Locally Advanced/Unresectable Pancreatic Cancer

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9.1 Introduction

Patients with locally advanced pancreatic cancer (LAPC) have evidence of unresectable primary disease and no clinical/radiological evidence of distant metastatic disease. The criteria for resectability of pancreatic cancer were reviewed in the previous chapter and are largely related to the amount of arterial involvement of the tumor. The determination of resectability is made after obtaining anatomic information from a multiphase CT of the chest, abdomen, and pelvis and a full review from

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a multidisciplinary clinic with significant input from surgical oncology. Unfortunately, if a patient's lesion is deemed unresectable, there is no strong consensus for management and treatment planning. Many patients with LAPC eventually develop symptoms related to progression of their primary tumor, but also have a high likelihood of micrometastatic spread. Although systemic therapy will address micrometastatic spread, there is a constant dilemma with regard to best timing and management of local disease with radiation therapy. Local control of primary disease remains important as approximately 30% of patients with pancreatic cancer died from local disease without evidence of metastases [1]. Local progression can become symptomatic (biliary obstruction, pain, portal hypertension, and gastric outlet obstruction) and have impact on patient's quality of life.

9.2 Locally Advanced (Unresectable) Disease

LAPC portends a poor prognosis with a median overall survival of 9–11 months [2, 3]. Although definitive treatment utilizing concurrent conventional fractionated radiation and chemotherapy has been trialed, patient outcomes remain unsatisfactory. In an LAPC case, treatment plans need to be tailored to every patient's need and circumstances. Patient's symptoms (e.g., pain, abdominal discomfort, jaundice) should be addressed upfront. The aims of treatment in LAPC are: (1) Improve quality of life by achieving locoregional control; and (2) Prolong survival by preventing development of distant metastatic disease and local progression. It is important to discuss the goals of treatment with patients and involve palliative care services, where feasible, early in the course of treatment.

9.2.1 Treatment Strategies for Unresectable Disease

9.2.1.1 Chemotherapy (Without Radiation)

Initial systemic combination chemotherapy is recommended for most patients, given that 30–50% of patients with LAPC develop evidence of distant metastasis within 3 months. Recent studies have shown gemcitabine-based combination chemotherapy to be more effective in improving survival compared to best supportive care or gemcitabine alone. FOLFIRINOX has also been studied in the neoadjuvant setting. Both gemcitabine-based and FOLFIRINOX studies in the neoadjuvant setting had included patients with LAPC, and some patients, albeit a very small number, had demonstrated a remarkable response to chemotherapy with tumor downstaging, enabling them to proceed to surgery. The duration of chemotherapy remained unclear, but is typically given for at least 6 months, provided that no demonstrable disease progression (imaging and biochemical) and patient had tolerated the regimen well with no dramatic impact on his/her quality of life.

9.2.1.2 Chemoradiation

The role and timing of radiotherapy are frequently debated in LAPC cases. Local control of primary disease remains important as approximately 30% of patients with pancreatic cancer died from local disease, as evident by an autopsy study by Iacobuzio-Donahue et al. [1]. With regard to adding a radiosensitizing agent during radiotherapy, there is evidence that concurrent chemoradiotherapy is superior to radiotherapy alone. An early study by the Gastrointestinal Tumor Study Group (GITSG) established that concurrent chemoradiotherapy improved survival rates compared to radiotherapy alone (1-year overall survival 46% vs. 10% in 60 Gy arms) [4]. At the MD Anderson Cancer Center, our approach is to deliver definitive concurrent chemoradiotherapy after a period, typically 2–6 months, of chemotherapy. This approach will: (1) address the high risk of micrometastatic disease and development of distant disease will significantly impact survival, (2) reduce overtreatment of patients who will eventually develop distant disease and may only have marginal benefit from a long treatment course (5.5 weeks), and (3) potentially reduce toxicity from radiotherapy. The recent Groupe Coopérateur Multidisciplinaire en Oncologie (GERCOR) LAP 07 randomized trial was aimed to investigate the role of chemoradiotherapy after chemotherapy in patients with LAPC [5]. This study demonstrated that there was no significant difference between the two groups in terms of overall survival, but those who received chemoradiotherapy had significantly improved local control (32% vs. 46%, $p = 0.03$). This study has its own limitations including that the chemotherapy regimen used was gemcitabine (±erlotinib) rather than FOLFIRINOX, and out of 88% available radiotherapy treatment plans available for quality assessment, 50% had minor deviations and 18% had major deviations [5]. Therefore, the results of this trial should be interpreted with caution.

9.2.1.3 Proton Therapy

Proton therapy may be utilized to deliver high doses of radiation with the aim of sterilizing the tumor in LAPC. The possible benefit and qualms of proton therapy were discussed in previous chapter. A dosimetry study comparing proton (double scattering and pencil beam scanning) with IMRT plans showed that proton therapy plans had significantly less low-dose scatter ($p < 0.01$) to organs at risk including small bowel, stomach, and duodenum than IMRT plans [6]. However, within the high-to-intermediate-dose regions, there were higher doses to the adjacent duodenum (<5%) and stomach (10%) than IMRT plans ($p < 0.01$) [6]. A phase I/II study on proton therapy (67.5 Gy/25 fractions) delivered with concurrent gemcitabine by Terashima et al. [7] found that the treatment was well-tolerated with ≤10% grade 3 toxicities and comparable 12-month progression-free, freedom from local progression, and overall survival rates of 64.3%, 81.7%, and 76.8%, respectively, to historical data. The majority of these patients had posttreatment endoscopy assessment. All patients received prophylactic lansoprazole and rebamipide pre- and during radiotherapy. Only 3% of patients exhibited grade ≥3 radiation-associated gastric and duodenal ulcers [8].

9.2.1.4 Stereotactic Body Radiation (SBRT)

SBRT enables the delivery of high doses of radiation delivered precisely to small area to achieve an ablative total dose to the tumor in only a few fractions (typically ≤7 fractions), while limiting dose to the surrounding organs at risk. A phase I dose escalation study by Koong et al. [9], which treated patients with LAPC with single fraction of 15 Gy, 20 Gy, or 25 Gy SBRT, found that the treatment was well-tolerated and provided good local control rate without any dose-limiting toxicity. Similar results were shown by Schellenberg et al. [10, 11] whereby patients treated with single fraction 25 Gy with sequential gemcitabine had 1- and 2-year survival of 50% and 20%, respectively. In terms of late toxicity, only 1 of 20 patients developed a duodenal perforation and three had ulcers (grade 2) that were managed medically [11]. Following these results, a multi-institutional trial investigating fractionated SBRT (33 Gy/5 fractions) with gemcitabine was performed and showed that fractionated SBRT was well-tolerated with low rates of acute and late ≥Grade 2 gastrointestinal toxicities (2% and 11%, respectively) which had 1-year overall survival of 59% [12].

9.3 Treatment Planning

Overall, patient setup, simulation, motion management, and treatment planning for LAPC are similar to resectable intact pancreatic cancer as described in the previous chapter. Here, we present specific treatment planning procedures for LAPC used at the MD Anderson Cancer Center, Houston, Texas, USA.

9.3.1 Pre-Simulation Instructions

Patients are instructed to fast at least 3 h prior to simulation and also for each fraction of radiation treatment to ensure reproducibility of stomach position and avoid daily variability in stomach filling (Fig. 9.1). The degree of stomach filling could potentially impact the tumor location and motion. Patients' allergies, particularly to iodine contrast, are clearly documented. Patients with allergy to iodine contrast should not be given intravenous (IV) contrast during simulation. For those who will receive IV contrast, a recent (usually within 2 weeks) renal function is obtained to ensure adequate renal function is documented prior to simulation. Intravenous contrast has the rare potential of causing contrast nephropathy complication.

For patients who will receive SBRT, treatment is given as per the radiation protocol on the ALLIANCE (discussed in the previous chapter). An endoscopy (gold standard) is performed to ensure there is no invasion of the duodenum which will preclude patient from SBRT. Previous studies have shown increased toxicity after invasion with direct duodenal invasion [12, 13]. Fiducial markers (preferably ≥3) are placed endoscopically at least 12 h prior to simulation and be placed within 1 cm and/or in the tumor. Although daily CT-on-rails imaging may be adequate for daily target alignment, the fiducial markers provide a second check/surrogate for daily target alignment during treatment with kV, cone-beam CT, or fluoroscopic image guidance.

