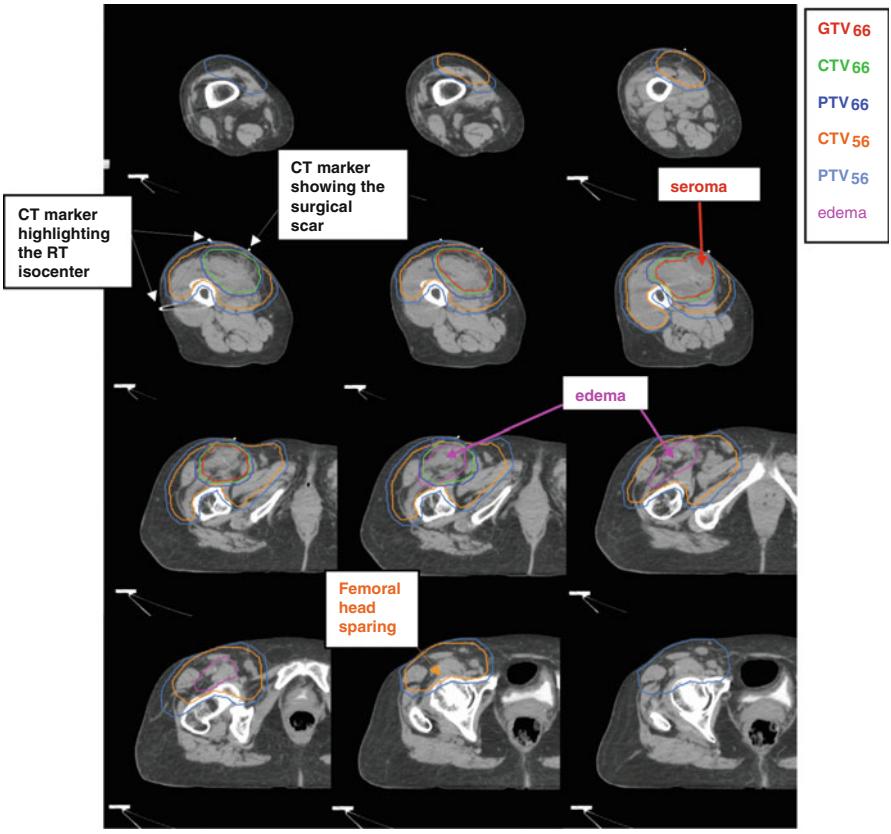

Fig. 30.3 A patient with a T2bN0M0 grade 3 pleomorphic rhabdomyosarcoma in the left thigh. This patient received postoperative RT for negative but close margins. CT simulation used 2.0-mm slice thickness. Edema was contoured at the superior aspect of the $_{postop}$GTV and included in the CTV_{56}. Shown are representative slices. CTV_{56} is limited by the femoral head and bone throughout the target. In some cases where the subcutaneous tissues have been contaminated, bolus may be applied to the surgical scar for a component of the treatment (e.g., 50 Gy)

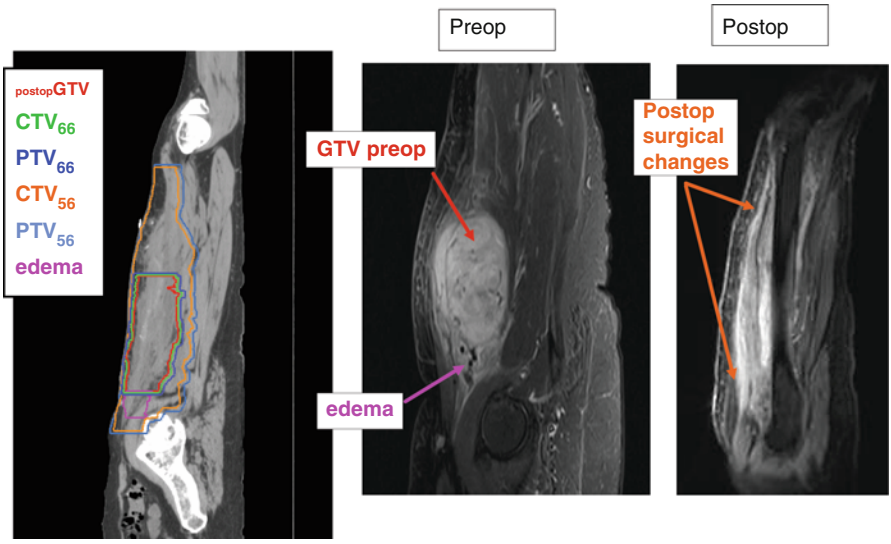

Fig. 30.4 Sagittal CT simulation view of the radiotherapy target volumes for this postoperative STS case and corresponding preoperative and postoperative MRI. Note the CTV_{56} is defined by edema and the postoperative surgical changes. Where the target may appear coincidental in this scaled anatomic illustration, the usual margins were applied (e.g., 0.5- to 1-cm PTV expansion). In addition, the preoperative imaging was imported and co-registered with the postoperative RT planning CT dataset in order to appreciate the original tumor extent for delineation of the $_{postop}$GTV

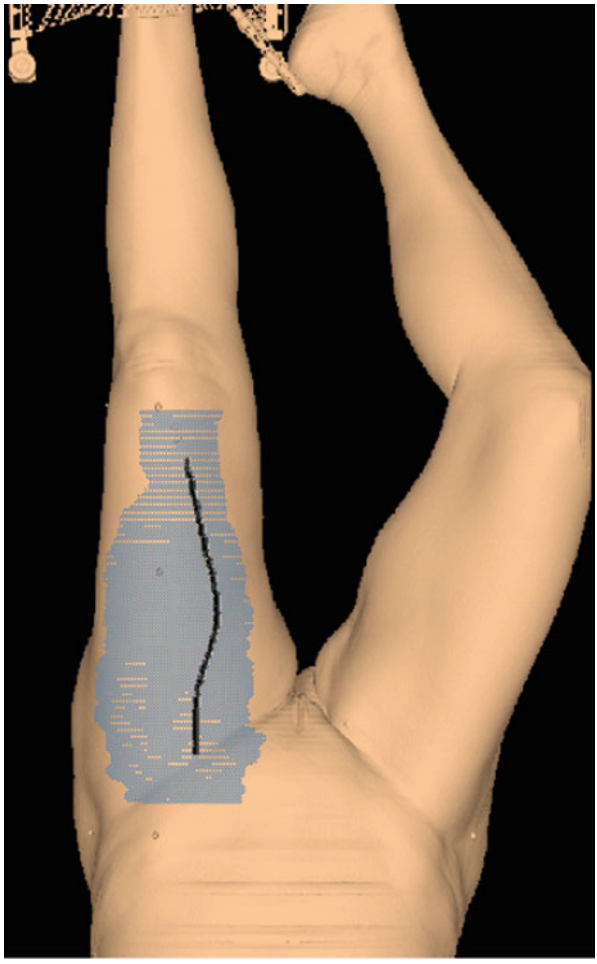

Fig. 30.5 The digitally reconstructed skin rendered image displaying the surgical scar and the planning target volume (PTV_{56}) shown in light blue that includes the surgical scar with a margin

Table 30.1 Suggested target volumes for preoperative extremity STS

Target volumes	Definition and description
GTV	Primary: all gross disease on physical examination and imaging. T1-weighted contrast-enhanced MRI preferable. Co-registration of the MRI and planning CT is facilitated by immobilizing the patient in the treatment position
CTV_{50*} (the subscript 50 denotes the radiation dose delivered)	Includes all areas at risk of subclinical spread defined by the distance from the GTV or edema
	Includes the GTV + a 4-cm margin in the longitudinal dimensions and a 1.5-cm margin in the radial dimension limited to but including any anatomic barrier to tumor spread, such as bone or fascia
	Suspicious peritumoural edema, best demonstrated on T2-weighted MRI, may contain microscopic tumor cells and should be contoured separately with an adequate margin (usually 1–2 cm)
	For cases of "unplanned excision," margins should include $_{postop}$GTV or any residual GTV + all surgically manipulated and disturbed tissues and violated fascia + 4 cm longitudinally and 1.5 cm radially limited to but including any barrier to tumor spread
PTV_{50*}	CTV_{50} + 0.5–1.0 cm, determined by individual institutional protocols and procedure

*Suggested gross tumor dose is 2.0 Gy/fraction to 50 Gy

Table 30.2 Suggested target volumes for postoperative extremity STS

Target volumes	Definition and description
$_{postop}$GTV	$_{postop}$GTV should identify the original site of the tumor Important to review and import presurgical imaging when contouring on the CT simulation scan for RT planning to ensure adequate coverage of the original tumor extent
CTV_{66*} (the subscript denotes the radiation dose delivered)	CTV_{66} should encompass the entire $_{postop}$GTV + immediate area of surgical change with a 1- to 2-cm margin in the longitudinal plane and a 1.5-cm margin in the transverse plane. This may, but not always, include all surgically disturbed tissues, scars, and drain sites
PTV_{66*}	CTV_{66} + 0.5–1.0 cm, determined by individual institutional protocols and procedure
CTV_{56*}	Includes all areas at risk of subclinical spread defined by the distance from the $_{postop}$GTV and additional disturbed tissues Includes the $_{postop}$GTV + a 4-cm margin in the longitudinal dimensions and a 1.5-cm margin in the radial dimension limited to but including any anatomic barrier to disease spread; additional disturbed surgical tissues and any scars or drain sites are ordinarily included with a 1- to 2-cm margin if they are not included in the CTV_{66} Suspicious peritumoural edema should be contoured separately and included with an adequate margin. Like surgically disrupted tissue, it is best identified from a recent postoperative MRI scan Discussion with the surgeon and review of surgical and pathology reports will facilitate the decision about whether or not a seroma, lymphocele, or hematoma should be included
PTV_{56*}	CTV_{56} + 0.5–1.0 cm, determined by individual institutional protocols and procedure

Table describes single-phase simultaneous boost technique. An alternative is the more traditional-phased shrinking field technique that delivers 50 Gy in 25 fractions to all areas of subclinical disease followed by a boost to deliver the final 16 Gy in 8 fractions using a second radiotherapy plan
*High-risk subclinical dose: 2.0 Gy/fraction to 66 Gy; for lower-risk subclinical regions 1.69 Gy/fraction to 56 Gy delivered to the CTV_{56}

Table 30.3 Suggested target volumes for retroperitoneal STS

Target volumes	Definition and description
GTV[a]	Primary: all gross disease on physical examination and imaging
CTV	Includes all areas at risk of subclinical spread defined by the distance from the GTV Includes the GTV + a 2-cm margin in the longitudinal dimensions and a 0.5–2.0-cm margin in the radial dimension limited to but including any anatomic barrier to tumor spread and critical anatomy. For example, if the tumor is approximating an intact liver, 0.5 cm of the liver is included 2-cm margins are usually used posteriorly to include fatty tissues and vessels Ipsilateral kidney may be sacrificed provided the contralateral kidney has acceptable function. In such a case, dose to the uninvolved opposite kidney should be kept as low as reasonably achievable Other organs at risk include the small bowel, liver, spinal cord, and lungs
PTV	CTV + 0.5 cm, determined by individual institutional protocols and procedure

[a]Suggested gross tumor dose range of 50 Gy/25 fractions to 50.4 Gy/28 fractions

