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Guidelines

EORTC-ROG expert opinion: Radiotherapy volume and treatment guidelines for neoadjuvant radiation of adenocarcinomas of the gastroesophageal junction and the stomach

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ABSTRACT

Purpose: The Gastro-Intestinal Working Party of the EORTC Radiation Oncology Group (GIWP-ROG) developed guidelines for target volume definition in neoadjuvant radiation of adenocarcinomas of the gastroesophageal junction (GEJ) and the stomach.

Methods and materials: Guidelines about the definition of the clinical target volume (CTV) are based on a systematic literature review of the location and frequency of local recurrences and lymph node involvement in adenocarcinomas of the GEJ and the stomach. Therefore, MEDLINE was searched up to August 2008.

Guidelines concerning prescription, planning and treatment delivery are based on a consensus between the members of the GIWP-ROG.

Results: In order to support a curative resection of GEJ and gastric cancer, an individualized preoperative treatment volume based on tumour location has to include the primary tumour and the draining regional lymph nodes area. Therefore we recommend to use the 2nd English Edition of the Japanese Classification of Gastric Carcinoma of the Japanese Gastric Cancer Association which developed the concept of assigning tumours of the GEJ and the stomach to anatomically defined sub-sites corresponding respectively to a distinct lymphatic spread pattern.

Conclusion: The GIWP-ROG defined guidelines for preoperative irradiation of adenocarcinomas of the GEJ and the stomach to reduce variability in the framework of future clinical trials.

Gastric and oesophageal cancers are highly lethal malignancies. Even if the incidence of distal Gastric Cancer (GC) has been decreasing over the past decades, the incidence of newly diagnosed proximal cancers (localized at cardia and gastroesophageal junction (GEJ)), has dramatically increased [1].

The mainstay of curative treatment of GC is a radical surgical resection [2]. More than half of all patients with advanced stage disease undergoing radical tumour resection relapse and die within five years [3] despite considerable progress in this surgical procedure in Japanese and Western countries [4]. Several clinical follow-up and autopsy series have shown high rates of loco-regional recurrences and systemic metastases [5,6]. This highlights the need of further efforts to standardize and optimize new multimodal strategies combining different neoadjuvant and/or adjuvant protocols [2,7].

There are two main pathological presentations of oesophageal cancer: squamous cell cancer (SCC) and adenocarcinoma (AC). ACs of the oesophagus were treated until recently similarly to squamous cell carcinomas of the oesophagus whereas ACs of the cardia were often mixed with GC [8]. An increasing amount of evidence supports the view that ACs of the junction have clearly to be considered separately to other tumours of the stomach and of the oesophagus as these tumours differ in terms of pathogenesis, epidemiology, prognosis as well as in the surgical approach [9–16].

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An important goal of *preoperative chemoradiation* is to reduce the primary tumour volume to facilitate surgery and increase R0 resections (resulting in a decreased local recurrence rate). Other theoretical benefits include a potentially earlier effect on micro metastatic disease and a change in the ability of tumour cells that may be spread at the time of surgical resection to implant at other locations. Moreover, patients may be diagnosed with rapidly growing metastatic carcinoma before surgery, thus avoiding unnecessary procedures and toxicity [17]. In addition, preoperative therapy may be better tolerated than postoperative therapy [18], and a pathologic evaluation of the response to preoperative treatment may offer important prognostic information [19].

The Gastrointestinal Working Party of the Radiation Oncology Group (GIWP-ROG) of the European Organization for Research and Treatment of Cancer (EORTC) has committed itself to develop guidelines for target volume definition in neoadjuvant radiation of AC of the GEJ and the stomach. The current assessment of target and organ at risk volume definitions, of imaging modalities and of the planning and verification procedures can be regarded as a guide to a clinical quality assurance concept.

Methods and materials

We performed a systematic review (MEDLINE (http://www.pubmed.com) search up to August 2008) of all reported data concerning prescription, planning, treatment delivery as well as the location and frequency of local recurrences and lymph node involvement in AC of the GEJ and the stomach. The members of the GIWP-ROG of the EORTC reached a consensus based on this extensive literature review resulting in the following guidelines.

