Chapter 5

Postoperative Radiotherapy : Delineation of Target Volumes and Organs at Risk

H Ben Salah[1]; J Daoud[1]*

[1]*Radiotherapy department, university Habib-Bourguiba hospital of Sfax Tunisia, Tunisia.*

***Correspondence to: H Ben Salah,** Radiotherapy department, university Habib-Bourguiba hospital of Sfax Tunisia, Tunisia.*

Email: bensalahh73@gmail.com

Abstract

It is imperative to review surgical and pathology reports and discuss with the surgeon, Prior to radiotherapy planning,to identify the areas considered to be at the highest risk for recurrence. The type of operation needs to be noted. Radiotherapy planning CT scans should be done with a patient in the supine position with arms over head, from top of diaphragm (for stomach) or carina (for tumor of oesogastric junction or cardia) to the bottom of L4. Preoperative CT scans should be used to aid identification of preoperative tumor volume and nodal groups to be treated. Clinical target volume for adjuvant radiation therapy for gastric cancer depends on the location of the primary disease as well as the status of lymph node metastasis.

1. Introduction

Postoperative radiotherapy was integrated into the routine care of gastric cancer patients since the results of INT0116 study was published [1] This trial showed a survival and locoregional control benefit of adjuvant radiochemotherapy. Recommendations for postoperative radiation fields design have been published [2,3]. However they were largely based on two-dimensional radiotherapy planning using bony anatomic landmarks. Their implementation in three-dimensional (3D) conformal RT practice is challenging, which results in a large inter- and intraobserver variability in target volume delineation [4,5]. There are no consensus guidelines for target volume definition for postoperative radiotherapy in gastric cancer. This makes 3D computed tomography (CT)-based contouring of a clinical target volume (CTV) very difficult. Even with an anatomical delineation atlas, substantial variations in the CTV delineation still occur between physiciens (**Figure 1**) [4,5].

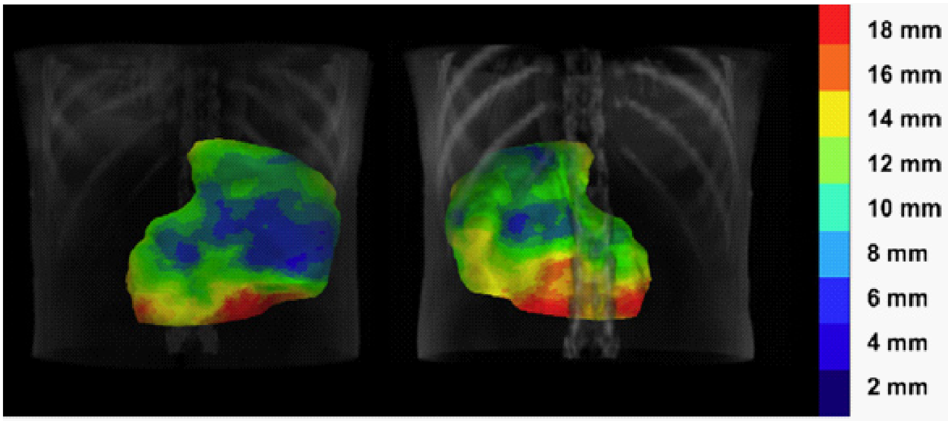


Figure 1: Anteroposterior and posterior views of a gastric cancer planning target volume. Red demonstrates large inter-observer variability and blue small variability [4].

2. Definition of Target Volumes

2.1. Cinical Target Volume (CTV)

The definition of target volumes is based on the characteristics of the tumor extension and the patterns of locoregional recurrence. Tumor extension includes invasion by contiguity, lymphatic extension and metastatic extension. Lymph node extension is very frequent conditioning the prognosis. Predicting lymph node involvement is difficult because of the submucosal or sub-serous lymphatics and abundant lymphatic chanels following the artery from the stomach. All lymph nodes schould be considered as a potential affected site [2,3,6]. In most studies of adjuvant radiotherapy, the target volume range is extremely diverse. Postoperative radiotherapy volume based on patterns of failure after radical surgery has been defined as the primary tumor bed, anastomosis site, duodenal stump, and regional lymph nodes [2,3]. If necessary, the remnant stomach in patients who underwent a subtotal gastrectomy has been often included [2,3].