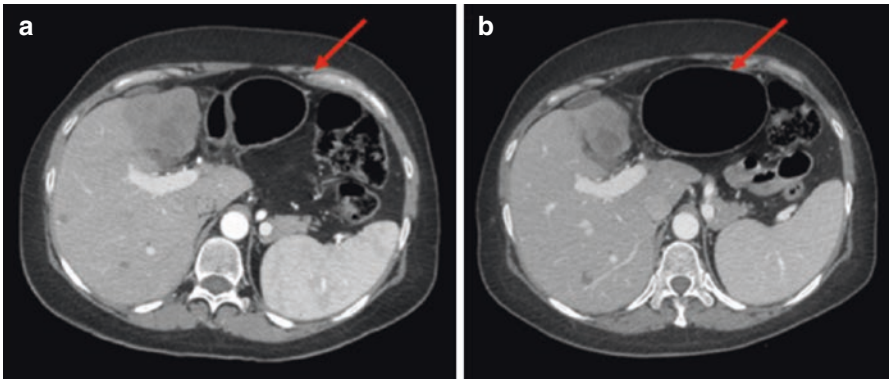

Fig. 9.1 These images depict the impact of stomach filling/bowel gas as depicted by the *red arrows* on movement of intra-abdominal organs

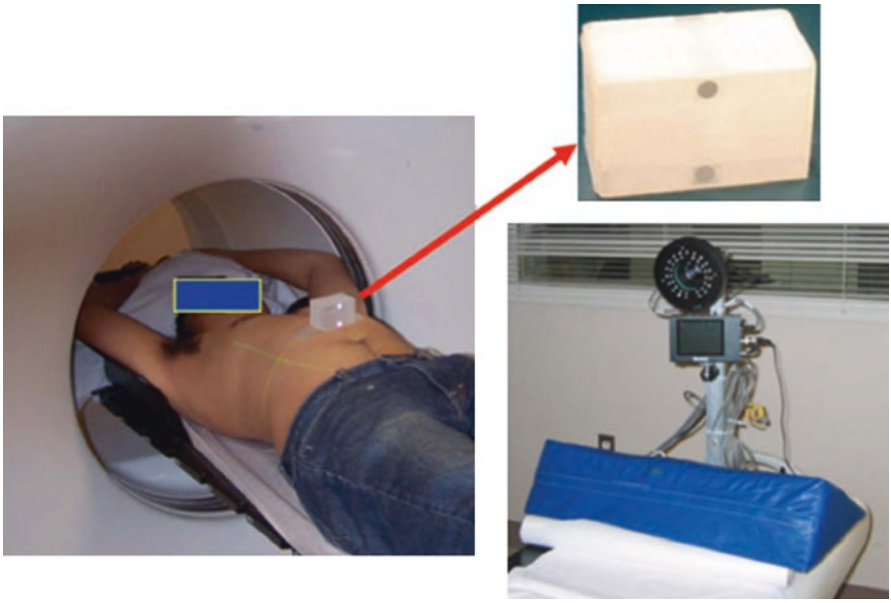

Fig. 9.2 Patient's position during simulation with RPM box taped on patient's abdomen. The RPM box has two dots which can be tracked by the RPM camera

9.3.2 Patient Setup

Patients are positioned supine, bilateral arms up, and immobilized with upper Vac-Lock (Civco Radiotherapy, Orange City, Iowa). A wingboard and Medtec leg holder (for photon treatment) or knee wedge (for proton treatment) are used for comfort and ensure reproducibility of treatment position. The Varian real-time patient monitoring (RPM) system is used to track respiration (Fig. 9.2). The RPM box is placed and taped onto the patient's abdomen in midline between the xiphoid process and

the umbilicus. The RPM camera is adjusted so that both dots on the RPM box are visible on the RPM computer and tracking is then commenced. The RPM box, positioned on the patient's abdomen, moves with patient's breathing, and therefore, is a surrogate marker used to track respiratory movement.

For conventional fractionated treatment (commonly 50.4 Gy/28 fractions), the RPM system will not be used. Free-breathing scans will be used for treatment planning. In other situations, it is acceptable and common to use respiratory gating to manage motion during conventionally fractionated therapy in an attempt to reduce normal tissue dose [14]. Our preference at UT MD Anderson is to plan on breath-hold scans, and this is explained in detail in the following sections.

9.3.3 Image Acquisition

Once the patient is comfortably positioned, an initial scout CT scan is performed and the scanning range is determined. Generally, scanning range extends from carina to iliac crests. Thin slices (2–3 mm) CT images were obtained.

Below is the workflow for image acquisition when breath-hold technique is implemented:

1. Perform scout CT
2. Determine scanning range (carina to iliac crest)
3. Perform free-breathing scan without contrast
4. Provide instructions and train patient to perform inspiration breath-hold. Each breath-hold should be comfortable and reproducible. It is not necessary and often not advisable to perform a "deep" inspiration hold, as this will often be challenging to reproduce during treatment. The aim of breath-hold is to reduce tumor motion, allowing reduction of planning target volume and dose to normal structures.
5. Once patient is comfortable with performing breath-hold, the breath-hold level is set in the RPM computer (between blue and orange bars). The bars should be set as narrow as feasible (Fig. 9.3).
6. Have practice runs with patient to ensure patient comfort, as well as consistency and reproducibility of breath-hold.
7. Perform 1–2 CT scans with breath-hold without contrast.
8. Perform breath-hold scans with contrast. We use 150 mL of iodine contrast (Optiray 320) at a rate of 5 mL/s. The first scan is performed at 30 s after commencement of IV contrast injection. Subsequent scans are performed at 30 s interval. Up to four scans are obtained.
9. The physician will select the optimal scan (best for tumor visualization and also considered to be most representative of all breath-hold scans) for treatment planning. The movement of the target between the various breath-hold scans gives a glimpse into patient compliance and the estimation of the variation that can occur even with breath-hold technique. This variation of target location during breathing should be accounted for as an ITV.
10. All CT images are exported to the treatment planning system.

If a patient is not able to perform breath-hold, a 4D-CT is performed.

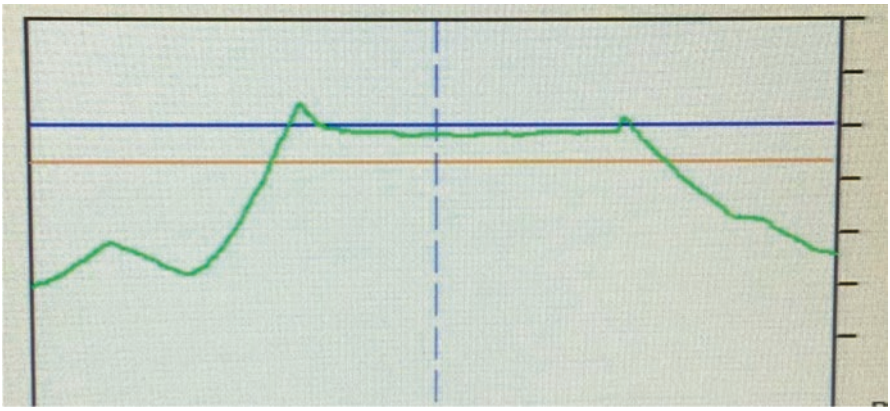

Fig. 9.3 Image showing the screen of RPM computer with the set level bars (*blue* and *orange* lines). The patient's respiratory movement is tracked and shown as the *green* line. Patient is instructed to try and maintain his/her breath-hold in between the *blue* and *orange* bars

9.3.4 Treatment Planning

9.3.4.1 Target Volumes for Conventional Dose/Fractionation (No Breath-Hold) Using Non-SBRT Techniques

- Figure 9.4 provides a contouring atlas for conventional dose/fractionation (50.4 Gy/28 fractions).
- Gross tumor volume (GTV) of the primary (GTVp) and pathological nodes (GTVn) are contoured.
- Contour:
  - Celiac artery (proximal 1–1.5 cm)
  - Superior mesenteric artery (SMA) (proximal 2.5–3 cm)
  - Porta hepatis (including the portal vein segment that runs anteromedial to the inferior venal cava to the bifurcation at the liver, and the liver hilum)
  - Duodenum (through the fourth portion)
  - Small bowel (particularly jejunum near the ligament of Treitz)
- Clinical target volume (CTV) = (GTV + celiac artery + SMA + porta hepatis) + 2 cm margin superiorly and inferiorly, and a 1 cm margin radially.
- Planning target volume (PTV) = CTV + institutional setup error (typically 0.5 cm margin).
- Dose/fractionation: 50.4 Gy in 28 fractions, 1.8 Gy per fraction, daily treatment 5 days per week over 5.5 weeks. This regimen is typically delivered with concurrent chemotherapy.