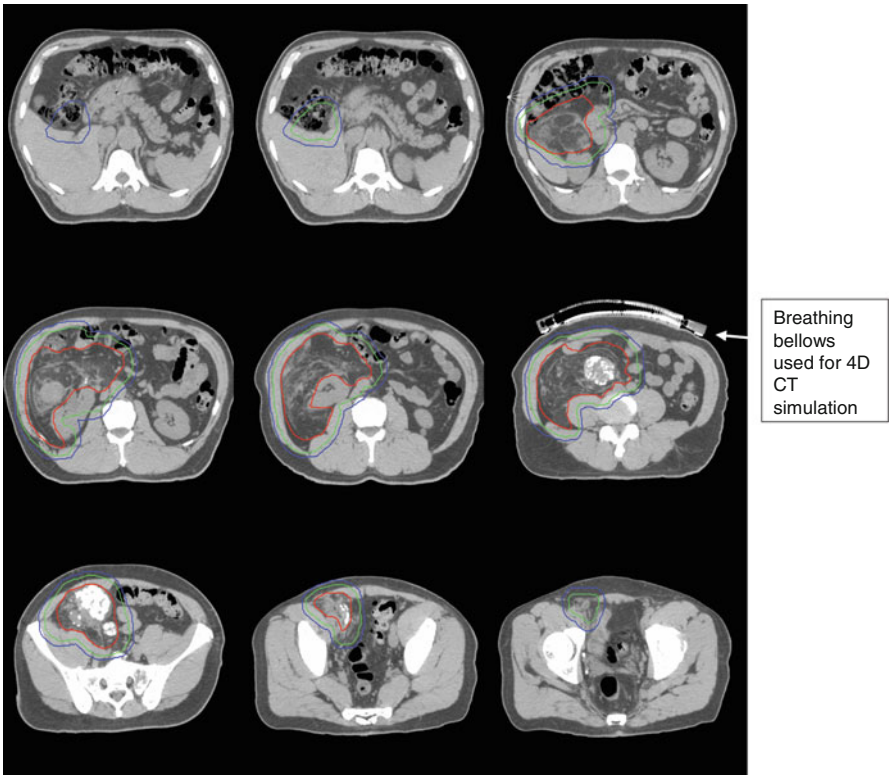

Fig. 30.6 An example of a right-sided T2bN0M0 grade 3 undifferentiated pleomorphic retroperitoneal sarcoma juxtaposed to the duodenum, the right kidney, and the iliac vessels. CT simulation used a 2.0-mm slice thickness. Representative slices are shown. Note the small amount of liver included in the CTV and PTV in the first three axial slices. Multifocal areas of calcifications within the tumor aided in daily image guidance for targeted IMRT. 4D CT simulation is encouraged

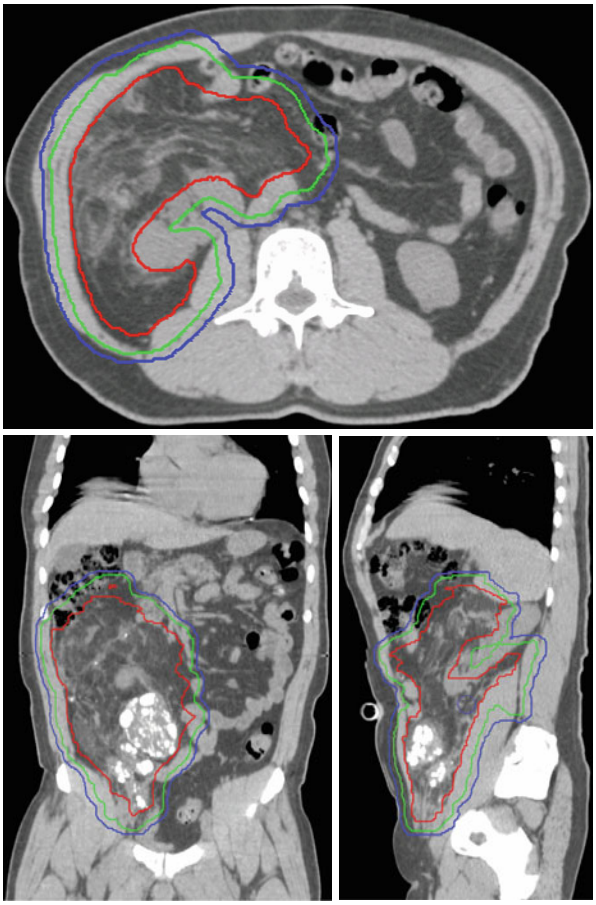

Fig. 30.7 An axial, coronal, and sagittal display of the right-sided retroperitoneal sarcoma. Note the bowel displacement by the tumor, one of the major advantages of preoperative radiotherapy in this setting

Pediatric Sarcoma

31

Arthur K. Liu and Arnold C. Paulino

Ewing's Sarcoma

General Principles of Planning and Target Delineation

- Tumor should be defined by physical exam, CT scan (preferable for definition of bony involvement), MRI (preferable for soft tissue involvement), and PET/CT if available.
- Immobilization during CT simulation will depend on the sites to be treated. For pelvic primaries, a custom Alpha Cradle or Vacloc bag should be used to immobilize the pelvis and upper legs. For thoracic primaries, the arms are often positioned up, and a custom Alpha Cradle/Vacloc bag or Wing Board are used.
- Target volumes include an initial target volume defined at presentation prior to chemotherapy or surgery (GTV1, CTV1, PTV1) and a volume reduction defined after chemotherapy and surgery (GTV2, CTV2, PTV2). See Table 31.1 for additional target definitions. Suggested doses (based on the Children's Oncology Group protocol AEWS1031) are given in Table 31.2. An example of volumes for a patient with a pelvic Ewing's sarcoma are shown in Fig. 31.1.

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Table 31.1 Ewing's sarcoma volume definitions

Initial target volumes	Definition and description
GTV1	Gross disease (including unresected enlarged lymph nodes) at presentation, prior to chemotherapy or surgery. GTV1 can be modified for tumors that extend into body cavities, such as the pelvis or thorax, which regress with chemotherapy. In these cases, the edge of GTV1 can be defined as the post-chemotherapy volume
CTV1	GTV1 + 1 cm. CTV1 includes involved (pathologically or clinically) nodal regions
PTV 1	CTV1 + institutional setup margin
Volume reduction	
GTV2	Residual tumor after induction chemotherapy. For definite radiation therapy, include all initial areas of bony involvement
CTV2	GTV2 + 1 cm
PTV2	CTV2 + institutional setup margin

Table 31.2 Ewing's sarcoma doses in 1.8 Gy per fraction

	PTV1 (Gy)	PTV2 (Gy)
Definitive RT (vertebral body)	45 (45)	10.8 (5.4)
Extraosseous with CR to chemotherapy	50.4	
Postoperative with microscopic residual with >90 % necrosis	0	50.4
Postoperative with microscopic residual with <90 % necrosis	50.4	0
Postoperative with gross residual	45	10.8

Rhabdomyosarcoma

General Principles of Planning and Target Delineation

- Tumor should be defined by physical exam, CT scan (preferable for definition of bony involvement), MRI (preferable for soft tissue involvement), and PET/CT if available.
- Immobilization during CT simulation will depend on the sites to be treated. For head and neck primaries, both the head and shoulders should be immobilized, for example, with a Med-Tec S-frame. For extremities, immobilization usually involves the use of a custom Alpha Cradle or Vacloc bag and needs to also account for the likely treatment angles.
- Target volumes include an initial target volume defined at presentation prior to chemotherapy or surgery (GTV1, CTV1, PTV1) and a volume reduction defined after chemotherapy and surgery (GTV2, CTV2, PTV2). See Table 31.3 for additional target definitions suggested doses are given in Table 31.4. Example volumes for a middle ear and hand rhabdomyosarcoma are shown in Figs. 31.2 and 31.3.

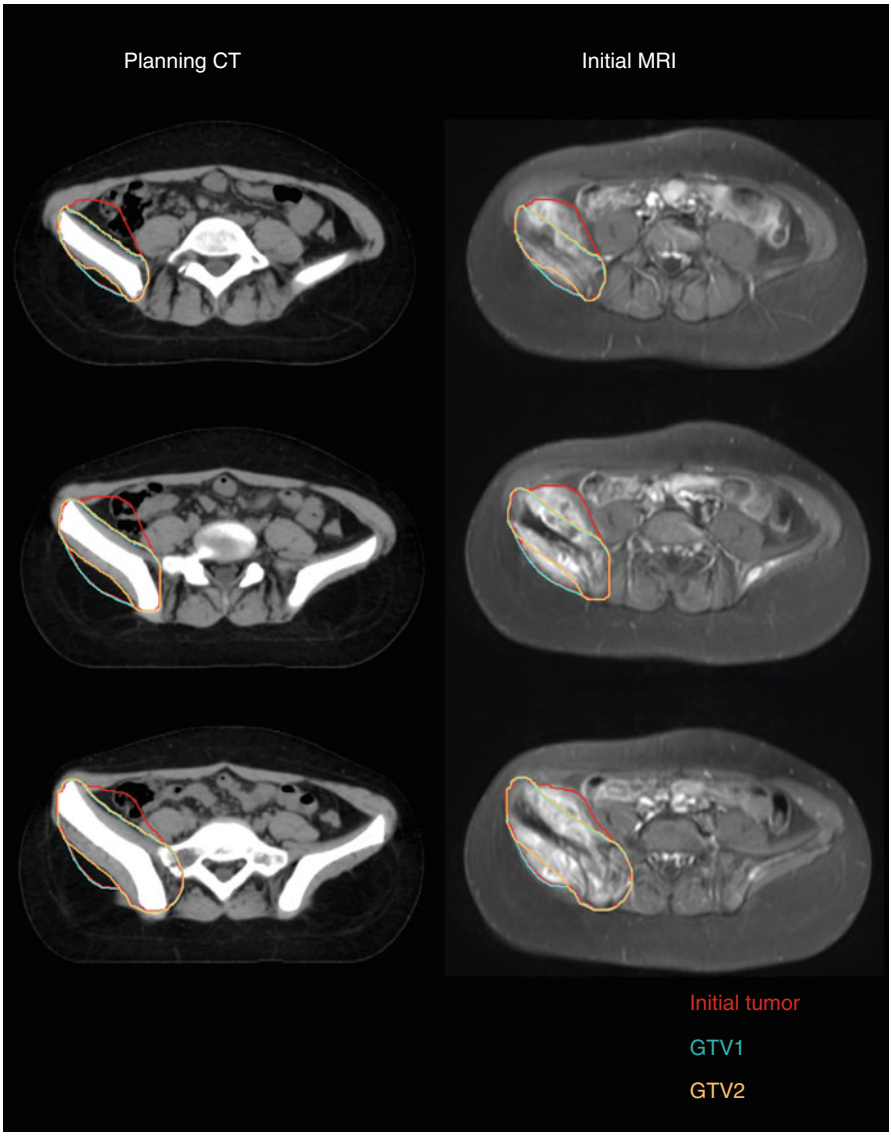

Fig. 31.1 A patient with Ewing's sarcoma involving the pelvis. The initial tumor (as defined by the MRI), GTV1, and GTV2 are shown on the planning CT and initial MRI. For clarity, CTV's are not shown but are GTV + 1 cm

Table 31.3 Rhabdomyosarcoma volume definitions

Initial target volumes	Definition and description
GTV	Gross disease (including unresected enlarged lymph nodes) at presentation, prior to chemotherapy or surgery. GTV can be modified for tumors that extend into body cavities, such as the pelvis or thorax that regress with chemotherapy. In these cases, the edge of GTV can be defined as the post-chemotherapy volume
CTV	GTV + 1 cm. CTV includes involved (pathologically or clinically) nodal regions
PTV	CTV1 + institutional setup margin