Tumors confined to one of the proximal, middle or distal thirds of the stomach were analyzed with subdivision according to the position of the tumor on the circumference by Maruyama [7]. The incidence of metastases to any perigastric node station was highest when the tumor was located close to it, even though there was little variation in the metastatic pattern along the lesser curvature between tumors in the different thirds [7]. Station numbers 2 (left cardial) and 5 (suprapyloric, right gastric artery) were low-incidence stations for all locations of tumors (**Table 1**). The position of the tumor on the stomach circumference had a similar impact, as shown for distal cancers (**Table 1**). Similarly tumors along the lesser curvature or on the anterior or posterior walls had splenic hilar node metastases in up to 6% [7].

Table 1: Incidence of node metastases from cancer s in various part of the stomach [7].

Lymph Node station Number	A N=339	M N=318	C N=150	A tumors on the			
				Lesser Curvature	Anterior Wall	Greater Curvature	Posterior Wal
1	7	16	31	11	0	3	7
2	0	1	13	(0-1)	(0-1)	(0-1)	(0-1)
3	38	40	39	42	27	32	33
4	35	31	11	25	44	49	26
5	12	3	2	15	3	7	0
6	49	15	3	39	32	62	30
7	23	22	19	25	21	23	11
8	25	11	7	34	9	25	15
9	13	8	13	16	3	12	7
10	0	2	10	(0-1)	(0-1)	(0-1)	(0-1)
11	4	4	12	7	0	1	0
12	8	2	1	12	3	6	0
13,14,15,16	(0-5)	(0-5)	(0-5)	(0-5)	(0-5)	(0-5)	(0-5)

A,M,C: distal,middle and proximal thirds of the stomach, respectively.

The inclusion of node stations in the CTV is based on these findings.

The 2002 Gastric Surgical Adjuvant Radiotherapy Consensus Report discussed gastric anatomy and pathways of tumor spread, described patterns of failure, and detailed treatment planning guidelines for adjuvant 2 D radiotherapy. This report mandated coverage of the gastric tumor bed, the anastomosis or stumps, and the regional lymphatics. Detailed recommendations was made in this report [2]. Administration of barium at the time of simulation was recommanded to identify the anastomosis and gastric stump. Review of preoperative computed tomography (CT) scans was mandatory to identify the preoperative location of the tumor and regional lymphatics, and placement of radiopaque clips at the time of surgical resection (**figure 2,3 and 4**) [2].

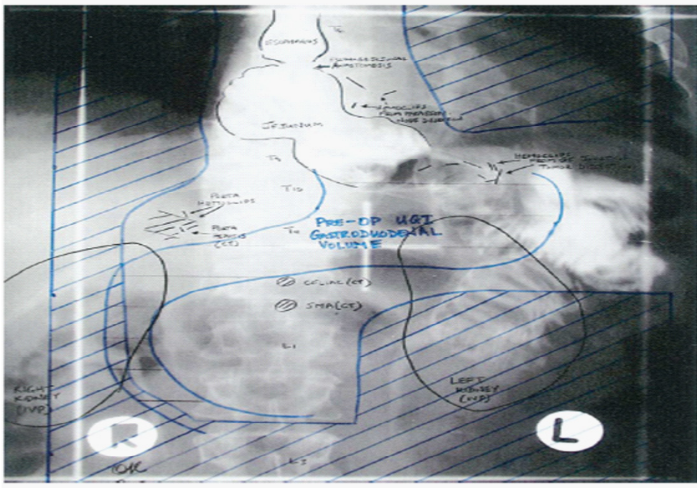


Figure 2: Simulation film for T4 (diaphragm invasion) cardial tumor with 4of 15 nodes involved with tumor. Preoperative CT identifies tumor bed. The anastomotic line is easily identified on barium swallow and by staple line. Regional lymph node location is reconstructed from CT scan.