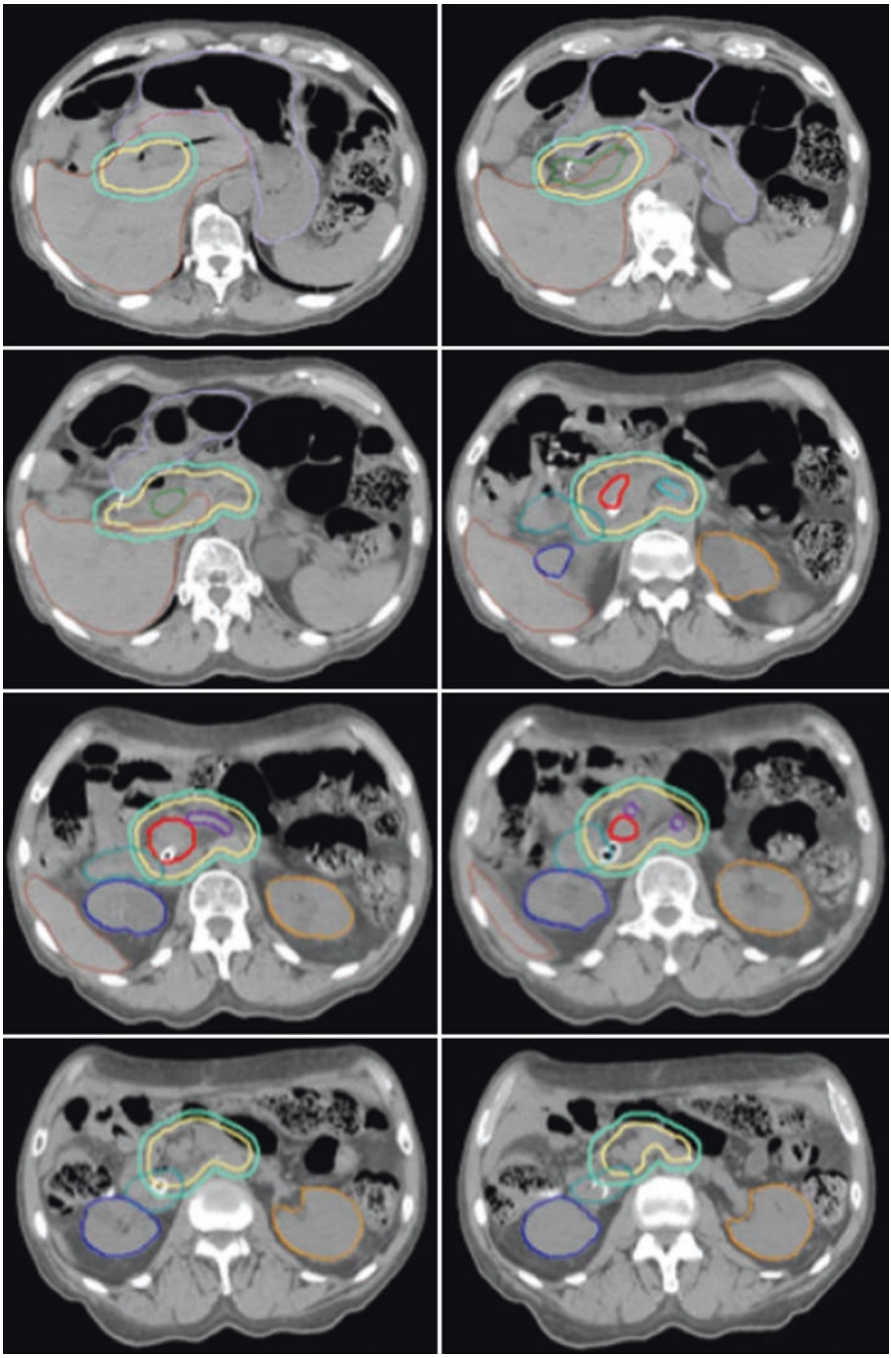

Fig. 9.4 Contouring atlas for conventional dose/fractionation (50.4 Gy/28 fractions). Target volumes: *Red*—GTV, *Yellow*—CTV, *Cyan*—PTV. Organs at risk: *Brown*—liver, *Green*—duodenum, *Blue*—right kidney, *Orange*—left kidney

9.3.4.2 Target Volumes and Dose/Fractionation for Non-SBRT Dose Escalation (Breath-Hold) Techniques

- Figure 9.5 provides a contouring atlas for dose-escalated regimens.
- GTV = primary tumor. Nodes are excluded from high dose treatment volumes.
- Internal target volume (I-GTV) = GTV expanded to encompass all GTV position seen on all breath-hold scans and combined to account for variable breath-hold positions and tumor motion.
- CTV is not generated in these cases
- Organs-at-risk are contoured and a planning organ at risk volume (PRV) is created for stomach, duodenum, and small bowel by adding a margin of 3 mm to these organs.
- PTV (high dose) = ITV + institutional setup error (typically 0.5 cm)—PRV
- A lower acceptable dose to the organs at risk is prescribed to the full PTV if the PTV extended into the PRV.
- Dose/fractionation
  - 60 Gy/15 fractions
  - 67.5 Gy/15 fractions
  - 70 Gy/28 fractions

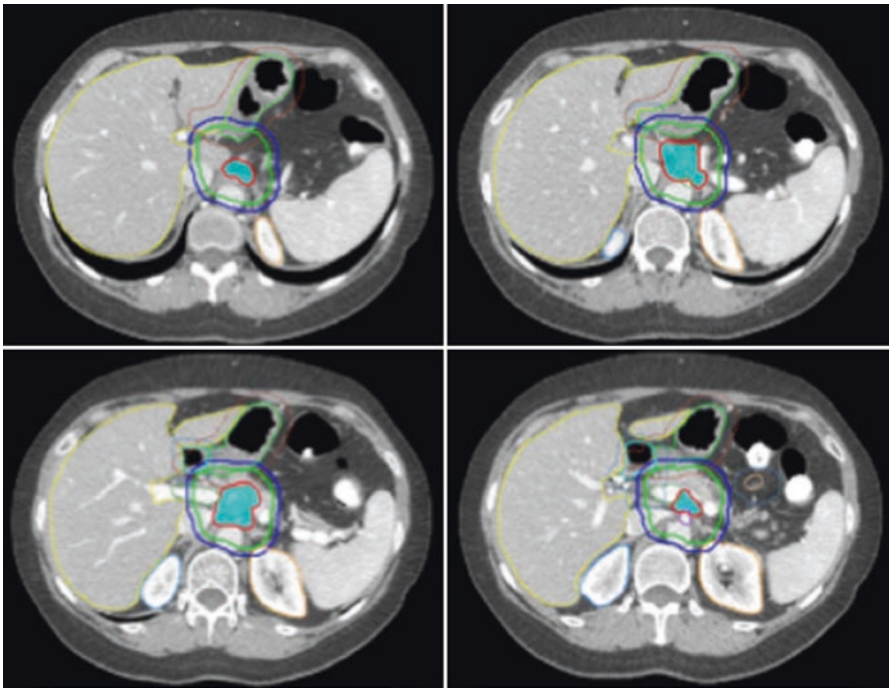

Fig. 9.5 Contouring atlas for dose-escalated regimens. Target volumes: *Red*—GTV, *Green*—CTV 37.5 Gy, *Dark blue*—PTV 37.5 Gy, *Cyan* filled—PTV 67.5 Gy. Organs at risk: *Yellow*—liver, *Light blue*—right kidney, *Orange*—left kidney, *Light green*—stomach, *Khaki*—small bowel, *Cyan* lined—duodenum

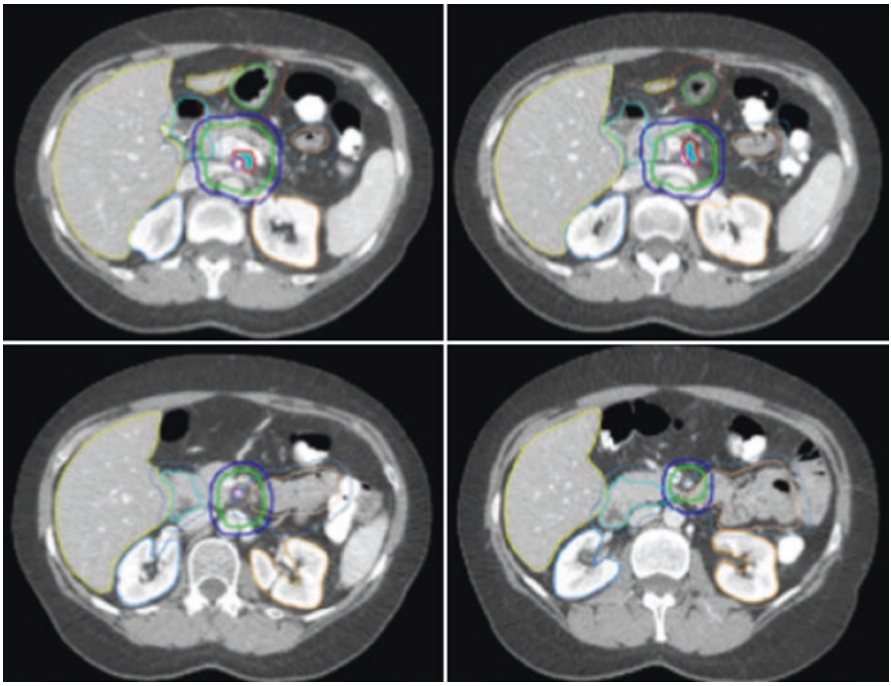

Fig. 9.5 (continued)

9.3.4.3 Target Volumes and Dose/Fractionation for SBRT Technique

We adopt the treatment planning procedures as the ALLIANCE study (NCT02839343).