Results

Guidelines for neoadjuvant radiotherapy of adenocarcinomas of the gastroesophageal junction and the stomach

Dose prescription and fractionation

- The regime consists of a total dose of 45 Gy in 25 daily fractions of 1.8 Gy on five days a week.
- Dose prescription and recording has to comply with the recommendations of the ICRU 50/62.

Treatment delay

- A maximum overall treatment time of 37 days shall be aimed for.

Treatment imaging, patient positioning and immobilization

- Planning CT is mandatory and has to be performed before the initiation of any induction chemotherapy. The intravenous administration of contrast medium is recommended. The oral administration of positive or negative contrast media for the planning CT is not recommended, but supported for an additional diagnostic CT.
- The slice-thickness must not be larger than 3 mm.
- In case of induction chemotherapy and more than 10% weight loss, a second planning CT is necessary.
- Patients should be treated supine. Legs with knee support, arms lifted above the head.
- Patient immobilization with thermoplastic device or vacuum cushion is recommended.

Treatment delivery technique

- A linear accelerator with 3D-CRT or IMRT capability with energy of 4–18 MV should be used.
- The volume should be treated by only one treatment plan (without superposition of different plans). Treatment with opposed pair fields alone is not acceptable.

Target volume definition

- Only one volume should be considered throughout radiotherapy and no cone-down or boost volume should be foreseen.
- The tumour site and extent should be defined by endoscopy, endoscopic ultra sound (EUS) and computed tomography (CT) prior to induction chemotherapy and assigned to one of the following six locations:
  - tumours of the gastroesophageal junction type; I; II; III (Fig. 1) or;
  - tumours of the proximal third of the stomach (with their tumour centre outside the gastroesophageal junction); tumours of the middle or distal third (Fig. 2).
- Gross tumour volumes (GTV) have to be delineated for the primary tumour (GTV_{tumour}) as well as for the involved lymph nodes (GTV_{nodal}). GTV_{tumour} has to include the primary tumour and the perigastric tumour extension.
- The global clinical target volume (CTV_{global}) will be obtained by the addition of the following structures (including the lymphatic spread ways in between these volumes):
  - CTV_{tumour}; which will be obtained by adding a margin of 1.5 cm to GTV_{tumour}

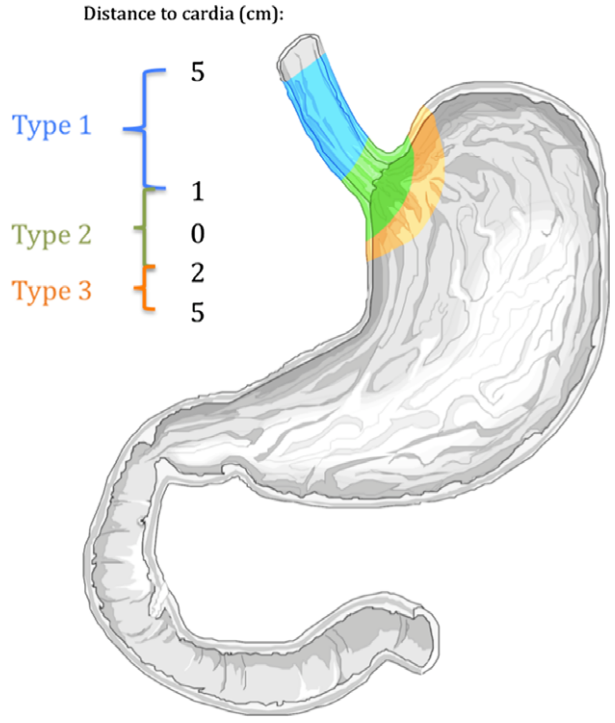


Fig. 1. Adenocarcinoma of the gastroesophageal junction. Based on the anatomic location of the tumour centre three subtypes can be defined [10]: Type I tumours have their tumour centres more than 1 cm above the anatomical gastroesophageal junction; Type II tumours are the true carcinomas of the cardia and have their tumour centres located within 1 cm oral and 2 cm aboral of the anatomical gastroesophageal junction; Type III tumours have their tumour centre more than 2 cm but not more than 5 cm below the anatomical gastroesophageal junction.