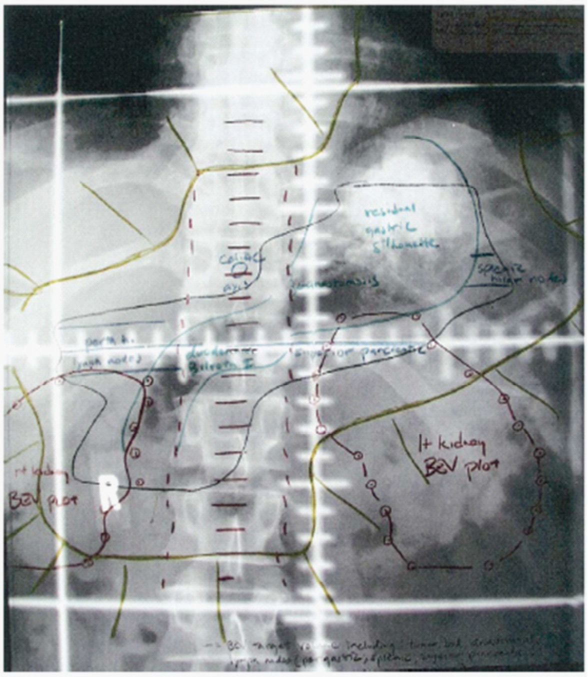


Figure 3: Simulation film for a T3 antral primary two of six regional nodes. The Billroth I anastomosis staple line is identified that connect the gastric remnant with the duodenum. Beam's-eyes-view reconstruction identifies the original tumor bed, the anastomosis and regional nodes (perigastric, retropancreatic, porta hepatis, celiac and pancreaticoduodenal nodes that are in an aberrant location because of the Billroth I procedure) at risk.Though splenic nodes are at relatively low risk, their proximity to residual perigastric nodes makes inclusion of these nodes not an issue of increased radiotherapy toxicity [2].

Tepper and Gunderson published a report entitled Radiation Treatment Parameters in the Adjuvant Postoperative Therapy of Gastric Cancer. This report provided detailed guidelines on appropriate radiation treatment volumes stratified by primary tumor site within the stomach (oesogastric jonction, proximal, middle and distal staomach) and by tumor (T) and node (N) stage[3].

Delineation of target volumes for tridimensional conformal radiotherapy requires intravenous contrast-enhanced planning CT with a 3-5mm slice thickness. This CT simulation is performed in the supine position with arms overhead, from top of diaphragm (for stomach) or carina (for tumor of oesogastric junction or cardia) to the bottom of L4. Patients should be fasted for 2–3 hours. Intravenous contrast is preferred to demonstrate blood vessels and guide clinical target volume (CTV) delineation, particularly for lymph nodes.The already defined lead marks are taped to the skin.

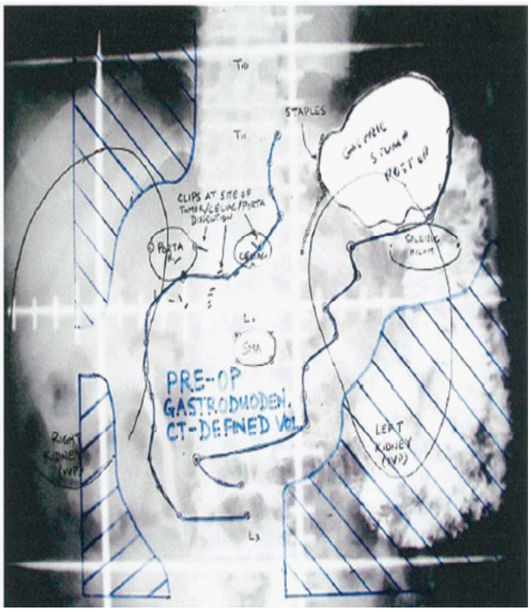


Figure 4: Simulation film for T3 antral tumor with two of five peritumoral lymph nodes metastatically involved. Simulation film shows areas at risk of locoregional relapse. Preoperative tumor bed is identified by preoperative CT scan: staple lines help locate duodenal stump and area of gastric transection. Regional lymphatics are identified from CT scan. Splenic nodes are included with tolerable kidney volumes [2].

The CTV is defined in the best conditions from the preoperative dosimetric scan and an image adjustment performed with the postoperative CT scan (**figure 5,6**) [8].

In the absence of a preoperative dosimetric scanner, a fusion of the diagnostic scanner and the scanner in the treatment position is performed [8].

Whatever the seat of gastric cancer - apart from cardiac tumors - all the stomach is included in CTV as well as anastomoses and lymph nodes.

These structures are contoured on each CT slice for delineation of the clinical target volume (CTV) [8].

Two CTV are described. A first CTV which includes the oes-jejunal or gastro-jejunal anastomosis, the gastric stump, the gastric bed reconstructed from a preoperative scan and lymph node areas. Ideally, clips are set up by the surgeon to delimit the operating bed, the initial site of the tumor and sites at risk of relapse (R2 residue, fixed lymph node groups). The second CTV includes sites at risk of relapse [8,9].

For most gastric cancers, L3 represents the lower limit of CTV. This lower limit allows the inclusion of nodes 5, 6, 7, 8, 9 and 12 [8,9].