- Figure 9.6 provides a contouring atlas for SBRT.
- GTV = primary tumor. Nodes are excluded from SBRT.
- I-GTV is generated to account for different breath-hold positions and tumor motion (see above).
- CTV is not generated for SBRT
- A tumor vessel interface (TVI) is contoured for each vessel (portal vein, SMA, common hepatic artery, celiac artery) separately that is in contact with the tumor (Fig. 9.7).
- Internal TVI (I-TVI) is generated by expanding the TVI to account for TVIs on all breath-hold scans.
- PRV is generated for stomach, duodenum, and small bowel by adding 3 mm margin to these organs. If possible, an ITV should first be generated from either 4DCT or multiple breath-hold scans. The duodenal and jejunal contours should be tightly adherent to the anatomy on CT and not a "bowel bag."
- Three PTVs are generated for different dose levels:
  - PTV1 = (I-GTV + I-TVI) + 3 mm to be treated to 25 Gy/5 fractions
  - PTV2 = PTV1—PRV to be treated to 33 Gy/5 fractions
  - PTV3 = (I-TVI + 3 mm)—PRV to be treated to 36 Gy/5 fractions
- Figures 9.7, 9.8, and 9.9 demonstrate SBRT planning target volumes with relation to adjacent normal structures.

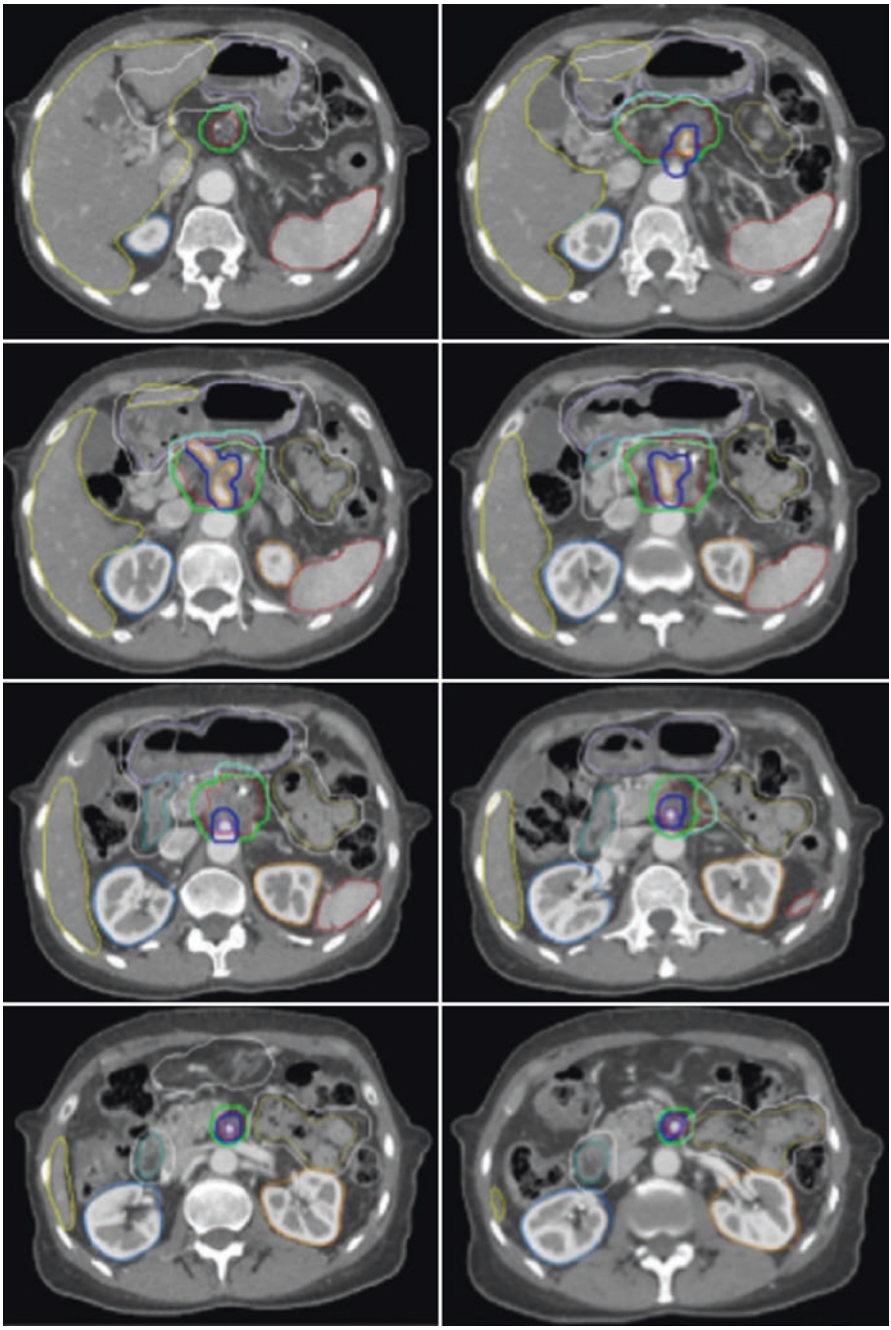

Fig. 9.6 Contouring atlas for SBRT. Target volumes: *Red*—GTV, *Cyan*—PTV1 (25 Gy), *Light green*—PTV2 (33 Gy), *Dark blue*—PTV3 (36–40 Gy). Organs at risk: *Yellow*—liver, *Dark green*—duodenum, *Purple*—stomach, *Orange*—Left kidney, *Light blue*—Right kidney, *Khaki*—Small bowel, *White*—PRV for stomach, duodenum, and small bowel

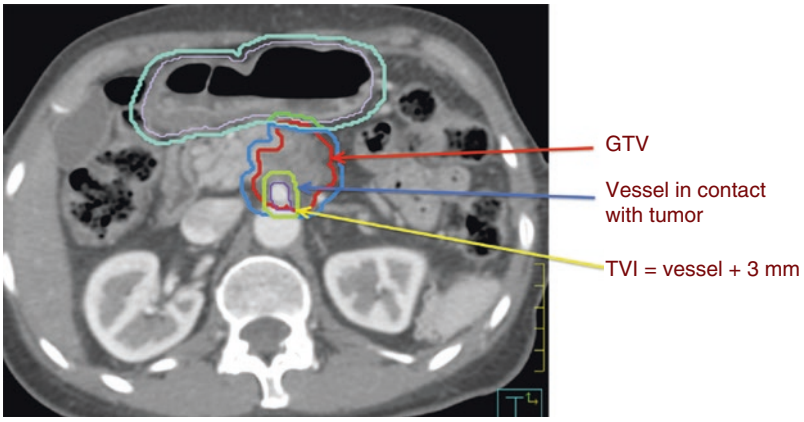

Fig. 9.7 SBRT treatment planning axial CT image illustrating the gross tumor volume (GTV in *red*) and tumor vessel interface (TVI in *neon green*) contours. The TVI will be treated to 36 Gy (maximum 40 Gy), the planning target volume (GTV plus margin, in *blue*) will be prescribed 33 Gy except for the region adjacent to the bowel (the region in *green* will be treated to 25 Gy)

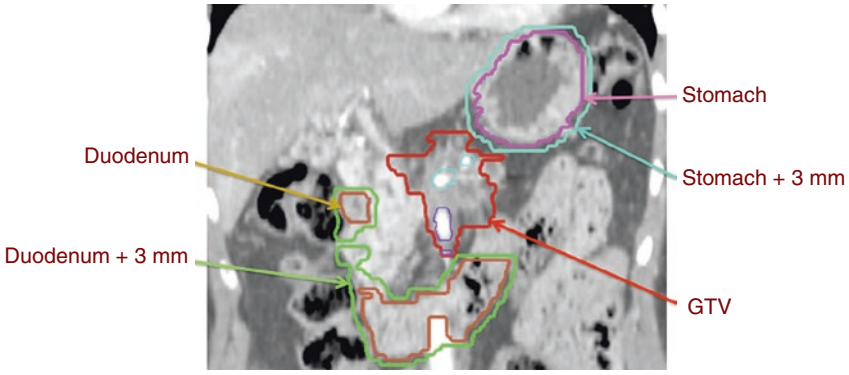

Fig. 9.8 SBRT treatment planning coronal CT image showing the planning organ-at-risk volume (PRV) generated by expanding the stomach (*purple*) and duodenum (*brown*) volumes by 3 mm