Table 31.4 Rhabdomyosarcoma doses in 1.8 Gy per fraction

Group	Histology	Dose (Gy)
I	Alveolar	36
II, node negative	Embryonal or alveolar	36
II, node positive	Embryonal or alveolar	41.4
III	Embryonal or alveolar	50.4 (except orbit 45)

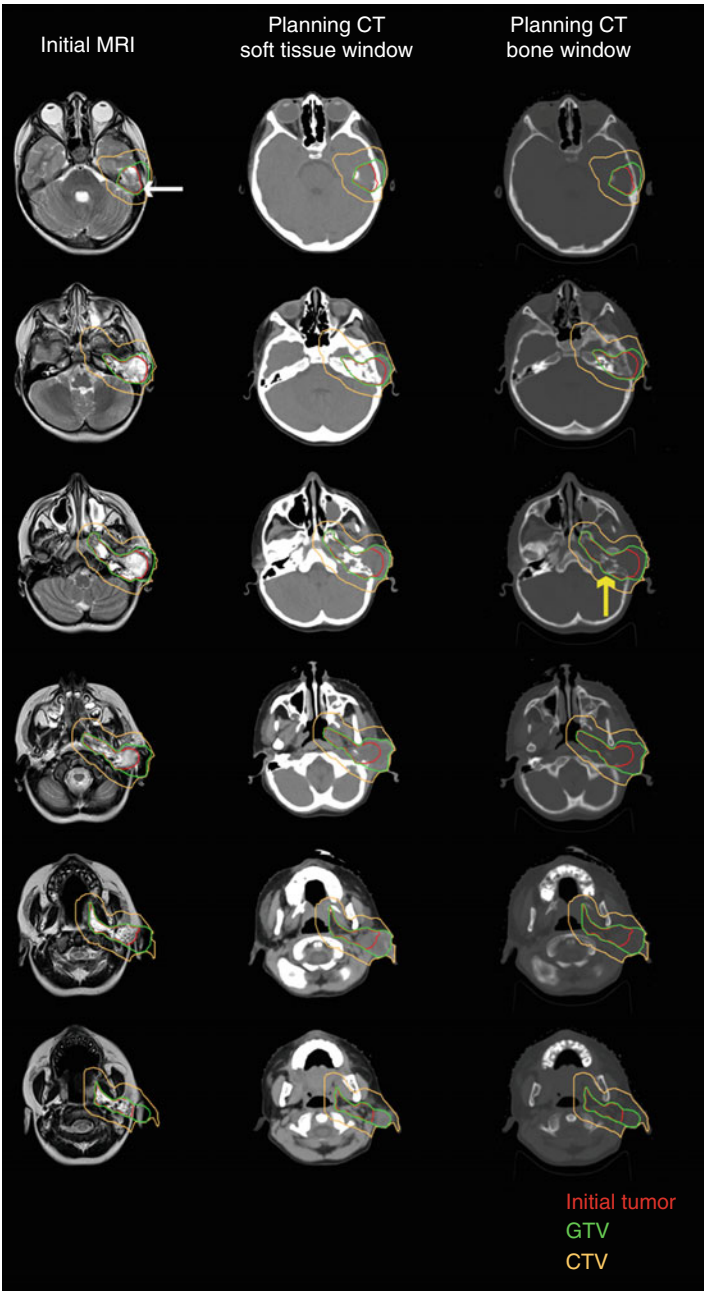

Fig. 31.2 A patient with rhabdomyosarcoma involving the middle ear. The initial tumor (as defined by the MRI), GTV, and CTV are shown on the initial MRI and planning CT (both bone and soft tissue windows). The patient has intracranial extension (*white arrow*) and significant bony destruction of the middle ear (*yellow arrow*)

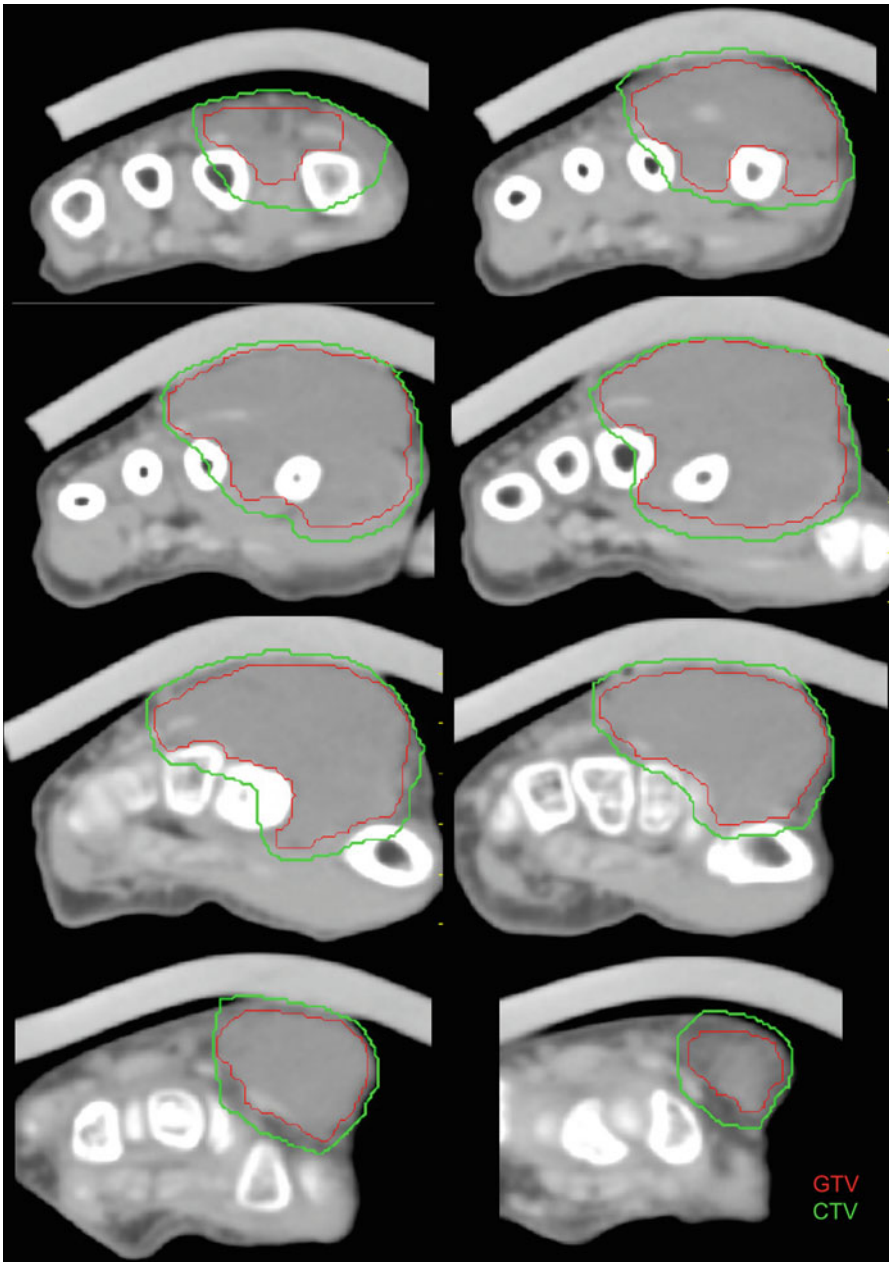

Fig. 31.3 A patient with alveolar rhabdomyosarcoma involving the hand. The patient was treated on week 4 of chemotherapy with very minimal shrinkage of the mass. The original mass prior to chemotherapy was the GTV. The CTV was an addition 1 cm to the GTV but was modified in a few areas to minimize morbidity. Bolus was used to increase dose to the surface

Further Reading

Curtis AE, Okcu MF, Chintagumpala M et al (2009) Local control after intensity-modulated radiotherapy for head-and-neck rhabdomyosarcoma. Int J Radiat Oncol Biol Phys 73:173–177

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Lin C, Donaldson SS, Meza JL et al (2012) Effect of radiotherapy techniques (IMRT vs. 3D-CRT) on outcomes in patients with intermediate-risk rhabdomyosarcoma enrolled in COG D9803-A report from the Children's Oncology Group. Int J Radiat Oncol Biol Phys 82:1764–1770

McDonald MW, Esiashvili N, George BA et al (2008) Intensity-modulated radiotherapy with use of cone-down boost for pediatric head-and-neck rhabdomyosarcoma. Int J Radiat Oncol Biol Phys 72:884–891

Wolden SL, Wexler LH, Kraus DH et al (2005) Intensity-modulated radiotherapy for head-and-neck rhabdomyosarcoma. Int J Radiat Oncol Biol Phys 61:1432–1438

Pediatric Central Nervous System Tumors

32

Jeffrey C. Buchsbaum and Arnold C. Paulino

Medulloblastoma

General Principles of Planning and Target Delineation

- Volumetric planning in the form of proton therapy, intensity-modulated radiation therapy (IMRT), and three-dimensional (3D) conformal therapy is the standard technique for definitive craniospinal irradiation (CSI) and boost radiation therapy for medulloblastoma. These volumetric methods each can be delivered using a number of techniques; however, accurate delineation of target volumes is universally required.
- In addition to thorough physical examination, adequate imaging studies (pre- and postoperative MRI of the brain and MRI of spinal axis with and without contrast) and cerebrospinal fluid (CSF) cytology from a lumbar tap should be obtained for diagnosis, staging, and planning.

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- CT simulation without contrast should be performed to help guide the GTV target and CTV CSI volume of the skull contents and the spinal canal contents per Table 32.1. Normal structures outside of the skull can be delineated sufficiently well to avoid contrast. Contrast may be used per institutional guidelines if MRI scans cannot be obtained. Planning system slice capacity is often the limiting factor. Digitally reconstructed radiograph (DRR) quality for use in image guidance generally improves with thinner slices at simulation.
- A mask and some form of body immobilization (i.e., Alpha Cradle, Vaculock bag) is needed for these cases if supine. If prone, a device to hold the face/head is useful as is table top padding, in addition to a mask. If anesthesia is used, an endotracheal (ET) tube is often selected for use in the prone patient. If supine, laryngeal mask airway (LMA) or nasal canula are often the devices selected for use. Both techniques are in use today at centers of excellence with the trend being toward a move to supine therapy.
- Two target volumes need to be defined: the craniospinal axis and the boost target volume.
- Fusion of MRI to CT is generally imperfect, so each slice of MR-based contours should ultimately be reviewed on the CT scan to make sure it seems plausible. The brain stem and optic chiasm can be slightly misregistered from MRI to CT.
- The location of the caudal margin of the spinal field has been the subject of discussion for years. It is recommended that one uses the spinal MRI for locating the thecal sac termination and lower border of the spinal field.
- For the boost field, there is an ongoing randomized trial comparing tumor bed with a margin vs (Table 32.2) the entire posterior fossa receiving the boost dose. Both examples are shown in this chapter Figs. 32.1, and 32.2.