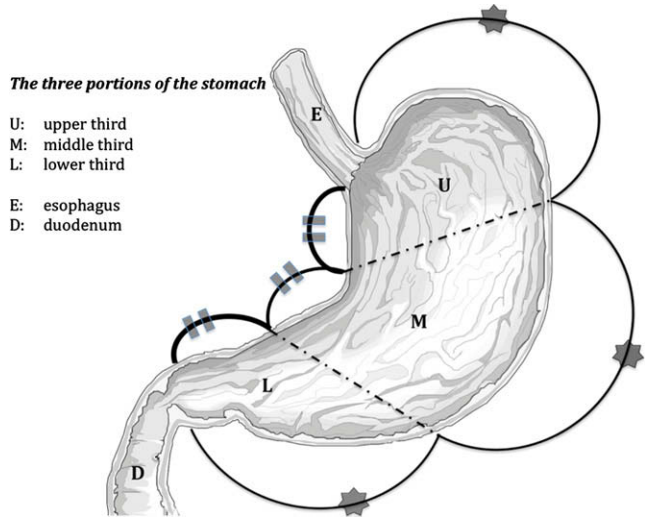


Fig. 2. Three portions are defined by subdividing both lesser and greater curvatures into three equal lengths. Tumours of the upper (or proximal), middle, lower (or distal) third have their main tumour masses in the respective parts of the stomach.

- CTV_{nodal}; which will be obtained by adding a margin of 0.5 cm to GTV_{nodal}
- *For GC only;* a $CTV_{gastric}$ which will be defined as
  i. GC of the proximal third of the stomach: $CTV_{gastric}$ = contour of the stomach with exclusion of pylorus and antrum (a minimal margin of 5 cm from the GTV has however to be respected).
  ii. GC of the middle third of the stomach: $CTV_{gastric}$ = contour of the stomach (from cardia to pylorus).
  iii. GC of the distal third of the stomach: $CTV_{gastric}$ = contour of the stomach with exclusion of cardia and fundus (a minimal margin of 5 cm from the GTV has however to be respected). In case of infiltration of the pylorus or the duodenum, CTV has to be expanded along the duodenum with a margin of 3 cm from the tumour.
- The elective lymph node stations ($CTV_{elective}$) corresponding to the specific tumour location as defined in Table 1 and illustrated in Figures 3–10. The $CTV_{elective}$ volume should be defined by a 5 mm margin around the corresponding vessels.

- An Internal Target Volume (ITV) should be included in the treatment planning process as recommended by ICRU 62 report [20] in order to take into account the target motion.
- A Planning Target Volume (PTV) should be defined according to the ICRU 50 and 62 report:

For GEJ tumours

- Individualized identification of the target volume motion has to be performed if possible.
- If no facilities allowing the evaluation of the target volume motion are present, the minimal recommended 3-D margins to be added from the CTV to get the ITV are: 1 cm radial margin; 1.5 cm distal margin and 1 cm proximal margin [21–24].
- PTV will then be defined as the ITV-volume plus a 3-D margin of 5 mm (except if the centre has defined its own measures of positioning inaccuracy).

For gastric tumours

- Individualized identification of the target volume motion has to be performed if possible.
- If no facilities allowing the evaluation of the target volume motion are present, the minimal recommended 3-D margins to be added from the CTV to get the ITV are: 1.5 cm to all directions [21].
- PTV will then be defined as the ITV-volume plus a 3-D margin of 5 mm (except if the centre has defined its own measures of positioning inaccuracy).