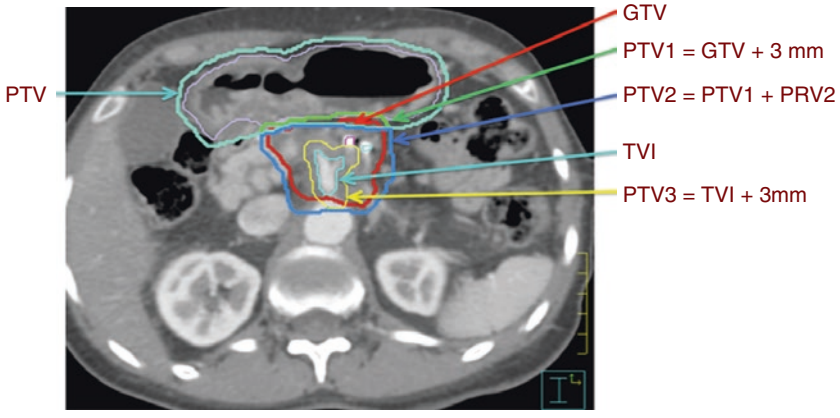

Fig. 9.9 Representative axial CT image depicting PTV1, PTV2, and PTV3 for SBRT treatment planning

9.3.4.4 Organs-at-Risk to be Contoured for Treatment Planning

- Duodenum
- Stomach
- Bowel bag (for conventional 50.4 Gy/28 fractions treatment)
- Small bowel loops (for dose escalation or SBRT). Make sure to account for jejunum near the ligament of Treitz.
- Large bowel loops (for dose escalation or SBRT)
- Liver
- Right and left kidneys
- Spinal cord
- Spleen
- Lungs
- Heart

9.3.5 Planning Aims and Dose Constraints

9.3.5.1 For Conventional Fractionation

Target coverage aims:

- PTV1: 50.4 Gy, V100% > 95%, V95% > 99%, V105% < 10%, Dmax < 120% (Table 9.1)

Table 9.1 Dose constraints for conventional fractionation

OAR	Constraints
Small bowel	Dmax < 50 Gy
Liver	Mean < 32 Gy, V20 < 60%, V30 < 33%
Combined kidneys	Mean < 18 Gy; V20 < 33% for each; if one exceeds, spare the other with V20 < 20%
Spinal cord	Dmax < 45 Gy
Spleen	Mean < 8Gy

9.3.5.2 For Dose-Escalated Regimens (67.5 Gy/15 Fractions)

Target coverage aims:

- For each PTV: V100% > 95%, V95% > 99%, V105% < 10%, Dmax < 120%

The priorities are first to meet dose constraints (ensuring that the treatment will be safe for the patient), secondly to optimize PTV coverage, and thirdly to try and delivery a high dose to the GTV/central core of tumor (accepting heterogeneity dose coverage) (Table 9.2).

Table 9.2 Dose constraints for 67.5 Gy/15 fractions (this will differ if a treatment dose/fractionation is used)

OAR	Constraints
Small bowel	Dmax < 40 Gy
Stomach Duodenum	Dmax < 45 Gy
Liver	Mean < 24 Gy
Common bile duct	Dmax < 60 Gy
Combined kidneys	Mean < 18 Gy; V20 < 33% for each; if one exceeds, spare the other with V20 < 20%
Spinal cord	Dmax < 30 Gy
Large bowel	Dmax < 50 Gy
Spleen	Mean < 6 Gy

9.3.5.3 For SBRT

Target coverage aims:

- PTV1: 25 Gy, Dmin >22.5 Gy
- PTV2: 33 Gy, Dmin >29.7 Gy
- PTV3: 36 Gy, Dmin > 32.4 Gy, Dmax 40 Gy

If the dose constraints cannot be met with the above target coverage, PTV1 will be reduced to 25 Gy/5 fractions with the aim of ≥90% PTV1 be covered by ≥95% of prescription dose and Dmax ≤ 110% of prescribed dose (Table 9.3).

Table 9.3 Dose constraints for SBRT

OAR	Constraints
Duodenum	V20 < 20 cc
	V35 < 1 cc
Small bowel (other)	V20 < 20 cc
	V35 < 1 cc
Stomach	V20 < 20 cc
	V35 < 1 cc
Liver	V12 < 50%
Combined kidneys	V12 < 25%
Spinal cord	V20 < 1 cc
Spleen	No constraint

9.3.6 Treatment Verification

For patients treated using conventional fractionation, daily kV-IGRT is used for treatment position verification.

For dose-escalated regimens and SBRT, patients are imaged daily using CT-on-rails (Fig. 9.10). CT-on-rails provides diagnostic high-quality on-board CT imaging which allow soft tissue to soft tissue matching with high accuracy. The ability to visualize soft tissue also allows dose escalation regimens to be delivered safely.

Workflow of CT-on-rails at the MD Anderson Cancer Center

1. Patient is brought into treatment suite, positioned, and set up on the treatment table with patient's head towards gantry (Fig. 9.10b).
2. Once setup has been established, the couch is rotated so that patient's head is towards the CT-on-rails (Fig. 9.10c).
3. Patient is imaged with CT-on-rails and the images are reviewed by the treating physician or trained therapists.
4. CT-on-rails images are compared to the planned CT images and contours (typically GTV) and isodose lines are displayed on both sets of images (Fig. 9.11).

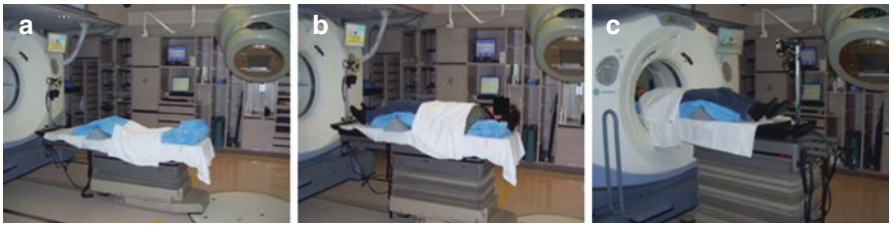

Fig. 9.10 Images depicting the CT-on-rails imaging process. (**a**)—setup before patient enters treatment room. (**b**)—patient positioned with head towards gantry. (**c**)—couch rotated 180° and patient positioned towards CT-on-rails

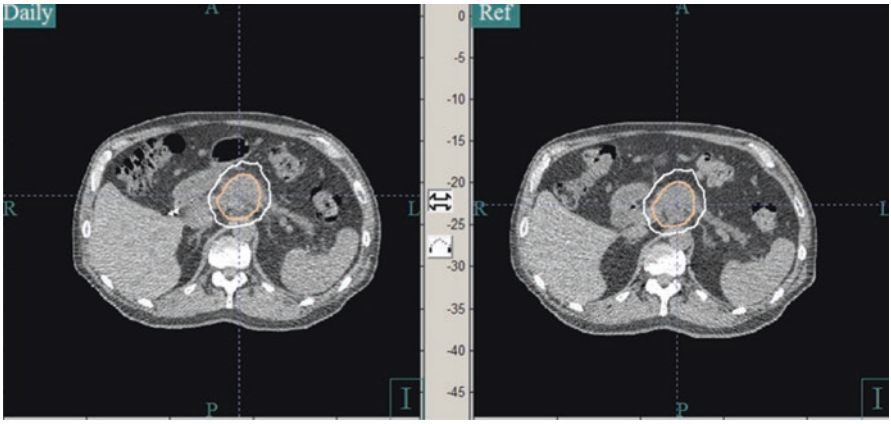

Fig. 9.11 Example of an image obtained from CT-on-rails ("Daily") compared to image obtained at simulation ("Ref"). *Khaki line*—GTV; *White line*—PTV

5. The CT-on-rails images are aligned to the planned images and couch shifts required are documented and made.
6. The couch is then rotated back so that patient's head is towards the gantry.
7. Treatment commenced.

During the whole process described above, patient is required to be in the treatment position.

9.3.7 Treatment Modalities

Table 9.4 describes the various radiation options and indications for the treatment of locally advanced pancreatic cancer (Figs. 9.12–9.15).

Table 9.4 Radiation treatment approaches for locally advanced pancreatic cancer

Technique	Indication	Fractionation schedules	Beam arrangement	Appropriate chemotherapy
3D CRT[a]	Definitive or consolidative therapy after chemotherapy	50.4 Gy; 1.8 Gy per fraction; 5 days per week	Three or four fields (APPA; right and left lateral)	Before radiation, and/or concurrent, and/or following radiation
IMRT VMAT[a]	Definitive or consolidative therapy before/after chemotherapy (IMRT/VMAT preferred over 3D CRT if available)	50.4 Gy; 1.8 Gy per fraction; 5 days per week	IMRT: Multiple coplanar isocentric beams VMAT: Volumetrically modulated coplanar arcs	Before radiation, and/or concurrent, and/or following radiation
Proton therapy[b]	Definitive or consolidative therapy before/after chemotherapy	50.4 Gy (RBE); 1.8 Gy per fraction; 5 days per week	Typically, three fields (posterior oblique: Right lateral oblique) with a 3-to-1 weighting to the posterior field to limit spinal cord dose	Before radiation, and/or concurrent, and/or following radiation
SBRT[b]	Consolidative therapy after chemotherapy	33 Gy; 6.6 Gy per fraction (or 25 Gy; 5 Gy per fraction if dose constraints not met with 33 Gy); Delivered over 5 days	Linac-based: IMRT: Multiple coplanar isocentric beams Cyberknife: Multiple noncoplanar nonisocentric beams	Before radiation, and/or following radiation