Table 32.1 Suggested target volume for the craniospinal (CSI) portion of the treatment

Target volumes	Definition and description
GTV_{CSI}	GTV is generally not defined for the CSI portion of treatment
CTV_{CSI}	The craniospinal volume or the area contained by the dura mater is outlined with a margin of 5–8 mm. The cribriform plate should be covered by a minimum of 5 mm. Because the spinal cord can in theory move in the canal, the CTV is often defined as the sum of the brain cavity of the skull and the entire spinal canal down to the end of the thecal sac plus a margin of at least 5–8 mm For growing children, the entire circumference of the bony spine is included in the CTV_{CSI} to avoid spinal asymmetry. Thus, vertebral bodies and the clivus are covered. See Fig. 32.3. One generally does not fully cover the sacrum laterally so as to shield the sacroiliac (SI) joints from dose if possible For fully grown patient contouring of the CTVcsi, please see Figs. 32.4, and 32.5.
PTV_{CSI}	CTV + 3–5 mm, depending on comfort level of daily patient positioning. One must discuss this issue with the medical physicists in the department because field width in some centers must be a minimum width for accurate dosimetry. This is typically 4 cm for photon planning but can vary quite a bit

Medulloblastoma with Tumor Bed Boost

Table 32.2 Suggested target volumes of the tumor bed boost within the posterior fossa for standard-risk cases

Target volumes	Definition and description
GTV_{boost}	Tumor bed and any gross residual tumor include all gross disease noted and cavity as noted on the MRI. Surgical defects caused by the procedure (the route to and from the tumor bed) are not considered the cavity. Several series support the safety of a "tumor bed boost" rather than full posterior fossa treatment (SJMB96 from St. Jude is one example)
CTV_{boost}	CTV_{boost} should encompass the entire GTV with a 1–1.5-cm margin
	Clinical limits to CTV expansion include the normal anatomic constraints to tumor spread which include the brain stem, the bone, and the tentorium. Because the brain stem can be invaded, a 2–3-mm portion of the brain stem adjacent to the tumor bed is included in the CTV
PTV_{boost}	CTV_{boost} + 3–5 mm. This depends on your institution's policies

Medulloblastoma with Posterior Fossa Boost

General Principles of Planning and Target Delineation for Full Posterior Fossa Boost

- The posterior fossa's anterior border includes the posterior clinoids, and the posterior fossa boost should include the entire contents of the posterior fossa with the tentorium serving as the mechanical border between supratentorial brain and posterior fossa.
- The brain stem in its entirety is included in the CTV.
- See www.qarc.org/cog/ACNS0331Atlas.pdf for clarification. See Figs. 32.6–32.8.

Ependymoma

General Principles of Planning and Target Delineation

- Volumetric planning in the form of proton therapy, IMRT, and 3D conformal therapy is the standard technique for definitive therapy for ependymoma. These volumetric methods each can be delivered using a number of techniques; however, accurate delineation of target volumes is universally required.
- In addition to thorough physical examination, adequate imaging studies should be obtained for diagnosis, staging, and planning similar to medulloblastoma. Unless contraindicated, all patients should undergo contrast-enhanced MRI

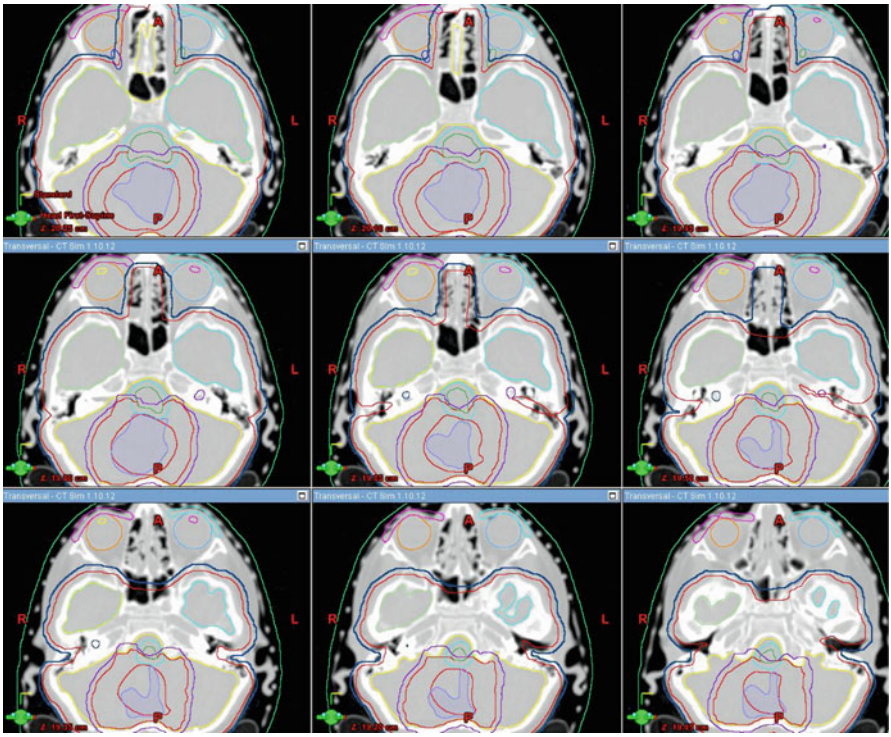
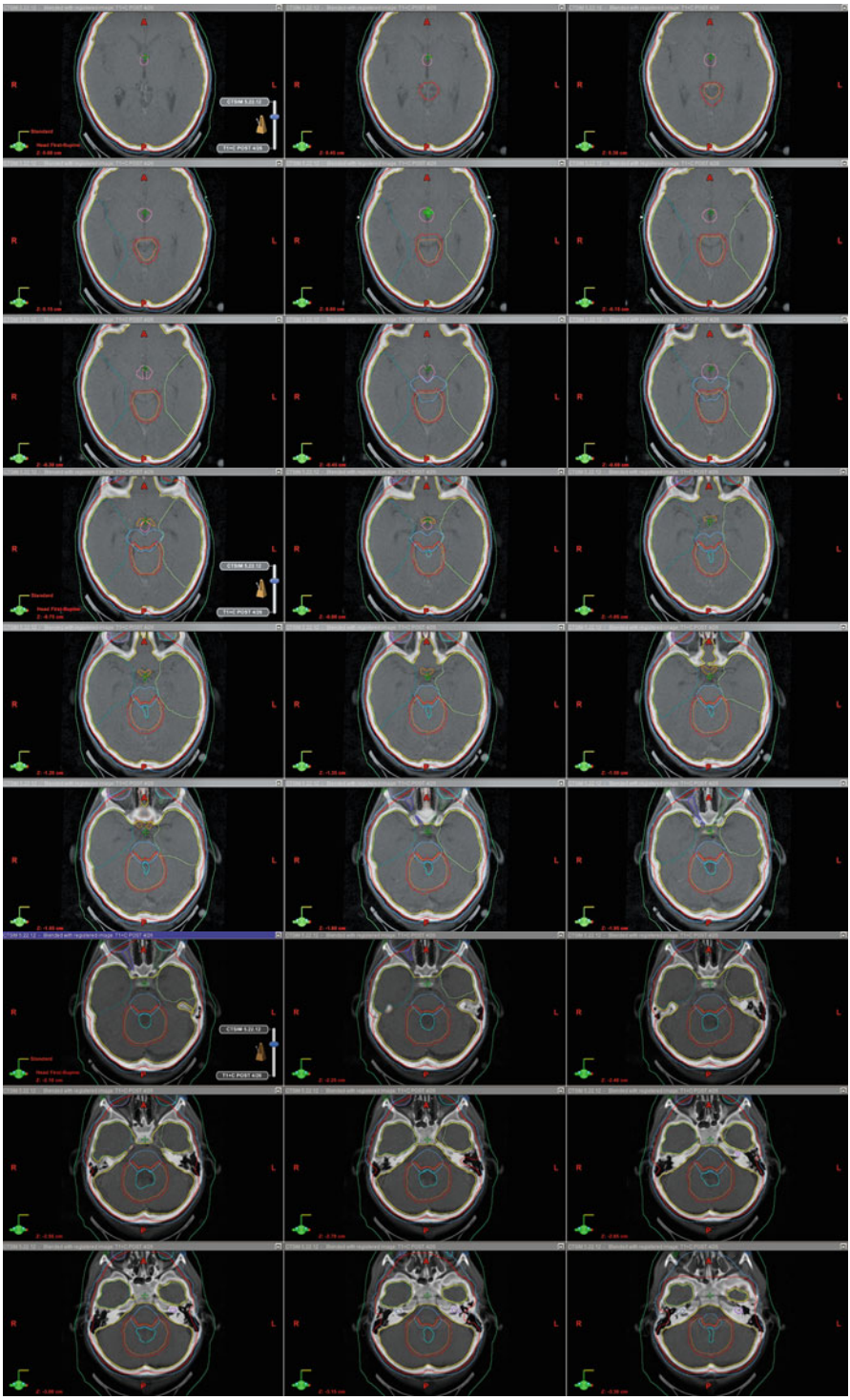


Fig. 32.1 A patient with standard-risk medulloblastoma. This patient was simulated using CT simulation with a 1.5-mm thickness on each slice. Note the 6 mm of coverage of the cribriform plate (the cobalt *blue line* is the PTV). Also note the contouring in the brain stem. The patient was treated with supine proton therapy. Oblique fields were used to avoid the anterior eye region. The craniospinal portion's CTV (*red orange*) is expanded to cover the full volume of the bone of the base of skull. The post-op GTV in the posterior fossa is highlighted in *blue violet*

scans of the brain and spine, preferably 1–3-mm slice thickness. Preoperative and postoperative scans of high quality are critical.

- CT simulation without contrast should be performed and fused with the preoperative and postoperative MRI scan to help guide the GTV and CTV. DRR quality for use in image guidance generally improve with thinner slices at simulation. An 18 month old's case is shown in Figs. 32.9 to 32.12. Collection of simulaiton data to at least the shoulders is recommended to help avoid collisions during treatment.
- An immobilization mask is needed for these cases. Patients are generally treated in the supine position. Given the young age of most of these patients, anesthesia is often used.

Fig. 32.2 MRI slices fused to a CT simulation from a similar patient. The postoperative GTV is shown in *aqua*



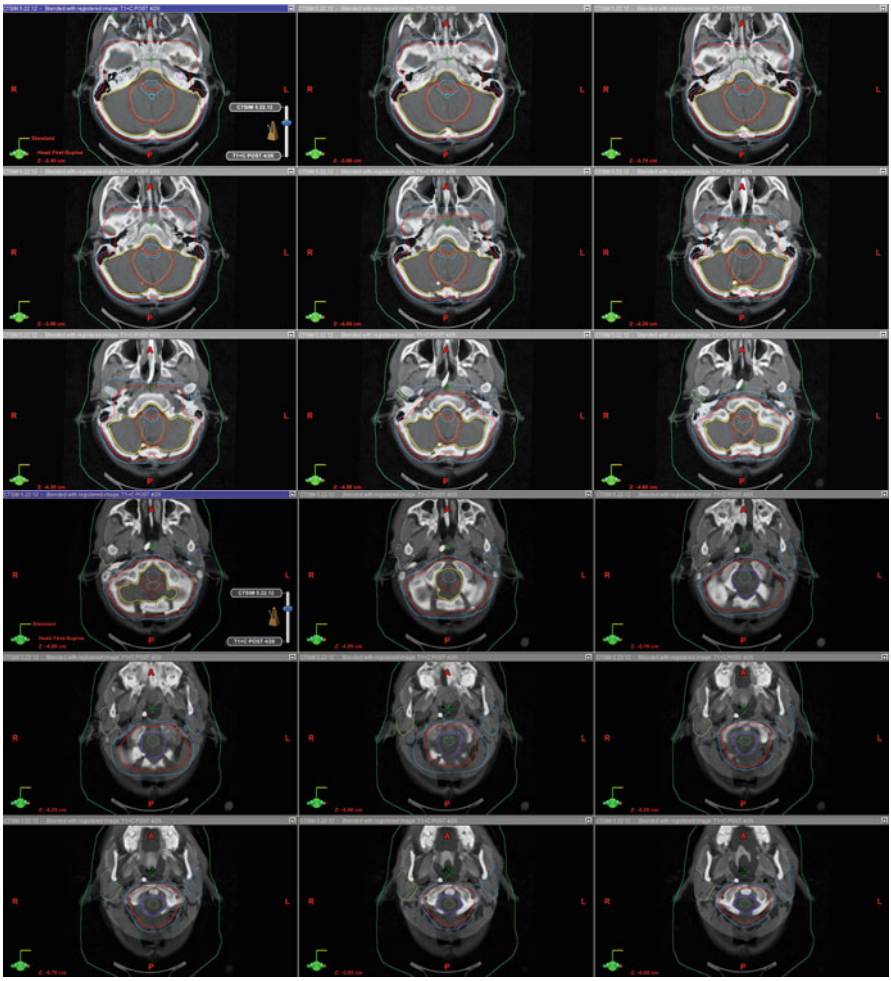


Fig. 32.2 (continued)

