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Contour Clinic

Elective Target Volume Delineation for Locally Advanced Pancreatic Cancer

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A 60-year-old man with no significant medical history was diagnosed with pancreatic ductal adenocarcinoma (PDAC). Imaging revealed a 4.0-cm mass in the pancreatic head with arterial involvement, including encasement of the proximal celiac artery (CA) and superior mesenteric artery (SMA) extending beyond the first jejunal branch, as well as abutment of the proximal splenic artery. There was also near-complete occlusion of the portal vein (PV) because of encasement at the confluence of the superior mesenteric vein (SMV) and splenic vein.

Staging classified the tumor as cT4N0M0, consistent with unresectable, locally advanced PDAC (LAPC). Because of the significant PV occlusion, the patient underwent portomesenteric venous stenting from the main PV to the SMV. A multidisciplinary team recommended initial systemic therapy with modified FOLFIRINOX. If the disease remained localized on interval assessment, consolidative chemoradiation was planned, consisting of 15 fractions delivering 6000 to 6750 cGy to the gross tumor and 3750 cGy to the elective regions, with concurrent capecitabine.

Patterns of Spread in PDAC and Implications for Target Volume Delineation

PDAC is a highly infiltrative malignancy with well-characterized patterns of locoregional spread. These include microscopic peritumoral infiltration, extrapancreatic tumor extension, perineural invasion, and regional lymph node (LN) involvement.[1] Direct tumor extension into adjacent organs and vascular structures is common and seen in nearly all cases of LAPC.[1,2] Perineural invasion is present in most patients and contributes to both locoregional symptoms and an increased risk of relapse.[1,3-5] Perineural spread typically follows the peri-pancreatic vasculature, eventually reaching the celiac or superior mesenteric ganglia (Fig. 1).

- Tumors of the pancreatic head and superior uncinate process often spread via the pancreatic head plexus I, which tracks alongside the superior pancreaticoduodenal arteries, gastroduodenal artery, common hepatic artery, and terminates at the right celiac ganglion.
- Tumors of the uncinate process or posterior-inferior pancreatic head spread via the pancreatic head plexus II, which courses along the inferior pancreaticoduodenal arteries to the SMA, superior mesenteric ganglion, and bilateral celiac ganglia.
- Caudal perineural spread along the SMA—referred to as the root of the mesentery pathway—may occur.[1]

Regional LN involvement is also frequent. Commonly affected LN regions in tumors of the pancreatic head, neck, or uncinate process include the following[6,7]:

- Pancreaticoduodenal
- Superior mesenteric
- Common hepatic
- Paraortic nodes

The hepatoduodenal ligament and celiac LNs are also at risk, although involvement is seen in <10% of patients with anatomically resectable disease.

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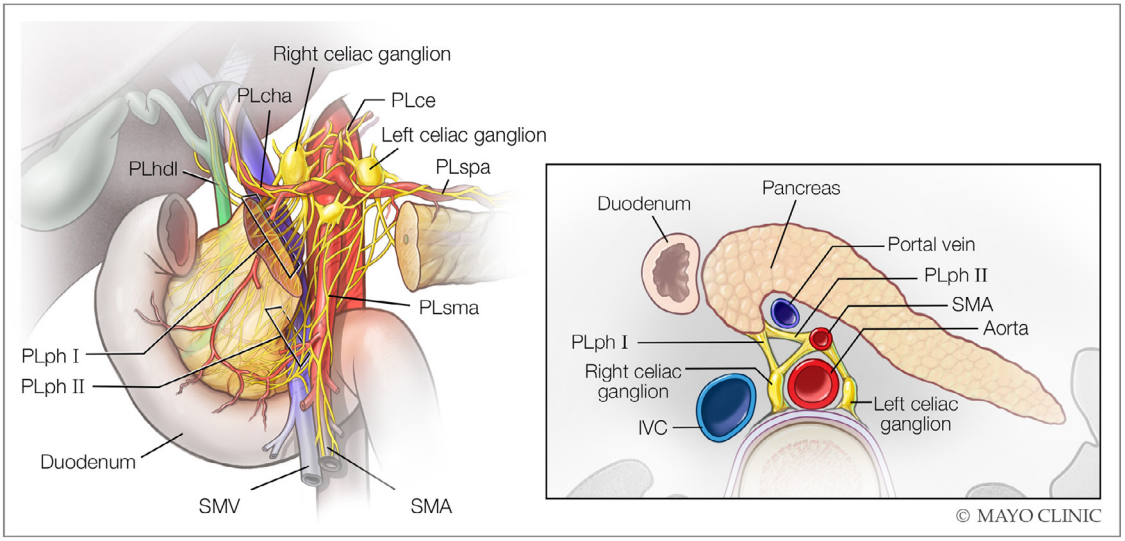