[a]High-energy photons (>10 MV) preferred as lower energy may result in more gastrointestinal toxicity
[b]May be appropriate for select cases

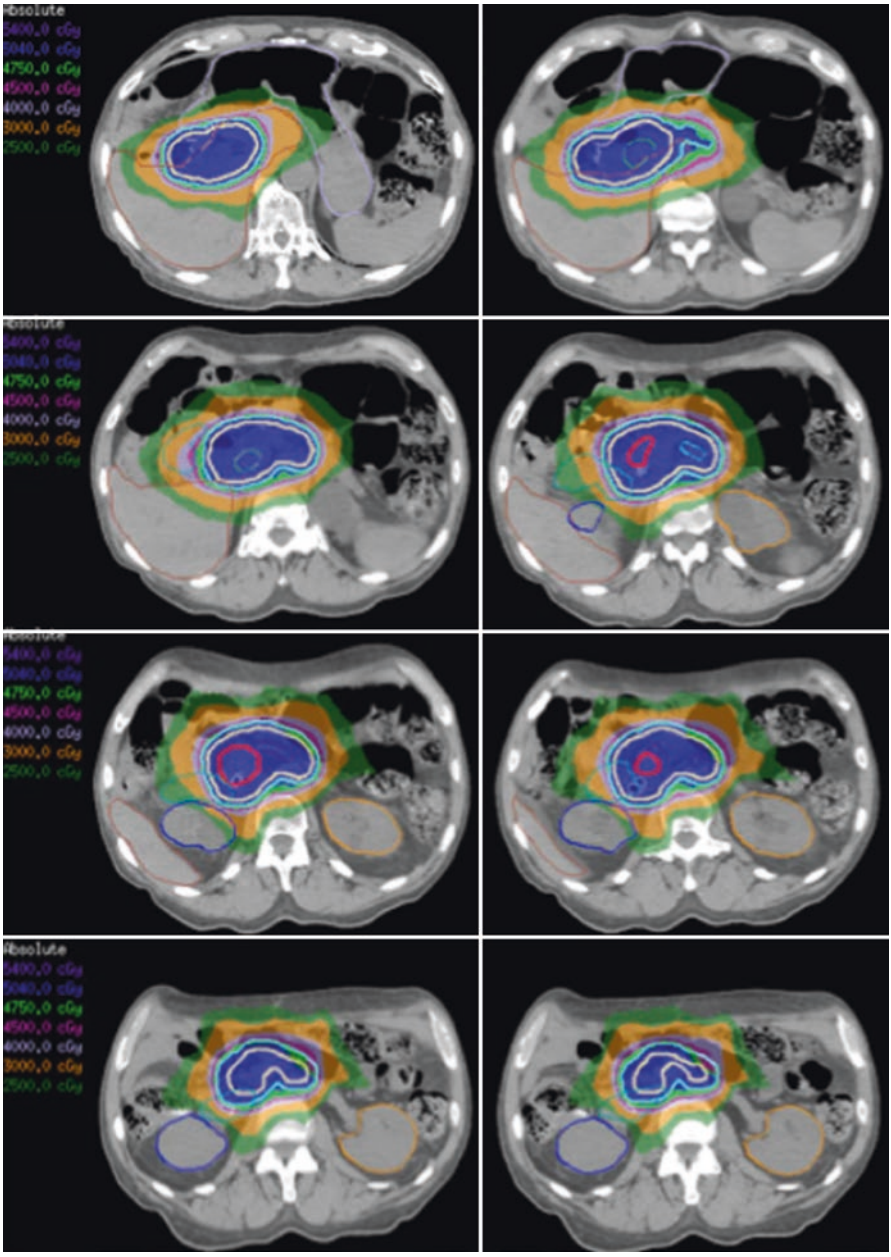

Fig. 9.12 Representative IMRT treatment plan for locally advanced, unresectable pancreatic cancer. Representative images of IMRT treatment plan and dose volume histogram (50.4 Gy/28 fractions). Dose volume histogram: *Cyan*—PTV, *Khaki*—CTV, *Purple*—Stomach, *Yellow*—Liver, *Dark blue*—Right kidney, *Red*—Spinal cord, *Orange*—Left kidney

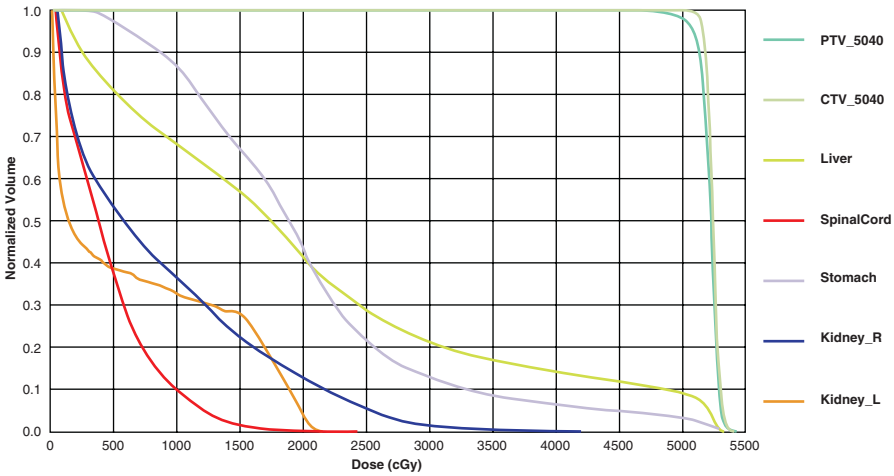

Fig. 9.12 (continued)

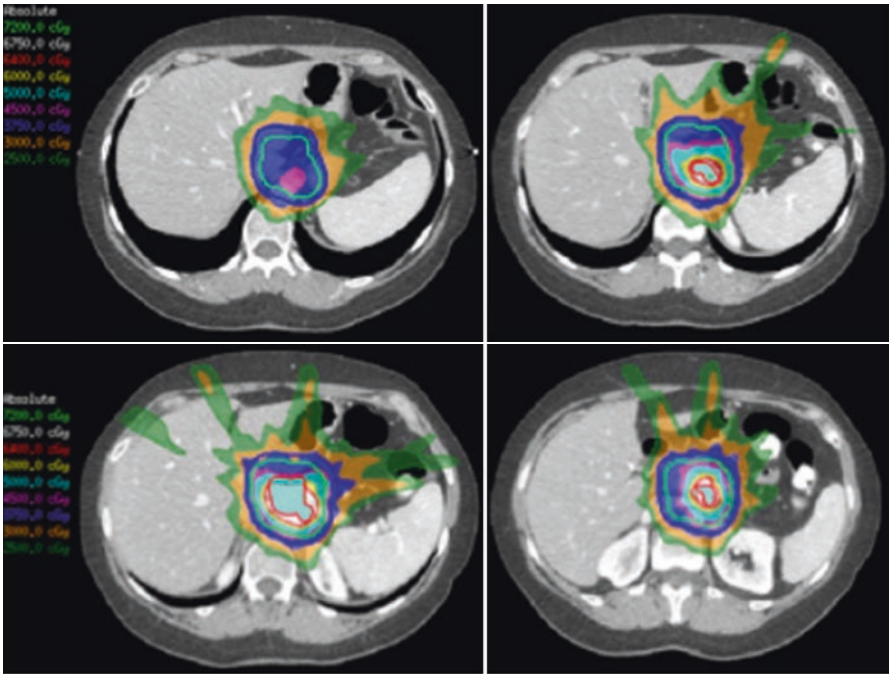

Fig. 9.13 Representative dose-escalated treatment plan for locally advanced, unresectable pancreatic cancer. Representative images of dose-escalated (in this case, 67.5 Gy/15 fractions) treatment plan and dose volume histogram. Dose volume histogram: *Red*—PTV 67.5 Gy, *Brown*—PTV 37.5 Gy, *Light green*—Stomach, *Dark green*—Small bowel, *Cyan*—Duodenum, *Orange*—Left kidney, *Yellow*–Liver, *Blue*—Right kidney, *Cherry red*—Spinal cord