Mineur and al detailed nodal sites included in the volume CTV 1 as follows in the **table 2**

Table 2 : nodal sites included in the volume CTV 1 according to Mineur [8].

Tumor site	Nodal sites included in CTV1
Cardia	1,2,3,7,8,9
Fundus	1,2,3,4,5,6,7,8,9,10,11
The lesser curvature or the greater curvature	1,2,3,4,5,6,7,8,9,10,11
The gastric antrum	1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16

Hennequin detailed nodal sites included in the volume CTV 1 as follows in the table 3

Table 3: nodal sites included in the volume CTV 1 according to Hennequin [9].

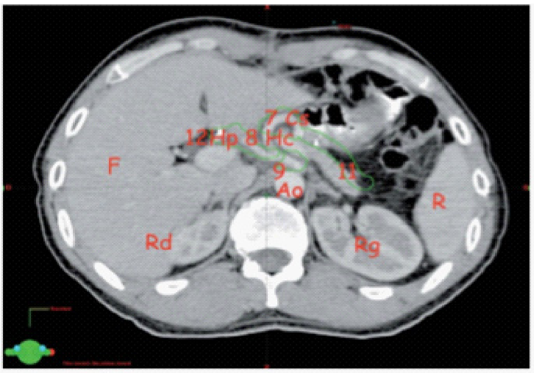
Tumor site	Nodal sites included in CTV1
Gastric body or fundus	1,2,3,4,5,6,7,8,9,10,11,12
Oesogastric junction	1,2,3,4,7,8,9,10,11
The gastric antrum	1,2,3,4,5,6,7,8,9

2.2. Planning target volume (PTV)

The margin defining PTV is 2 cm [8,9,10]. This margin corresponds to the positioning errors and to the movements of organs. The median displacements of the critical organs are 6 mm in a cranio-caudal axis and 2 mm in the other directions. Wysocka et al. Recommended a caudal-caudal margin of 1 cm and a margin of 5 mm in the other axes with an individual approach for patients with high respiratory amplitude [11]. Caudry et al. Have proposed to reduce this margin to 10 mm under the condition of rigorous control of patient placement (restraint, laser, supine position, portal imaging) [12].

3. Delineation of Target Volumes

As radiation treatment fields become increasingly conformal in an attempt to limit dose to normal critical structures, it becomes increasingly important to accurately identify treatment volumes on CT-based planning images. Based on studies evaluating the patterns of relapse after surgical resection, general guidelines have been proposed to aid in definition of the clinical target volume for adjuvant radiation treatment fields based on location, T stage of the primary tumor, and N-stage. For node positive disease, wide coverage of the tumor bed, residual stomach, resection margins, and nodal drainage regions have been generally recommended. Mineur has published illustrative figures of the delineation of CTV (**figure 5,6**)[8].



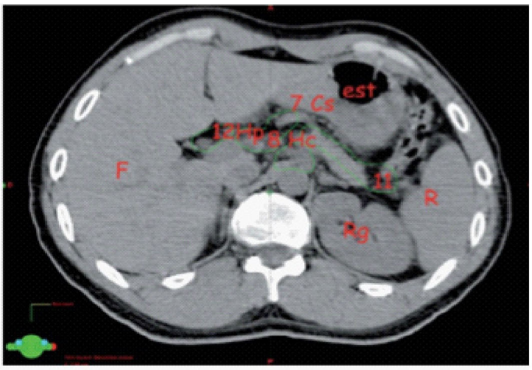


Figure 5: CT delimitation of the subdiaphragmatic lymph node territories involved in stomach cancers on preoperative and postoperative CT. 7: left gastric artery (Cs), 8: common hepatic artery (Hc); 9: celiac trunk; 11: splenic artery lymph nodes; 12: hepatic artery (Hp). AO: descending aorta; Rd: right kidney; Rg: left kidney; F: liver [8].