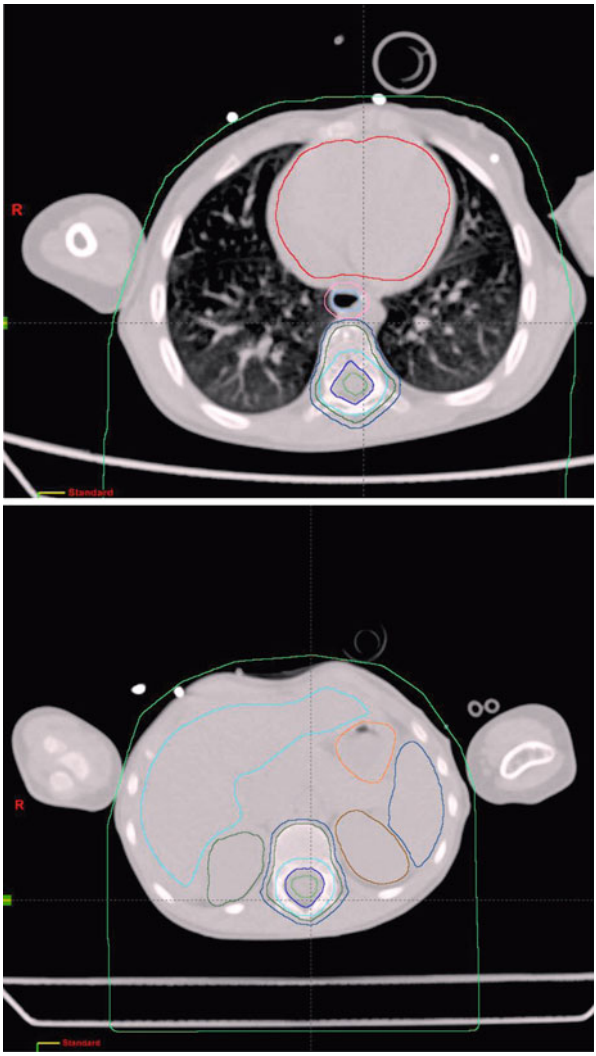


Fig. 32.3 Example of a CTV displayed on bone windows of the spine in a growing child. The CTV could cut across the vertebral body in a fully grown child

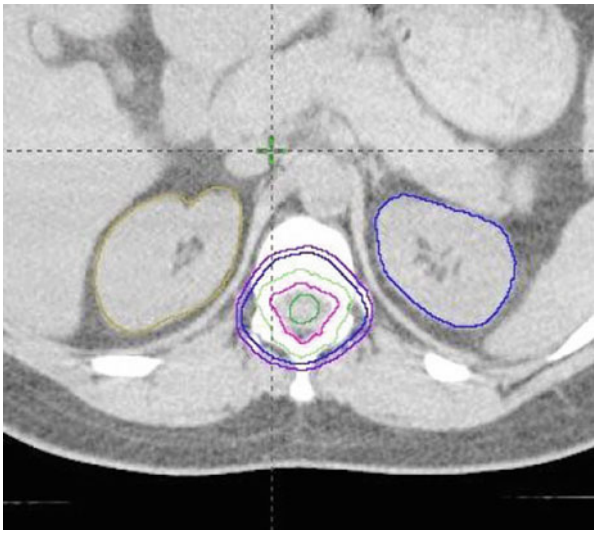


Fig. 32.4 This shows how the spine field changes for a fully grown patient. Note how the CTV (*blue*) and PTV (*purple*) lines are not outside of the bone anteriorly

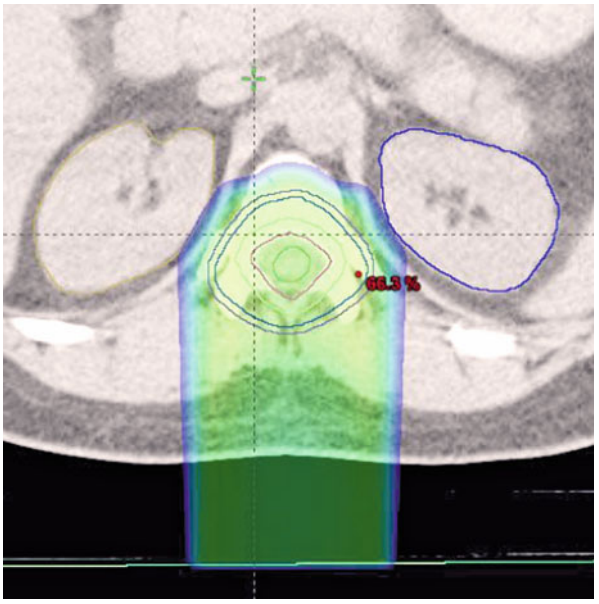


Fig. 32.5 Dose is directly shaped in IMRT and proton plans via contouring – making attention to detail critical. In this case, the contouring physician shaped things in a way that would cause the kidneys to be spared

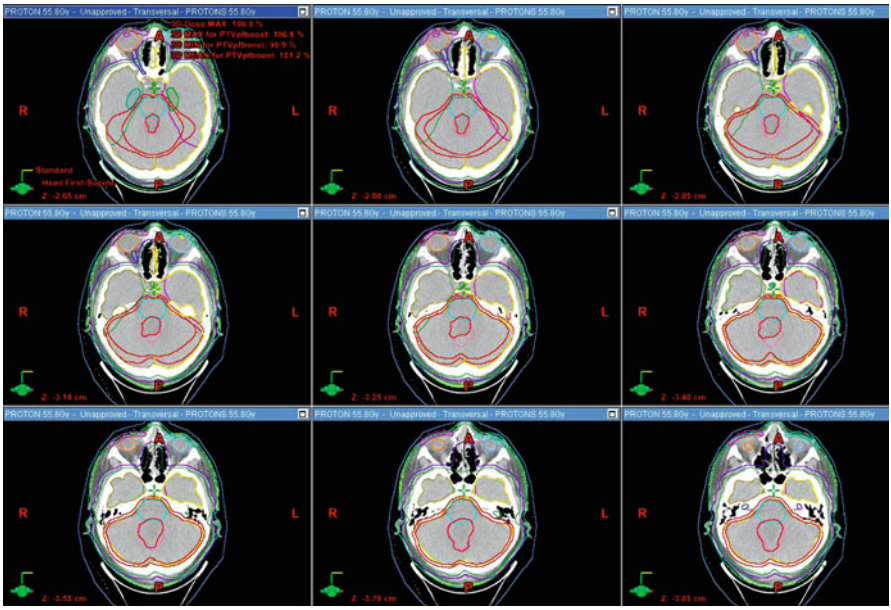


Fig. 32.6 The posterior fossa contours in a series of CT slices. The posterior fossa (inner *orange red*) is the CTV; a margin on 3–5 mm is added to the CTV to create the PTV (outer *orange red*). The tumor bed is outlined in *red*

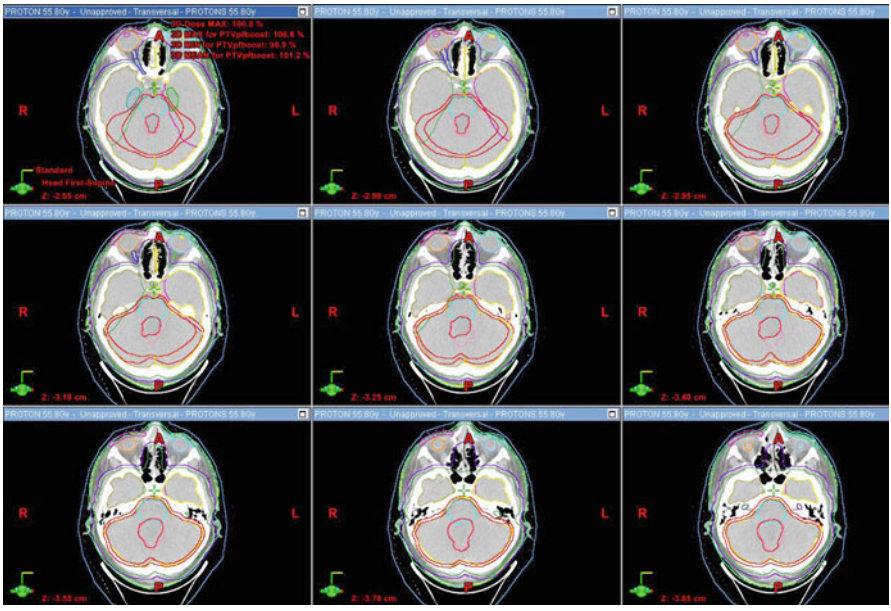


Fig. 32.7 The posterior fossa contours can be seen in this series of MRI slices fused to the simulation CT. These are from the above patient. MRI fusion is critical for these cases. The CTV is bounded by the tentorium in these images. The posterior fossa (*orange*) is the CTV; a margin on 3–5 mm is added to the CTV to create the PTV (*orange red*). The tumor bed is outlined in *red*