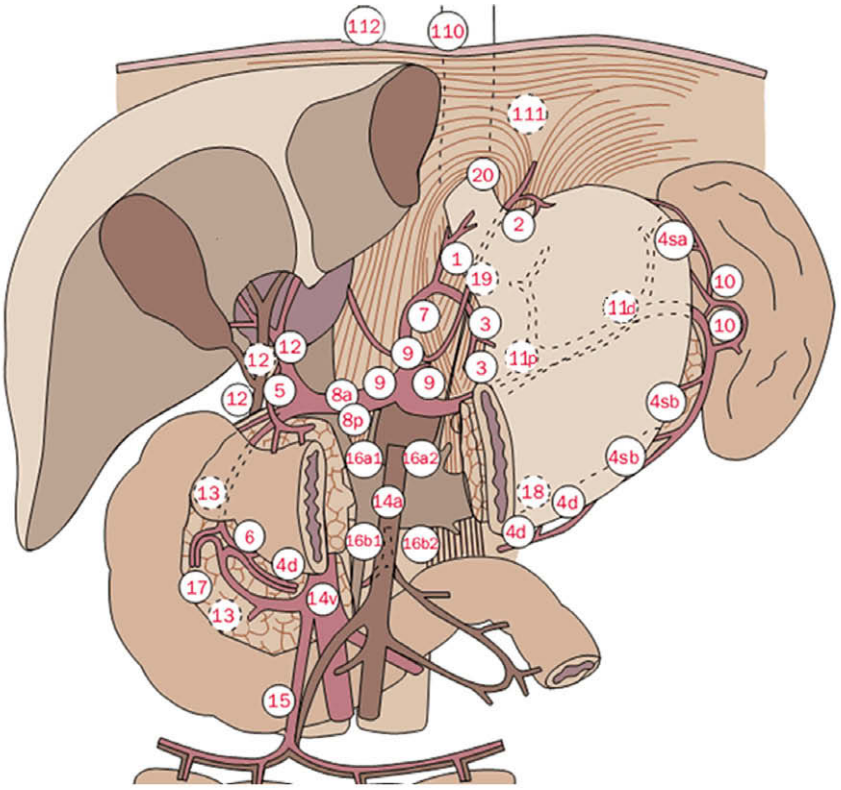
- All margins should be added in 3D.

Organ at risk (OAR) volume definition and dose limitation

- The complete volumes of the lungs, the liver, the kidneys and the heart have to be delineated. Spinal cord must be outlined along the whole volume interested by the beams plus 2 cm above or below this volume.
- Whenever possible, without missing the PTV, attempts should be made to limit the dose to all organs-at-risk.
- The maximal spinal cord dose must not exceed a total dose of 45 Gy. In case of combined modality treatment with oxaliplatin this dose should not exceed 40 Gy [25–29].
- The combined lung volume receiving more than 20 Gy has to be less than 20% (V20 < 20%). Furthermore the combined lung volume receiving less than 5 Gy should be higher than 2300 cc. (<10% chance of postoperative pulmonary complication [30,31]).
- The whole heart must not have more than 30% exposed to a total dose of 40 Gy and not more than 50% exposed to a total dose of 25 Gy.
- At least 70% of one physiologically functioning kidney should receive a total dose of less than 20 Gy (V20 < 70%). For the contralateral kidney the volume exposed to more than 20 Gy has to be less than 30% (V20 < 30%) [32,33].
  - The glomerular filtration rate of each kidney has to be taken into account in case of suspicion of a decreased renal function. Overall, not more than 50% of the combined functional renal volume should receive more than 20 Gy.
  - Caution is requested if the treatment is combined with oxaliplatin, as there are no reports of the effect of combined treatment of oxaliplatin and radiation on renal function and only scarce reports of renal failures following oxaliplatin delivery [34,35].
- The liver must not have more than 30% of its volume exposed to more than 30 Gy (V30 < 30%) [36].

Treatment planning

- 3D treatment planning with inhomogeneity corrections should be performed.
- The use of DVH for planning is mandatory.
- The dose volume histograms (DVH) of all delineated volumes (target and OAR) have to be calculated using a calculation grid of 3 mm maximum on an appropriate calculation mode using a high point density.
- Use of shielding blocks/MLC is mandatory.
- The coverage and homogeneity of the PTV should conform to ICRU 50/62 criteria. The dose homogeneity within the volume has to be kept within −5% and +7% of the prescribed dose.
- The PTV should be encompassed by the 95% isodose-volume.
- Underdosage is only allowed if requested by the proximity of serial OAR. In this situation a maximum of 5% of the PTV volume should receive less than 95% of the prescribed dose.
- The ICRU "hot spot" (i.e. the dose outside of the PTV with a volume of at least 1.8 cc) should not exceed the prescription dose by more than 7%.