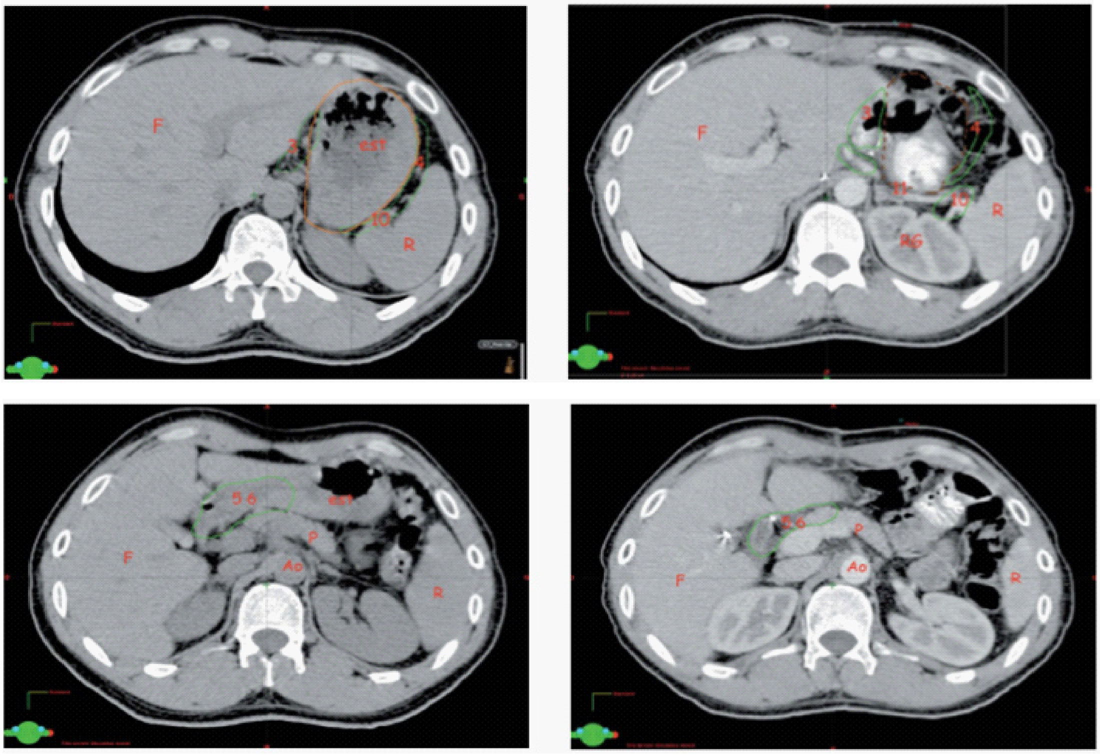


Figure 6: repositionning of the stomach on the postoperative CT after adjustment (brown dotted line) and identification of lymph node territories, view with representation of areas 3,4 (small and large curvature, 7 (left gastric artery) 10,11 (splenic artery and hilum) [8]

By inclusion of the preoperative tumor bed and resection margin, more often than not the preoperative perigastric lymph node drainage basin is naturally included within the target volume [13]. A gastric lymph node (LN) contouring atlas is meant to supplement the previously established guidelines for definition of CTV in the adjuvant treatment of gastric cancer [13]. This report serves as a template for the delineation of gastric lymph node stations to aid in the definition of elective clinical target volumes to be used in conformal treatment planning [13].

Although generally the radiographic definitions of gastric LN stations described for intact gastris anatomy can be applied in the postoperative setting (**figure 7**), due to the potential for differences in postsurgical anatomy it is important to discuss radiographic identification of gastric LN stations in the setting of the most common oncologic surgeries employed for resection of gastric cancers (**figure 8,9,10**)