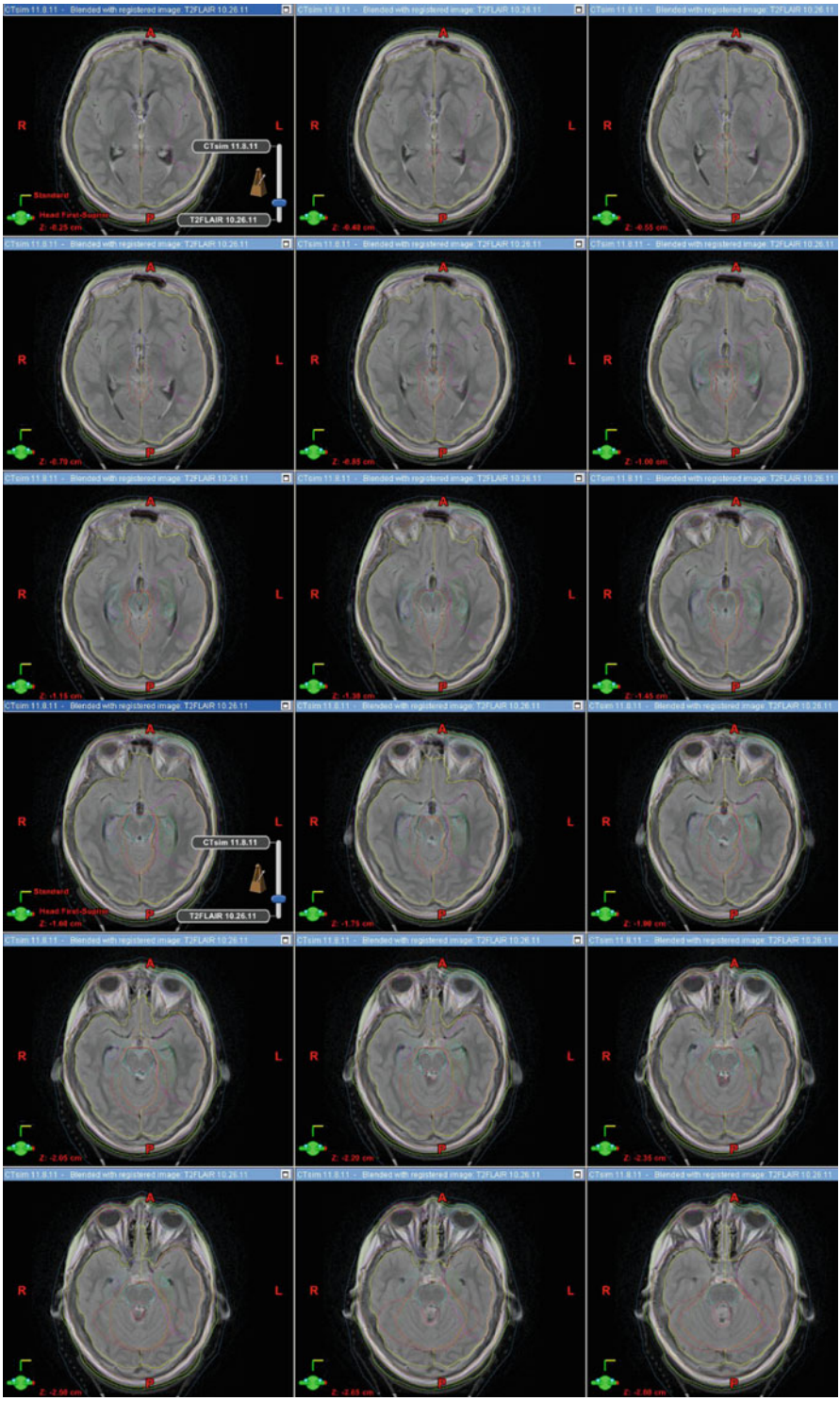


Fig. 32.7 (continued)

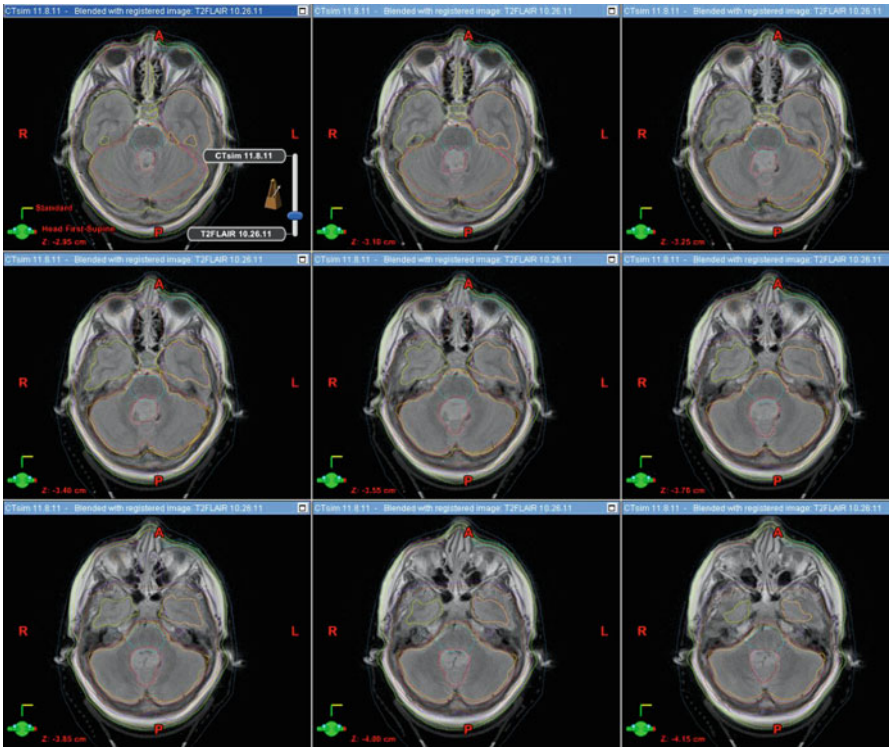


Fig. 32.7 (continued)

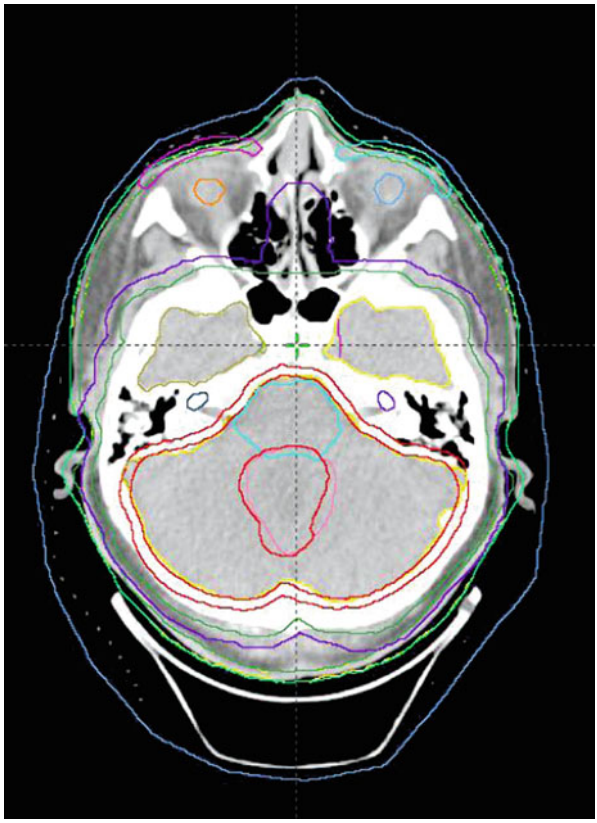


Fig. 32.8 Details of the posterior fossa boost contours at the level of the cochleae (*blue* and *purple*). Note the craniospinal PTV in *purple* is covering the full bones of the base of skull and still is coving some areas of the cribriform plate to make sure it is covered by at least 5 mm. The craniospinal CTV is in *green*

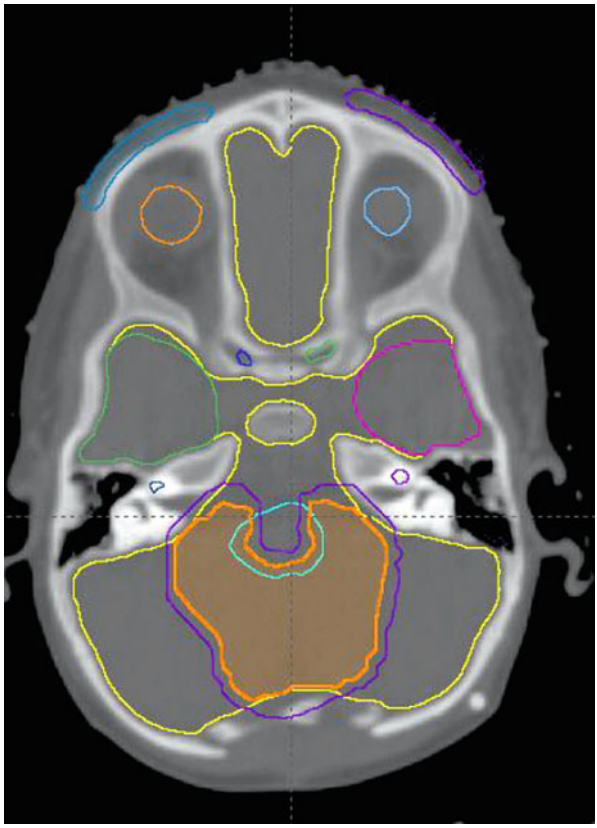


Fig. 32.9 Contouring of an 18-month-old boy with ependymoma using the standard of care margins and dosing described above. Note that the surgery caused the pre-op volume to change as the reconstruction of the skull brought the bone surface "in." Note that the brain stem was in contact with the tumor but was not formally invaded, so the CTV was taken into the brain stem 3 mm. Also note the size of the frontal lobe in this infant. Using lateral fields for a CSI or leukemic field on this patient would require treatment of the entire globes. CTV is in *orange*. PTV is in *purple*

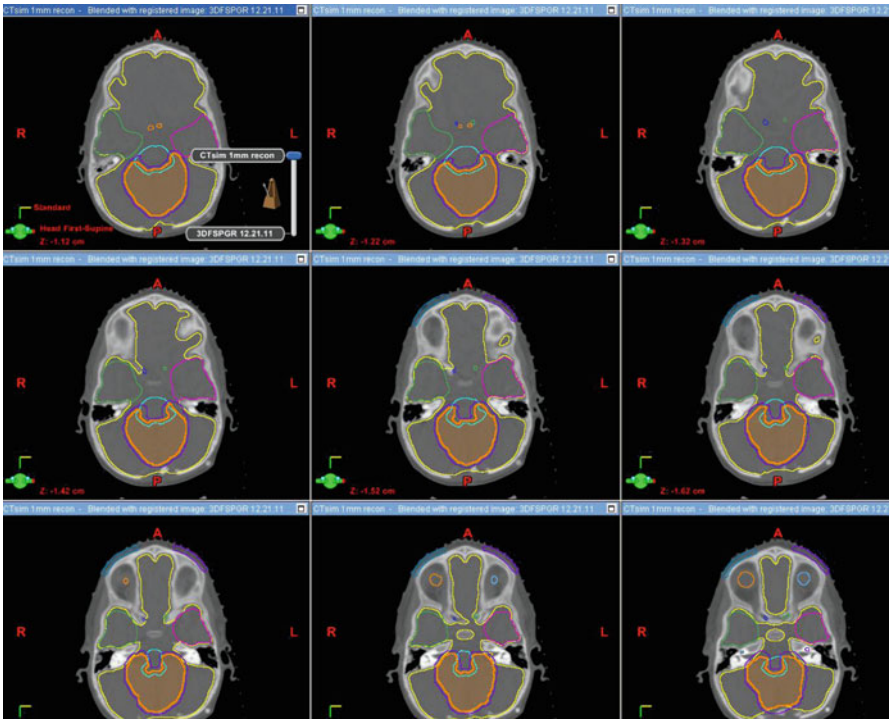


Fig. 32.10 Multi-window view of the contours in Fig. 2.9. In planning these cases, the hypothalamus, temporal lobes/hippocampi, and cochleae are avoided as much as possible. IMRT and proton therapy are often used to avoid these structures