Figure 1 Main nerve structures of the mesopancreas. Reproduced with permission from Jethwa et al.[1]
Abbreviations: PLce = celiac artery nerve plexus; PLcha = common hepatic artery nerve plexus; PLhdl = hepatoduodenal ligament nerve plexus; PLphI = pancreatic head plexus I; PLphII = pancreatic head plexus II; PLphII = pancreatic head plexus II; PLsma = superior mesenteric artery nerve plexus; PLspa = splenic artery nerve plexus.

How We Do It: Contouring Strategy for Unresectable Pancreatic Cancer

The patient was simulated under breath-hold conditions with intravenous (IV) contrast. Three breath-hold computed tomography (CT) scans were acquired. The primary pancreatic tumor was contoured on the planning CT, guided by the registered scan with IV contrast, as pancreatic tumors typically appear hypoenhancing compared with normal pancreatic parenchyma. Although CT imaging often underestimates peritumoral spread, subtle areas of haziness extending into peripancreatic fat are frequently observed.[2,8] These regions, suggestive of microscopic infiltration, are included in the gross tumor volume. To account for respiratory motion, an **i**nternal gross tumor volume (iGTV) was generated from all 3 breath-hold scans. The entire circumference of vessels adjacent to the tumor—at the tumor-vessel interface—was also contoured. The combination of iGTV and tumor-vessel interface defined the high-risk clinical target volume. An additional 0.5-cm isotropic margin was added to generate the planning target volume**,** which received a prescribed dose of 6000 cGy. A heterogeneous dose distribution was requested with a goal of ≥6750 cGy to regions of gross tumor away from gastrointestinal luminal organs.

There is no universal standard for defining an elective clinical target volume (CTVlow) in definitive radiation therapy (RT) for LAPC.[9-11] Historically, elective regions were omitted because of the predominance of progression within gross tumor and distant sites. However, with improved systemic therapy and RT dose escalation techniques, which are associated with relatively improved control of the gross primary tumor, recent practice trends favor inclusion of elective volumes also to improve control of subclinical disease.[12,13]

CTVlow includes a 0.5 to 1.0-cm isotropic expansion from the iGTV and incorporates elective nodal and perivascular/perineural regions at high risk of microscopic disease, inclusive of the following:

- **CA:** From origin to trifurcation with 0.5- to 1-cm margin, extended to include the common hepatic artery and gastroduodenal artery takeoff
- **SMA:** From aortic origin to below the first jejunal branch, and extended to include ∼1 cm distal to gross tumor extension
- **PV:** Medial PV extended laterally at least 0.5 to 1 cm from the celiac axis and SMA, inclusive of the portosplenic confluence
- **SMV:** At levels of SMA coverage
- **Retroperitoneal and paraortic nodes:** At levels of SMA coverage

This strategy targets high-risk pathways for lymphatic and perineural spread, including the pancreatic head plexus I and II and the root of the mesentery pathway**.** Our approach is similar to a "triangle volume"-based approach, a surgical concept emphasizing the role of perineural and lymphatic routes in locoregional progression of pancreatic head, neck, and uncinate tumors.[14] The triangle is anatomically defined by the space bordered by the CA, SMA, CHA, PV, and SMV.