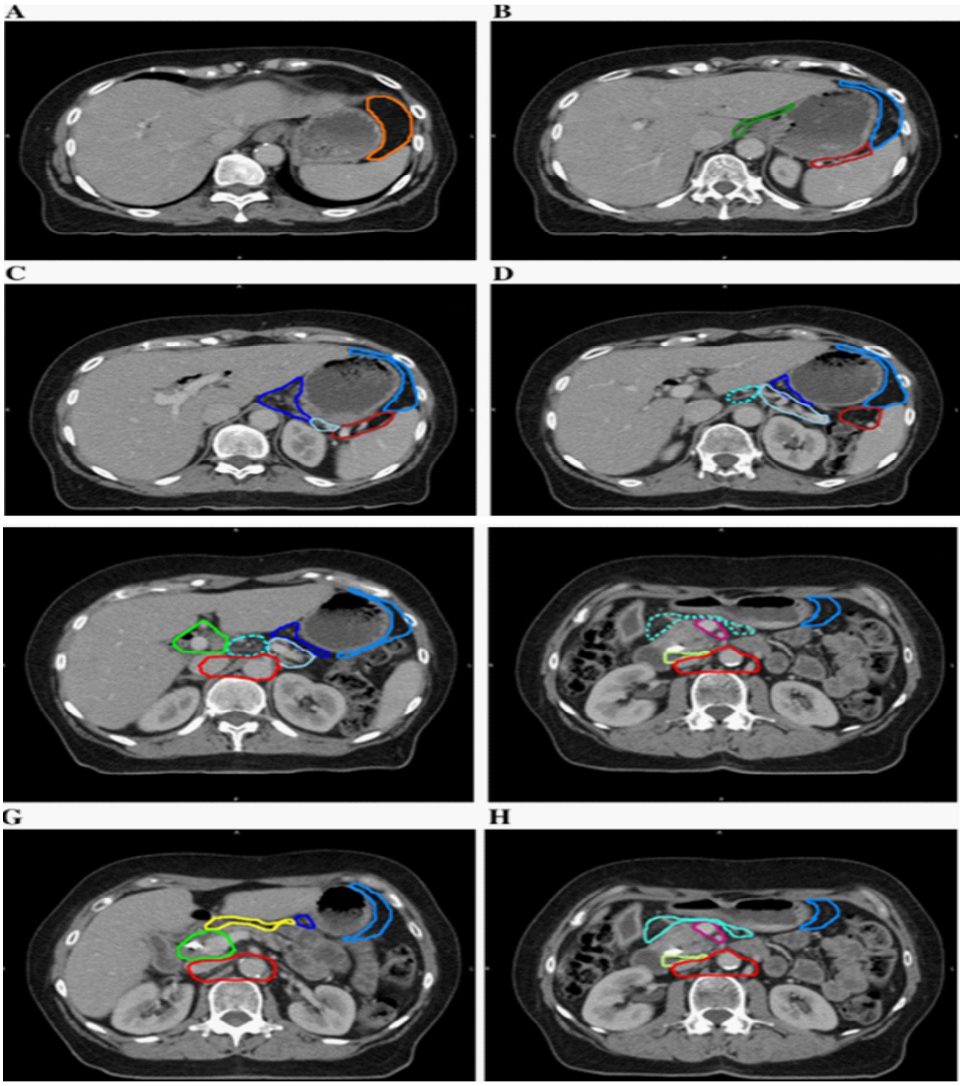


Figure 7: intact gastric anatomy. (A) left paracardial (orange); (B) greater curvature (blue), splenic hilum (brown), right paracardial (forest green); (C) greater curvature (blue), lesser curvature (dark blue), splenic hilum (brown); (D) greater curvature (blue), lesser curvature (dark blue), splenic (sky blue), splenic hilum (brown), left gastric (aquamarine, dashed); (E) greater curvature (blue), lesser curvature (dark blue), splenic (sky blue), left gastric (aquamarine, dashed), paraortic (red), hepatoduodenal (bright green); (F) greater curvature (blue), lesser curvature (dark blue), splenic (sky blue), paraortic (red), hepatoduodenal (bright green), common hepatic (dark purple), celiac (pink); (G) greater curvature (blue),), lesser curvature (dark blue), paraortic (red), hepatoduodenal (bright green), suprapyloric (yellow); (H) greater curvature (blue),), paraortic (red), pancreatic (lime green), superior mesenteric (violet), infrapyloric (green dashed).