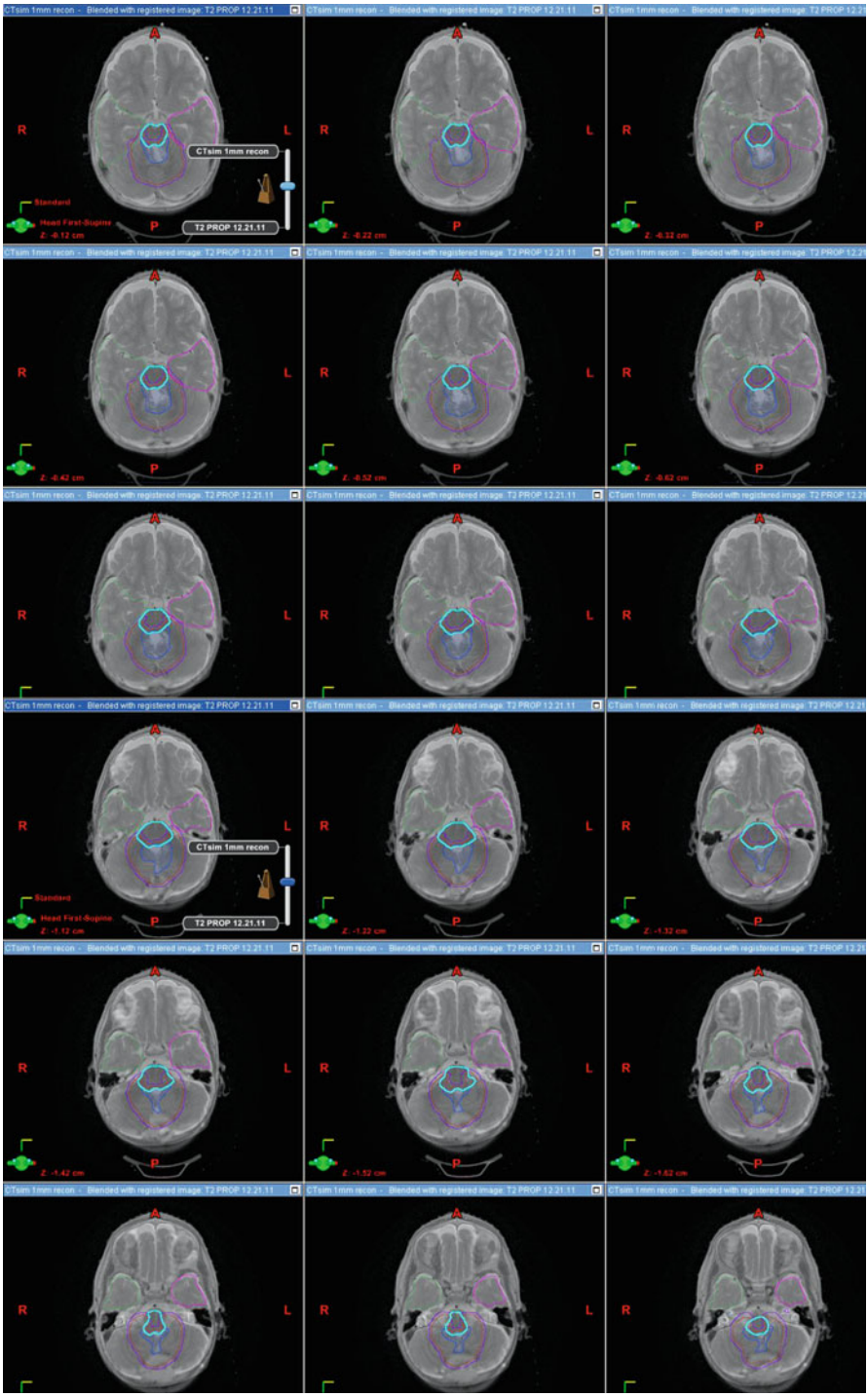


Fig. 32.11 MRI slices from the above patient's plan fused to the above CT scan. Brain stem is outlined in *aqua*

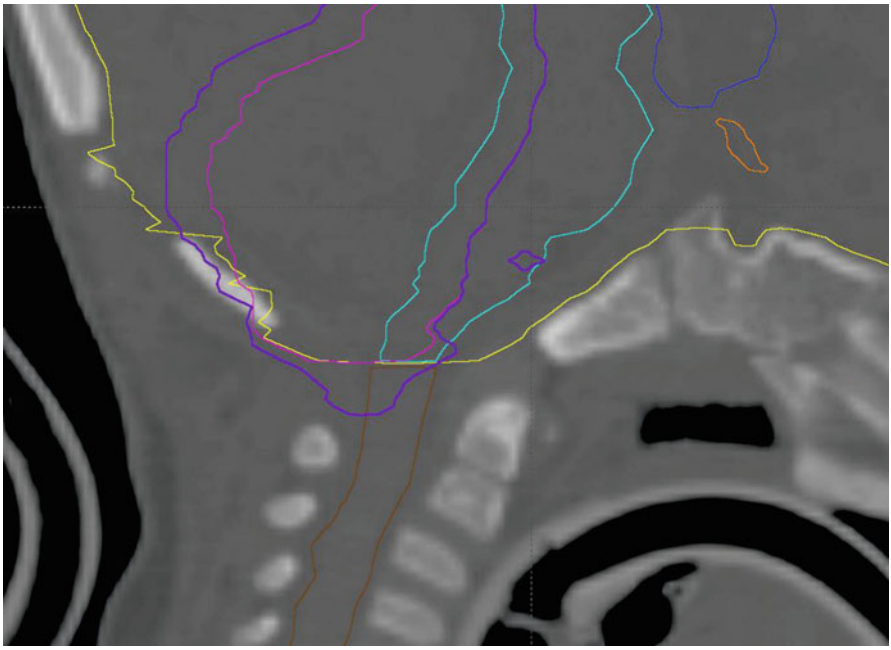


Fig. 32.12 Sagittal view of the same ependymoma infant showing the use of a PTV_{54} (*purple*) and a $PTV_{59.4}$ (*pink*). The spinal cord is in *brown* and the brain stem is in *aqua*

Table 32.3 Suggested target volumes for ependymoma treatment

Target volumes	Definition and description
GTV	GTV is generally defined by the postoperative cavity and any tiny amount of tumor that remains. If a large amount of tumor remains, exploring the ability to re-resect the case is felt to be in the best interest of the patient. Seeing the preoperative volume will help to avoid contouring resection defects that do not reflect true tumor volume. In a sense, one wants GTV to represent anywhere there is tumor or where tumor may have been present
CTV_{54} and $CTV_{59.4}$	CTV expansion is usually 10 mm added to the GTV. One has to take normal anatomic barriers such as bone and tentorium into consideration. A volume reduction is performed after a dose of 54 Gy to minimize dose to the spinal cord in posterior fossa ependymoma. The initial field is the CTV_{54}, while the boost field is $CTV_{59.4}$. For the $CTV_{59.4}$, the portion of the spinal cord included in the CTV_{54} is removed to prevent overdosage which may result in spinal cord injury
PTV_{54} and $PTV_{59.4}$	The PTV is expanded to include the CTV with a 3–5-mm margin with the exception of the $PTV_{59.4}$where a 3–5-mm margin is not added distally on the spinal cord

- Target volumes include gross tumor volume preoperatively and the postoperative resection cavity; clinical target volume (CTV) should be delineated on every slice of the planning CT. The current standard of care is to use the guidelines from COG ACNS0121. These were based on a published series from St. Jude. The CTV is the GTV (postoperative bed and any small residual) with a 1-cm margin. A 3–5-mm margin is then added to the CTV and basedon institutional preference. This is summarized in Table 32.3.
- Critical in these cases is a willingness to explore re-resection in the situation where the initial reseciton leaves significant tumor. It is not uncommon for some centers with more experience to perform re-resection as survival outcome is correlated with the degree of tumor removal.

Pure Germinoma

General Principles of Planning and Target Delineation

- Volumetric planning in the form of proton therapy, IMRT, and 3D conformal therapy is standard for definitive therapy for pure germinoma. These volumetric methods each can be delivered using a number of techniques; however, accurate delineation of target volumes is universally required. See Figs. 32.13 to 32.15
- In addition to thorough physical examination, adequate imaging studies should be obtained for diagnosis, staging, and planning such as in medulloblastoma. Unless contraindicated, all patients should undergo contrast-enhanced MRI scans of the brain and spine, preferably 1–3-mm slice thickness. Pre-chemotherapy and post-chemotherapy scans of high quality, when applicable, are critical.
- CT simulation without contrast should be performed to help guide the whole ventricular volume and primary tumor volumes. Contrast may be used per institutional guidelines if MRI scans cannot be obtained. Slices should be thin (1 mm if possible). DRR quality for use in image guidance generally improves with thinner slices at simulation. Collection of simulation data to at least the shoulders is recommended to help avoid collisions during treatment. One must have the CT scan data be of high enough contrast to allow resolution of the ventricles.
- An immobilization mask is needed for these cases. Patients are usually treated in the supine position.
- Target volumes include gross tumor volume pre-chemotherapy and post-chemotherapy, the ventricles, and the normal structures of elegant brain that are nearby (hearing, hormonal systems, visual pathways, memory and learning pathways, and the brain stem).
- One often gets imaging on therapy via simulations with high-contrast CT to make sure the ventricle shape is stable and that the tumor is responding. It is recommended to collect such a scan in the last week of the whole ventricular phase to help with final boost dosing.
- The current standard of care when treating with radiotherapy alone is to treat the full ventricular volume plus the initial tumor volume with a margin of 1.5 cm

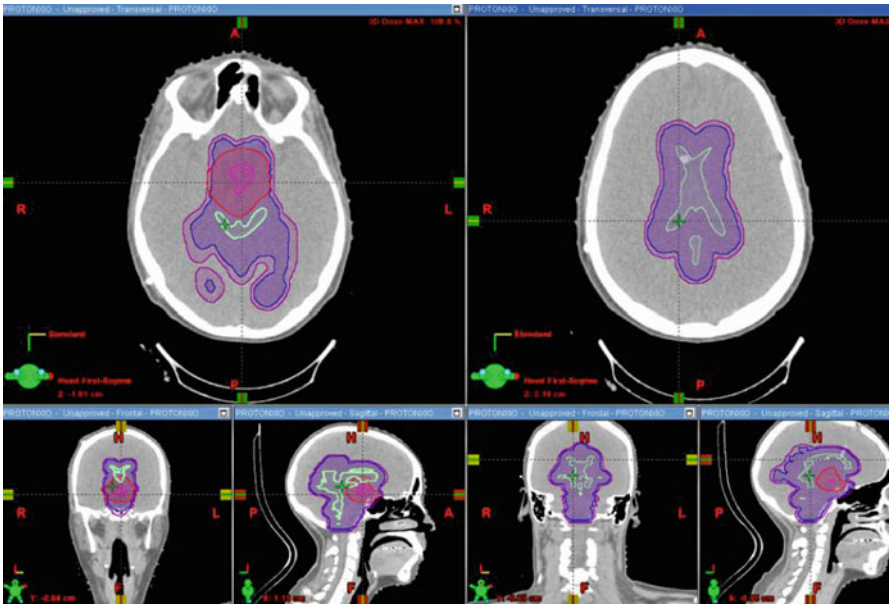


Fig. 32.13 Whole ventricular used for treatment of a pure germinoma of the suprasellar region. $CTV_{ventricles}$ (*blue*), $PTV_{ventricles}$ (*purple*), GTV (*pink*), PTV_{boost} (*red*)