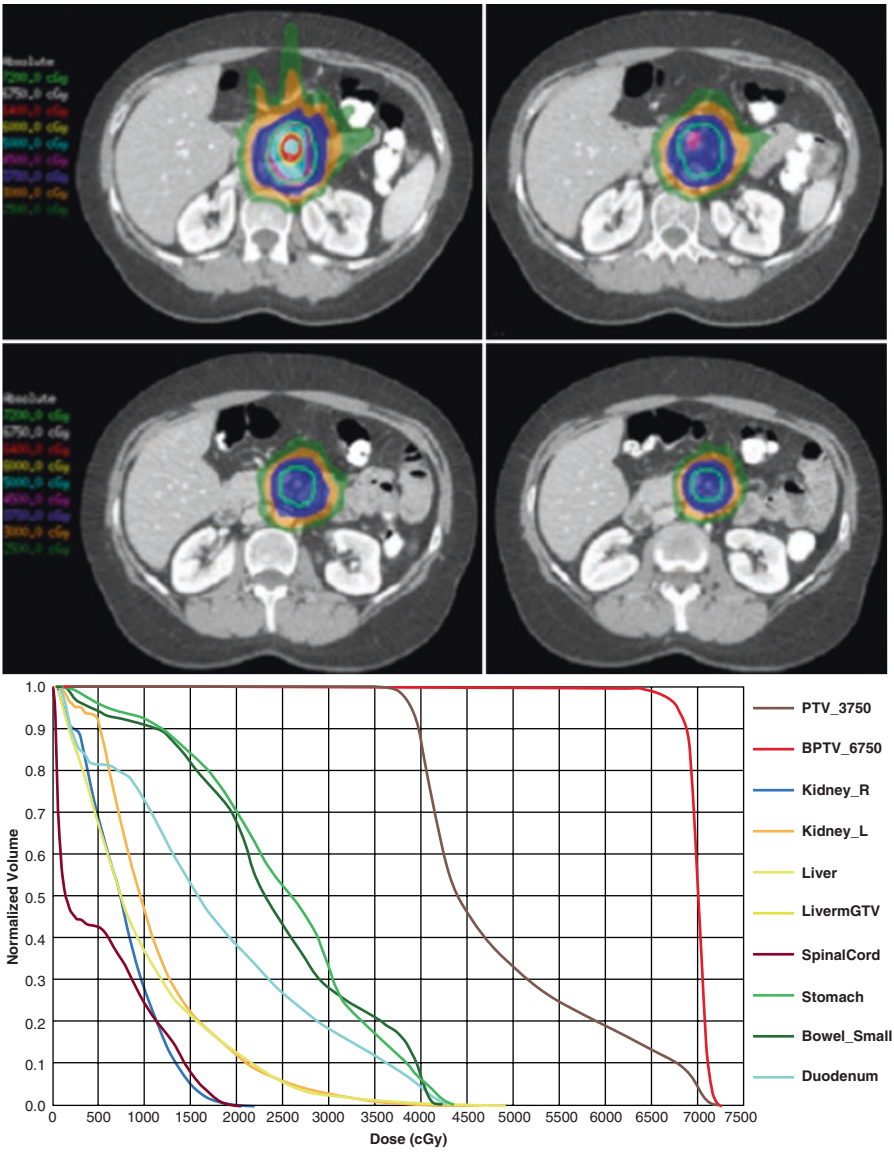

Fig. 9.13 (continued)

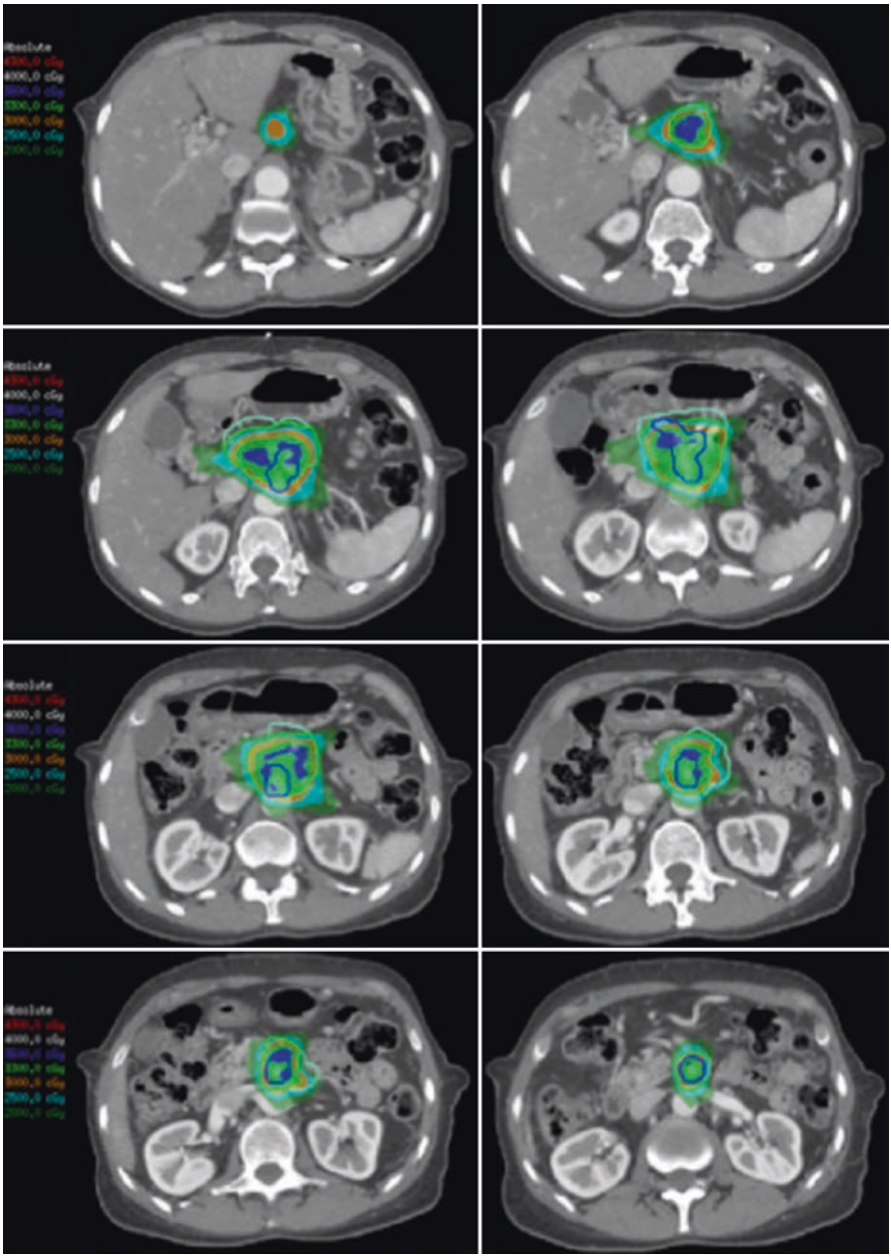

Fig. 9.14 Representative SBRT treatment plan for locally advanced, unresectable pancreatic cancer. Representative images of SBRT treatment plan (33 Gy/5 fractions) and dose volume histogram. Dose volume histogram: *Red*—PTV1 (25 Gy), *Brown*—PTV2 (33 Gy), *Blue*—PTV3 (36–40 Gy), *Light green*—Small bowel, *Cyan*—Right kidney, *Dark green*—Duodenum, *Orange*—Left kidney, *Yellow*—Liver, *Purple*—Stomach, *Khaki*—Spinal cord

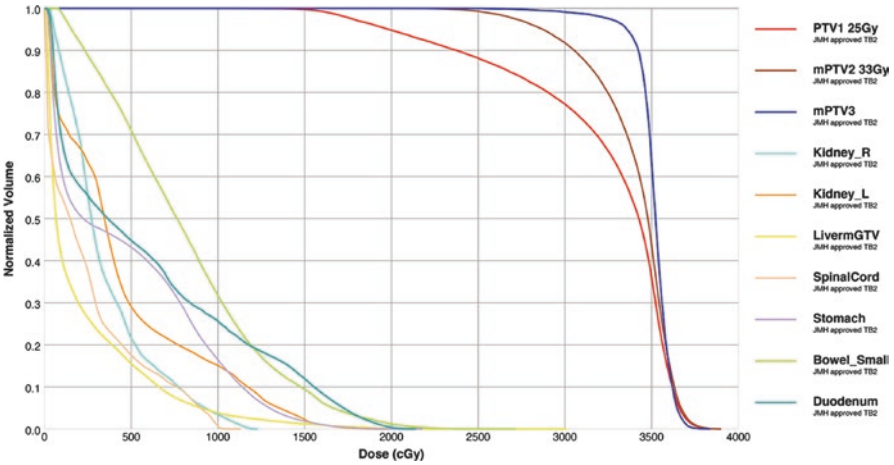

Fig. 9.14 (continued)