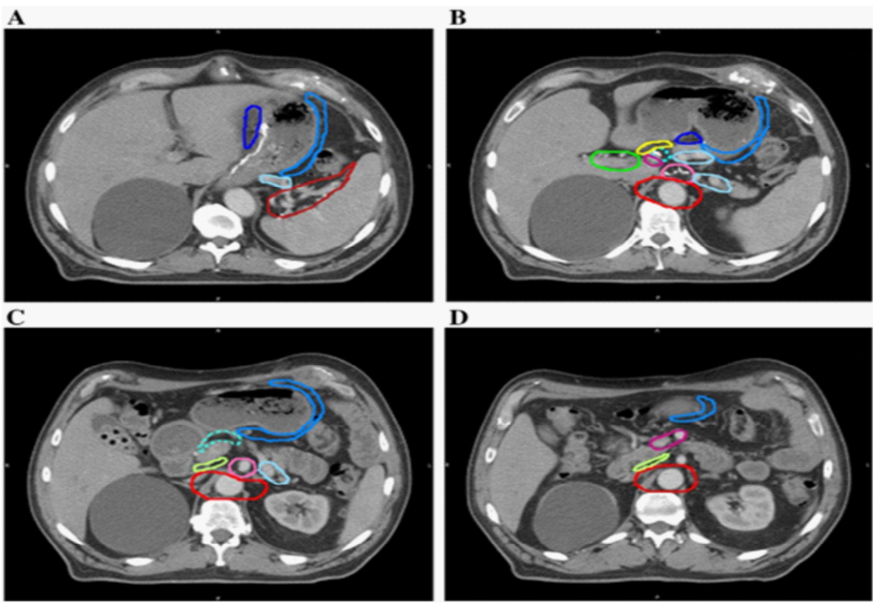


Figure 8: Ivor-Lewis eosophagogastrectomy. (A) Greater curvature (blue), lesser curvature (dark blue), splenic hilum (brown), splenic (sky blue); (B) greater curvature (blue), lesser curvature (dark blue), splenic (sky blue), hepatoduodenal (bright green), suprapyloric (yellow), celiac (salmon pink), common hepatic (dark purple), left gastric (aquamarine, dashed), paraortic (red); (C) greater curvature (blue), pancreatic (lime green), celiac (salmon pink), splenic (sky blue), paraortic (red), infrapyloric (green dashed); (D) greater curvature (blue), superior mesenteric (violet), pancreatic (lime green), paraortic (red); (E),), pancreatic (lime green), paraortic (red).

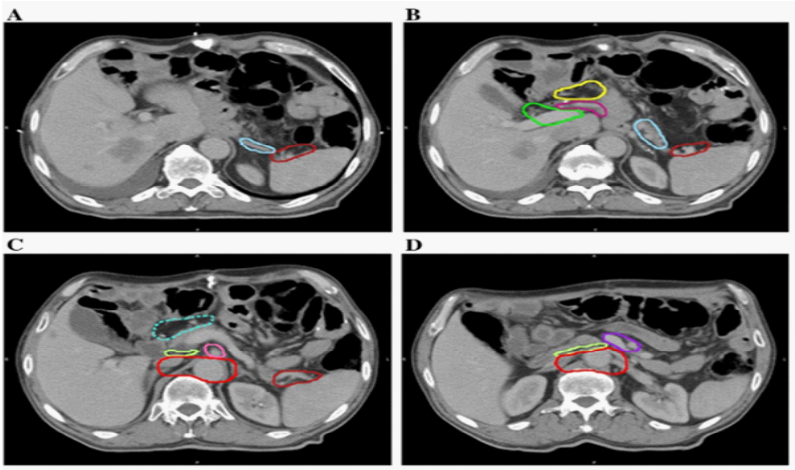


Figure 9: Total gastrectomy with roux-en-Y esophagojejunostomy. (A) splenic hilum (brown), splenic (sky blue); (B) splenic hilum (brown), splenic (sky blue), hepatoduodenal (spring green), common hepatic (dark purple), suprapyloric (yellow); (C) splenic hilum (brown), paraortic (red), celiac (salmon pink), pancreatic (lime green), infrapyloric (green dashed); (D) paraortic (red), pancreatic (lime green), superior mesenteric (violet).