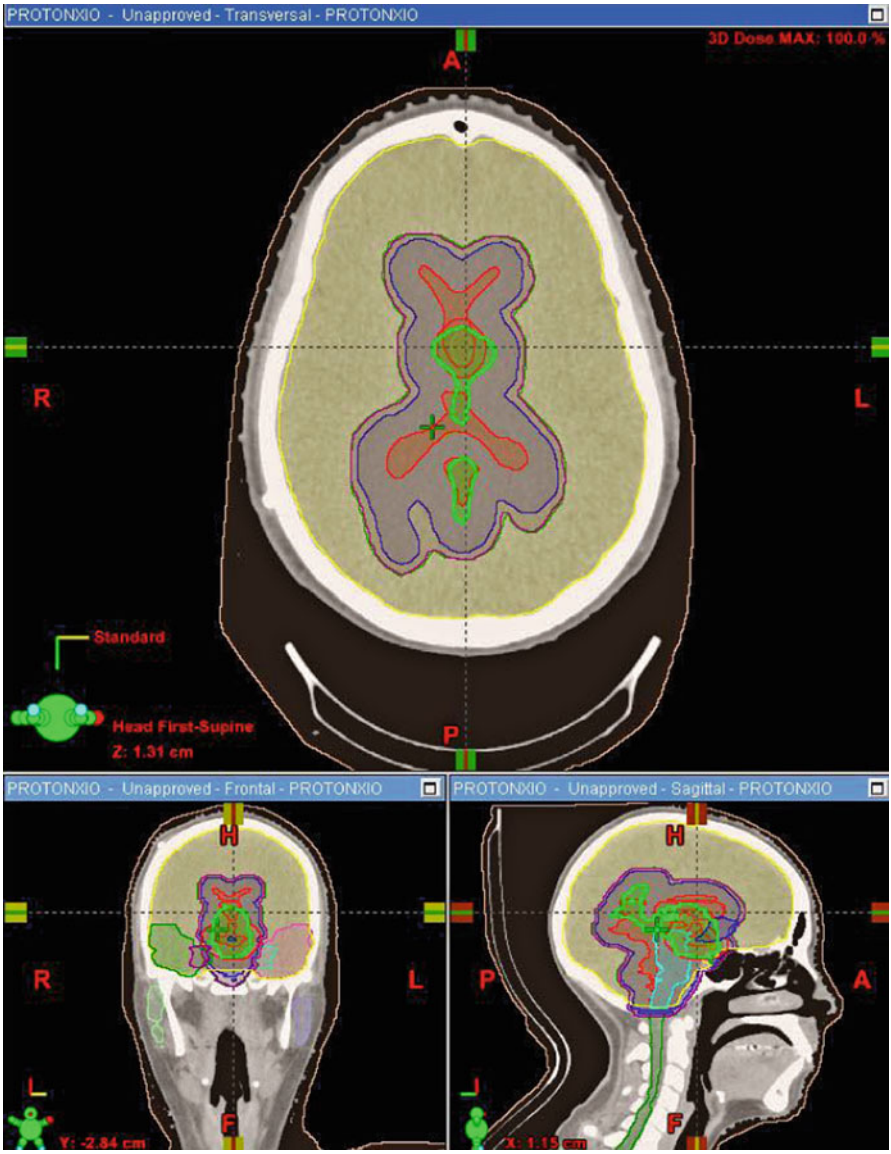
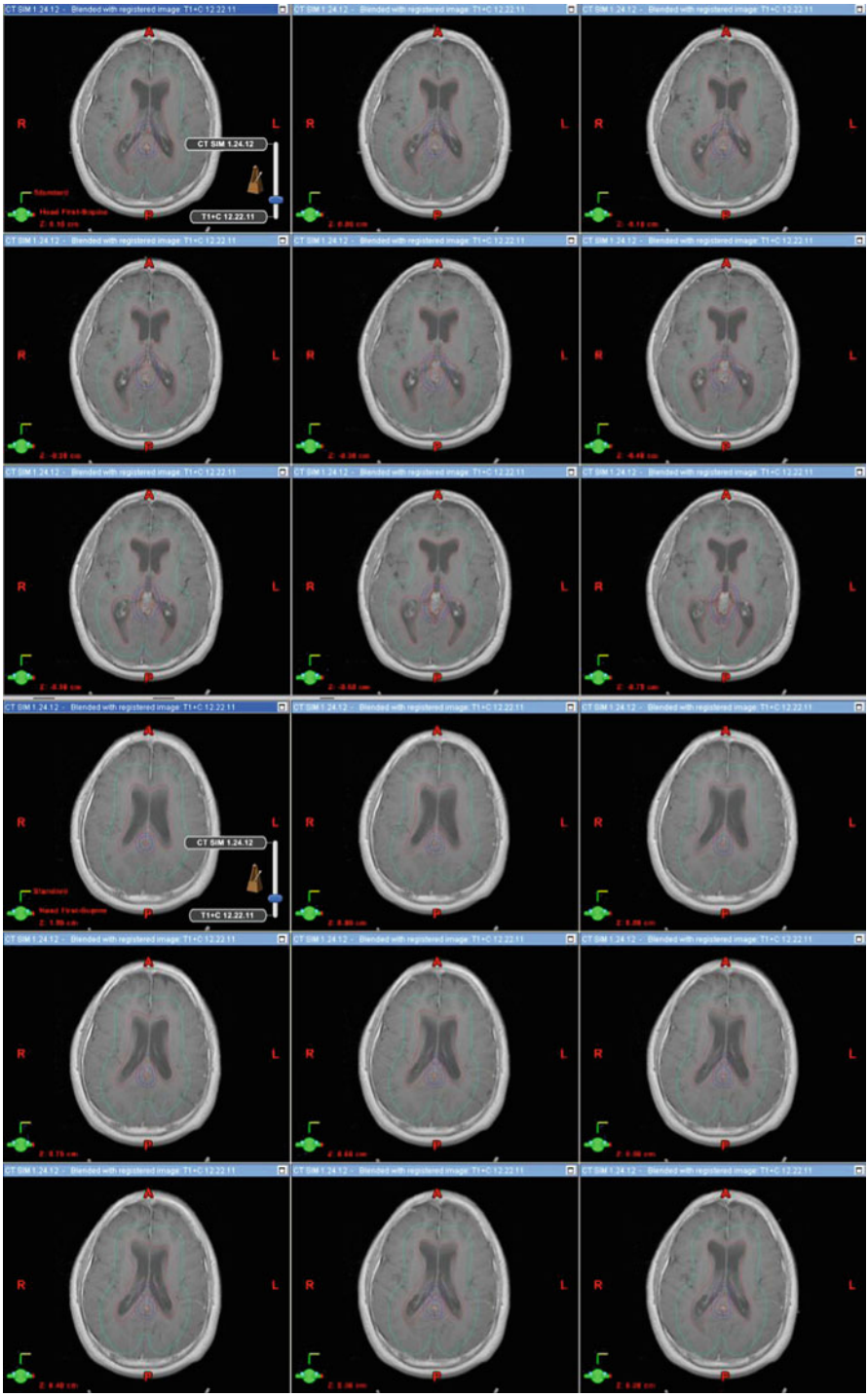


Fig. 32.14 Detailed view of the contours used in whole ventricular therapy in orthogonal views. The ventricles at simulation are in *red*. The preoperative tumor volume is in *green*. The $CTV_{ventricles}$ (*blue*) and $PTV_{ventricles}$ (*purple*) are shown as being carved out of the brain contour that is in *yellow*. The brain stem is in *aqua*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T1+C 12.22.11
A
R
L
P

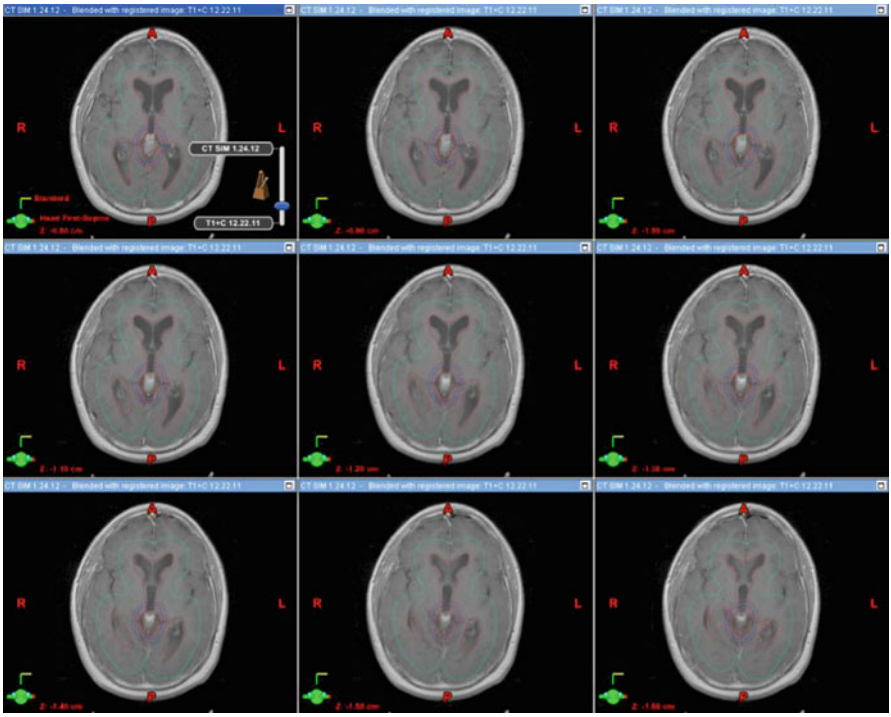

Fig. 32.15 (continued)

Fig. 32.15 MRI slices of a whole ventricular irradiation case for a different patient. Shown are the ventricles (*red*), the gross tumor volume of the lesion (*red*), and the planning target volumes. $CTV_{ventricles}$ (*green*), $PTV_{ventricles}$ (*aqua*), CTV_{boost} (*blue*), PTV_{boost} (*purple*)

Table 32.4 Suggested target volumes for whole ventricular treatment with boost of pure germinoma

Target volumes	Definition and description
GTV	GTV is generally defined as the primary tumor, usually located in the pineal or suprasellar region
$CTV_{ventricles}$ and CTV_{boost}	$CTV_{ventricles}$ is usually the ventricles and primary tumor with a 10–15-mm margin. One has to take bone and tentorial constraints into consideration. For the whole ventricular portion of treatment, there is variability nationally on what is defined as this volume, in particular the CSF space anterior to the brain stem. Because the dose is so low for this portion and this technique is something we are using as a move from CSI, it is probably safest to be generous if in doubt. The CTV_{boost} is the GTV with a 10–15-mm margin
$PTV_{ventricles}$ and PTV_{boost}	PTVs are expanded to cover the CTV listed above by the customary amount in one's clinic, usually 3–5 mm

($CTV_{ventricles}$) to 24 Gy in 16 fractions. A cone-down boost volume of 21 Gy in 14 fractions is then employed on the post-chemotherapy volume plus a 1–1.5 cm (CTV_{boost}). PTVs are per institutional standard and are usually the CTV with a 3–5-mm margin. These are summarized in Table 32.4.

- The other treatment option for pure germinoma is induction chemotherapy followed by radiotherapy. In the case of a complete response on MRI after induction chemotherapy, the initial tumor with a 1- to 1.5-cm margin (CTV) can be treated to 30 Gy in 20 fractions. In the case of stable disease or partial response, patients are treated with whole ventricular irradiation followed by a boost with doses and volumes as described above.
- For intracranial germinoma with leptomeningeal dissemination,, craniospinal radiation therapy should be employed, and target delineation for the CSI field is similar to medulloblastoma.

Further Reading

Merchant TE, Li C, Xiong X et al (2009) Conformal radiotherapy after surgery for paediatric ependymoma: a prospective study. Lancet Oncol 10:258–266

Paulino AC, Mazloom A, Teh BS et al (2011) Local control after craniospinal irradiation, intensity-modulated radiotherapy boost, and chemotherapy in childhood medulloblastoma. Cancer 117:635–641

Raggi E, Mosleh-Shirazi MA, Saran FH (2008) An evaluation of conformal and intensity-modulated radiotherapy in whole ventricular radiotherapy for localized primary intracranial germinomas. Clin Oncol (R Coll Radiol) 20:253–260

Roberge D, Kun LE, Freeman CR (2005) Intracranial germinoma: on whole-ventricular irradiation. Pediatr Blood Cancer 44:358–362

Wolden SL, Dunkel IJ, Souweidane MM et al (2003) Patterns of failure using a conformal radiation therapy tumor bed boost for medulloblastoma. J Clin Oncol 21:3079–3083

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