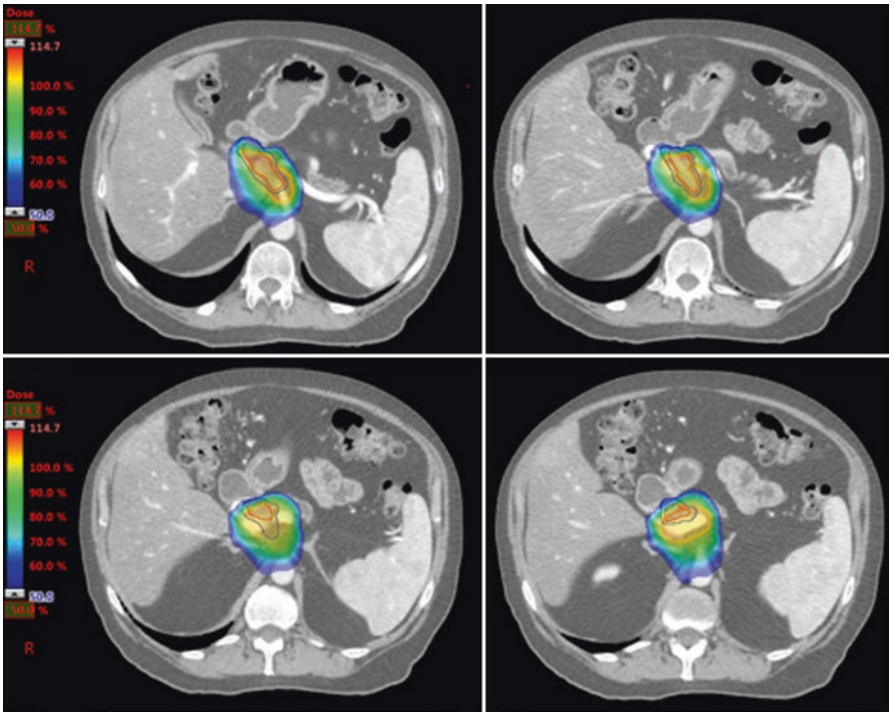

Fig. 9.15 Representative proton treatment plan for locally advanced, unresectable pancreatic cancer. Representative images of proton SBRT treatment plan (33 Gy/5 fractions) and dose volume histogram. Dose volume histogram: *Purple*—PTV1, *White*—PTV2, *Khaki*—PTV3, *Dark green*—Duodenum, *Yellow*—Liver, *Light green*—Small bowel, *Orange*—Left kidney, *Blue*—Right kidney, *Purple*—Stomach, *Red*—Spinal cord

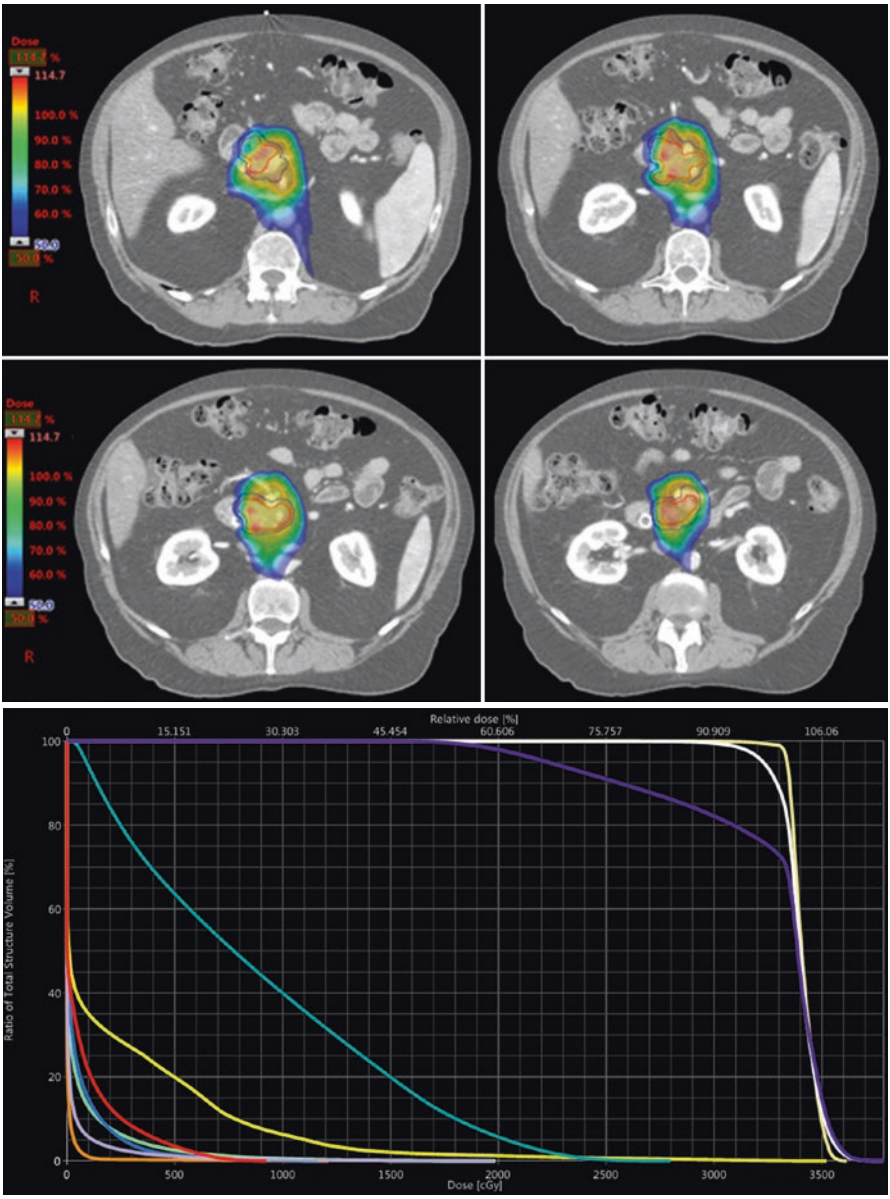

Fig. 9.15 (continued)

9.3.8 Treatment Plan Optimization and Special Considerations

To achieve satisfactory target coverage and dose to organs at risk, treatment plans must be optimized. Strategies to optimize treatment plans and special considerations for SBRT and proton therapy were described in detail in the previous chapter.

9.4 Summary

The optimal treatment and sequencing of chemotherapy and radiotherapy for locally advanced pancreatic cancer remained controversial. Without surgery, the prognosis in this group of patients is poor, and therefore, a frank discussion with patient with regard to goals of treatment upfront and an early referral to palliative care service, if feasible, is of importance. These patients have high risk of systemic progression warranting consideration of chemotherapy as first line of treatment. Achieving local control with radiation therapy following chemotherapy appears to translate into a survival benefit in some studies. However, the exact role and timing of radiation is yet to be established.

There are different radiation treatment modalities that can be considered when planning radiotherapy for patients with locally advanced pancreatic cancer. The choice of modality used will depend on the availability of equipment/technology, dose/fractionation, and dose to normal tissues. IMRT, VMAT, and proton therapy tend to have improved dose distribution to target volumes, while minimizing radiation dose to normal tissues than 3D CRT. SBRT can be considered in this group of patients, provided that patient has no invasion of the duodenum, and adequate respiratory/tumor motion management, immobilization, and on-board imaging are available (Fig. 9.16).

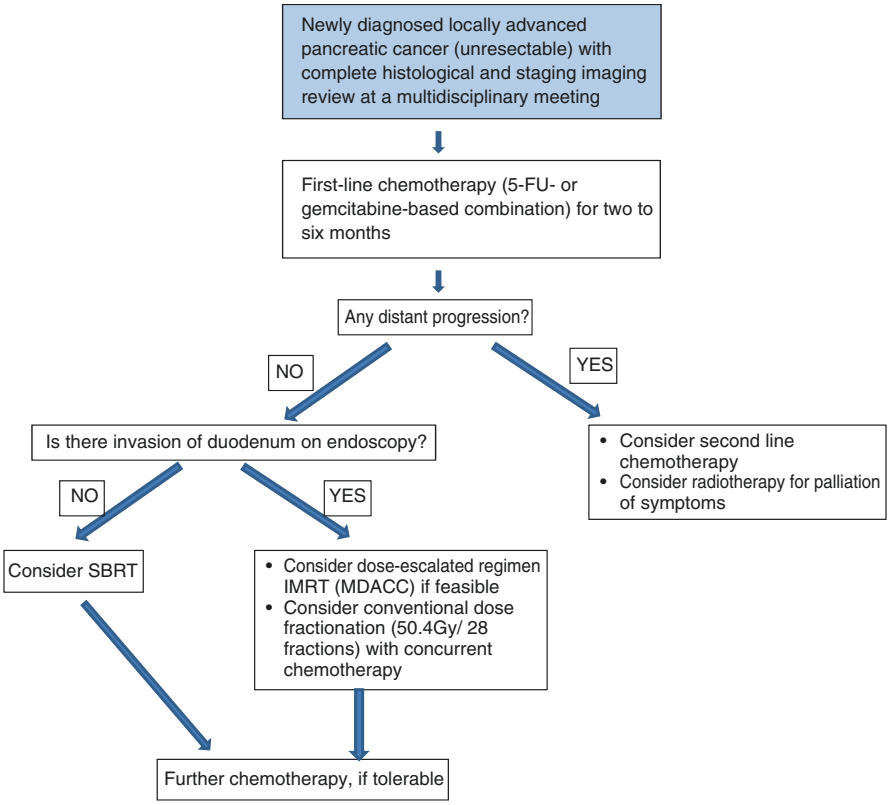

Fig. 9.16 Treatment algorithm designed to help choose clinical scenarios appropriate for particular treatment modalities in the setting of locally advanced pancreatic cancer

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