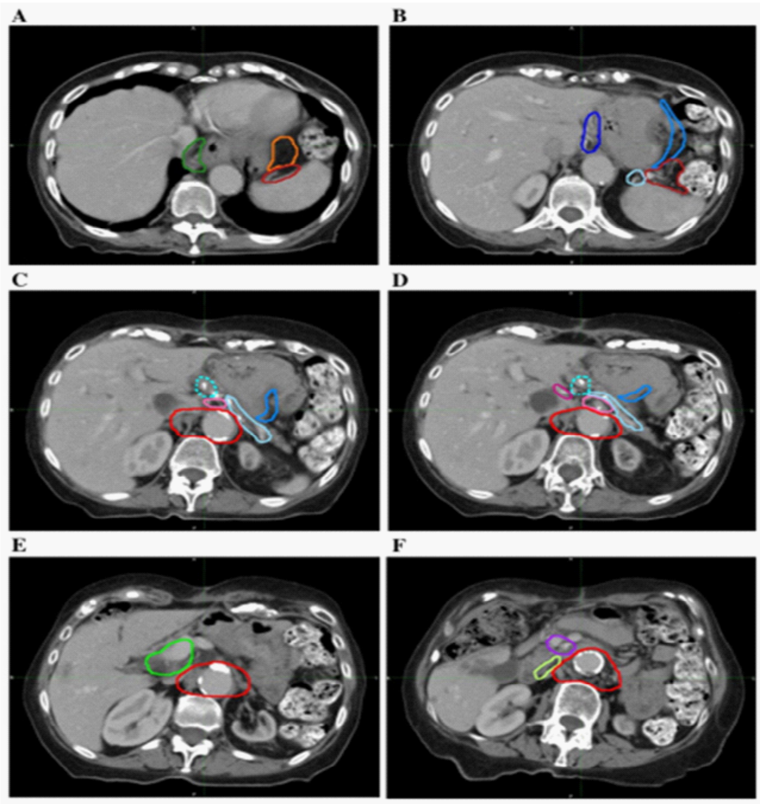


Figure 10: Subtotal gastrectomy. (A) R paracardial (forest green), L paracardial (orange), splenic hilum (brown); (B) lesser curvature (dark blue), greater curvature (blue), splenic (sky blue), splenic hilum (brown), (C) greater curvature (blue), splenic (sky blue), paraortic (red), left gastric (aquamarine, dashed), celiac (salmon pink); (D) greater curvature (blue), splenic (sky blue), paraortic (red), left gastric (aquamarine, dashed), celiac (salmon pink), common hepatic (dark purple); (E) hepatoduodenal (spring green), paraortic (red); (F) pancreatic (lime green), paraortic (red), superior mesenteric (violet).

4. Organes at Risk

Organs at risk are kidneys, liver, heart, lung, and spinal cord. Their delineations is easy.

5. References

1. Macdonald JS, Smalley SR, Benedetti J, Hundahl SA, Estes NC, Stemmermann GN, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med. 2001; 345: 725–730.

2. Smalley SR, Gunderson L, Tepper J, Martenson JA Jr, Minsky B, Willett C, et al. Gastric surgical adjuvant radiotherapy consensus report: rationale and treatment implementation. Int J Radiat Oncol Biol Phys. 2002; 52: 283–293.

3. Tepper JE, Gunderson LL. Radiation treatment parameters in the adjuvant postoperative therapy of gastric cancer. Semin Radiat Oncol. 2002; 12: 187–195.

4. Jansen EPM, Nijkamp J, Gubanski M, Lind PA, Verheij M. Interobserver variation of clinical target volume delineation in gastric cancer. Int J Radiat Oncol Biol Phys. 2010; 77: 1166–1170.

5. Moretones C, Leo ´n D, Navarro A, Santacruz O, Boladeras AM, Macia ` M, et al. Interobserver variability in target volume delineation in postoperative radiochemotherapy for gastric cancer. A pilot prospective study. Clin Transl Oncol. 2012; 14: 132–137.

6. Japanese Gastric Cancer Association. Japanese Classification of Gastric Carcinoma-2nd English edition. Gastric Cancer. 1998; 1: 10–24.

7. Maruyama K, Gunven P, Okabayashi K. Lymph node metastases of gastric cancer : general pattern in 1931 patients. Ann Surg. 1989; 210: 596-602.

8. Mineur L, Jaegle E, Pointreau Y, Denis F. Cancer de l’estomac. Cancer/Radiother. 2010; 14: 84-93.

9. Hennequin C , Quero L , Mineur L. Cancer de l’estomac : doses et volumes-cibles. Cancer / Radiother 2008; 12: 659-662.

10. Matzinger O, Gerber E, Bernstein Z, Maingon P, Haustermans K, Bosset JF, et al. EORTC-RTOG expert opinion: radiotherapy volume and treatment guidelines for neoadjuvant radiation of adenocarcinomas of the gastroesophageal junction and the stomach. Radiother Oncol. 2009; 92: 164-175.

11- Wysocka B, Kassam Z, Lockwood G, Brierley J, Dawson LA, Buckley CA, et al. Interfraction and respiratory organ motion during conformal radiotherapy in gastric cancer. Int J Radiat Oncol Biol Phys. 2010; 77: 53-59.

12- Caudry M, Ratoanina JL, Escarmant P, Maire JP. Target volume in radiotherapy of gastric adenocarcinoma. Cancer Radiother. 2001; 5: 523-533.

13-Wo JY, Yoon SS, Guimaraes AR, Wolfgang J, Mamon HJ, Hong TS. Gastric lymph node contouring atlas: A tool to aid in clinical target volume definition in 3-dimensional treatment planning for gastric cancer. Pract Radiat Oncol. 2013; 3: 11-19.