No. 1	Right paracardial LN
No. 2	Left paracardial LN
No. 3	LN along the lesser curvature
No. 4sa	LN along the short gastric vessels
No. 4sb	LN along the left gastroepiploic vessels
No. 4d	LN along the right gastroepiploic vessels
No. 5	Suprapyloric LN
No. 6	Infrapyloric LN
No. 7	LN along the left gastric artery
No. 8a	LN along the common hepatic artery (Anterosuperior group)
No. 8p	LN along the common hepatic artery (Posterior group)
No. 9	LN around the celiac artery
No. 10	LN at the splenic hilum
No. 11p	LN along the proximal splenic artery
No. 11d	LN along the distal splenic artery
No. 12a	LN in the hepatoduodenal ligament (along the hepatic artery)
No. 12b	LN in the hepatoduodenal ligament (along the bile duct)
No. 12p	LN in the hepatoduodenal ligament (behind the portal vein)
No. 13	LN on the posterior surface of the pancreatic head
No. 14v	LN along the superior mesenteric vein
No. 14a	LN along the superior mesenteric artery
No. 15	LN along the middle colic vessels
No. 16a1	LN in the aortic hiatus
No. 16a2	LN around the abdominal aorta (from the upper margin of the celiac trunk to the lower margin of the left renal vein)
No. 16b1	LN around the abdominal aorta (from the lower margin of the left renal vein to the upper margin of the inferior mesenteric artery)
No. 16b2	LN around the abdominal aorta (from the upper margin of the inferior mesenteric artery to the aortic bifurcation)
No. 17	LN on the anterior surface of the pancreatic head
No. 18	LN along the inferior margin of the pancreas
No. 19	Infradiaphragmatic LN
No. 20	LN in the esophageal hiatus of the diaphragm
No. 110	Paraesophageal LN in the lower thorax
No. 111	Supradiaphragmatic LN
No. 112	Posterior mediastinal LN

Fig. 3. The classification of the lymph node stations of the stomach and the perigastric region according to the JGCA [58].

Treatment verification

- Daily patient set-up shall be performed using laser alignment to reference marks on the skin of the patient. As a minimum requirement, an off-line set-up correction protocol must be in place that requires imaging at least once a week.
- It is highly advised to adhere to the adapted "shrinking action level" (SAL) or extended "no action level" (eNAL) off-line protocols as described in the literature [37,38].
- Daily on-line set-up verification and correction is also allowed but not mandatory.
- A non-daily on-line correction protocol is not allowed.
- The protocol can be based on bony anatomy. However, soft-tissue or marker based set-up corrections are to be preferred.
- If the total portal imaging dose is expected to exceed 2% (0.9 Gy) of the prescribed dose, this should be taken into account during planning.

Discussion

Parameters of interest for radiotherapy planning include traditionally the gross tumour volume (GTV), the clinical target volume (CTV) and the planning target volume (PTV). However, the International Commission on Radiation Units and Measurements (ICRU) Report 50 (1993) and ICRU Supplement to Report 62 (1999)