Hill et al[13] applied this concept to RT planning, showing that most recurrences occurred within this triangle, thus supporting its inclusion in elective CTV design. Our contouring strategy applies similar themes of encompassing

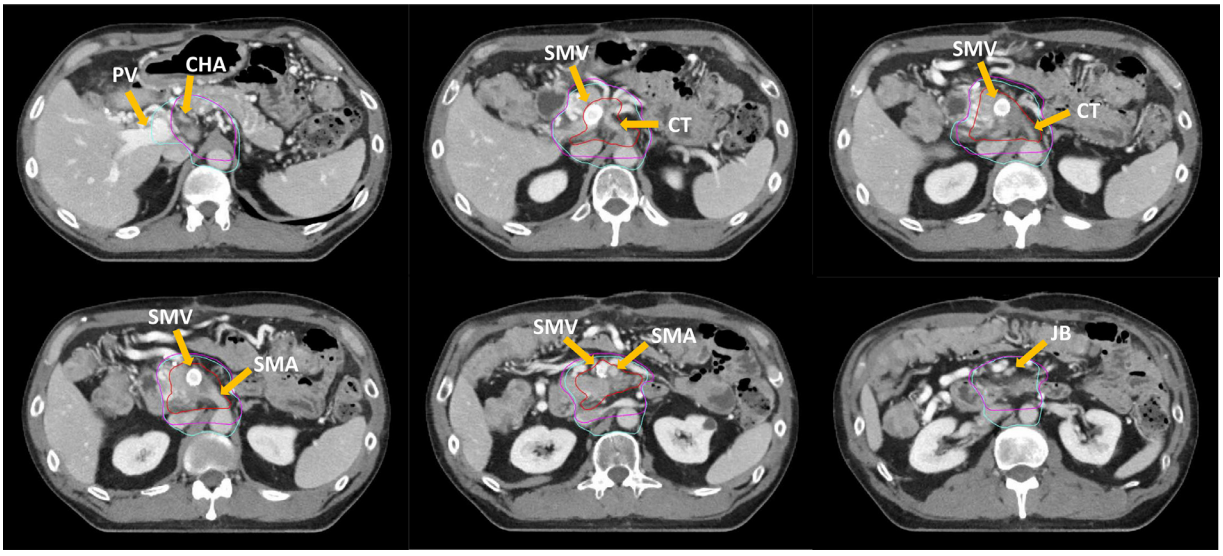

Figure 2 Representative axial slices of the radiation plan. The figure demonstrates the gross tumor volume (red) and CTVlow, the triangle volume (light blue). An elective clinical target volume based on the NRG GI011 contouring atlas (magenta) is shown for comparison.

Abbreviations: CHA = common hepatic artery; CT = celiac trunk; JB = first jejunal branch; PV = Portal vein; SMA = superior mesenteric artery; SMV = superior mesenteric vein (with stent in place).

the highest-risk pathways of perineural and lymphatic spread as the "triangle volume"-based approach and is also similar to the approach that will be used in the upcoming NRG GI011 trial investigating dose-intensified RT for LAPC.[15]

As discussed in the NRG GI011 contouring atlas,[15] posterior coverage of the aorta and the extent of inclusion of the porta hepatis were 2 regions of the CTVlow that varied the most among the participating radiation oncologists. With the understanding that perineural tracks do extend posteriorly around the aorta approximating the vertebral bodies, that retroperitoneal/paraortic LN metastasis are seen in practice, and that modern radiation techniques allow for improved dose-conformality without substantial detriment to organs at risk when extending target volumes posteriorly to encompass the aorta, our standard practice is to include the entire aorta approximating the anterior aspect of the vertebral bodies (as shown in Fig. 2). Additionally, we do encompass the porta hepatis/hepato-duodenal ligament extending to the bifurcation of the main PV in patients with involved porta hepatis lymphadenopathy or to encompass the next echelon of LN spread in those with common hepatic lymphadenopathy as this next echelon is at heightened risk of occult involvement in such patients.

Disclosures

Krishan R. Jethwa reports honoraria from RadOncQuestions.com, LLC. The other author declares that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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