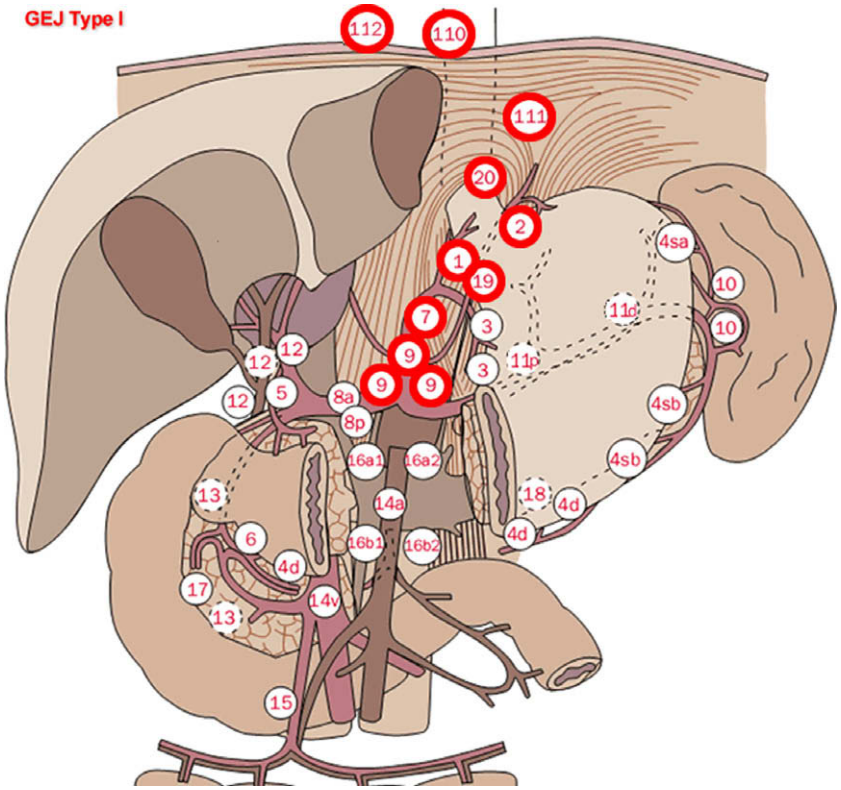


Fig. 4. Corresponding elective lymph node stations for tumours of the gastroesophageal junction. Type I: 1 right paracardial LN; 2, left paracardial LN; 7, LN along the left gastric artery; 9, LN around the celiac artery; 19, infradiaphragmatic LN; 20, LN in the oesophageal hiatus of the diaphragm; 110, paraoesophageal LN in the lower thorax; 111, supradiaphragmatic LN; 112, posterior mediastinal LN.

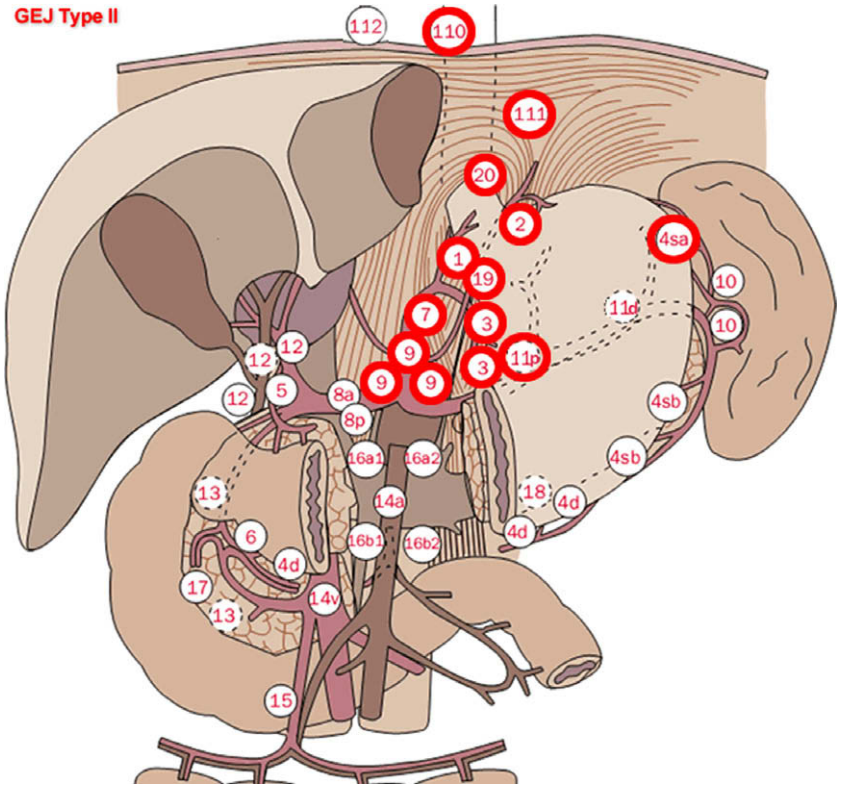


Fig. 5. Corresponding elective lymph node stations for tumours of the gastroesophageal junction Type II: 1, right paracardial LN; 2, left paracardial LN; 3, LN along the lesser curvature; 4sa, LN along the short gastric vessels; 7, LN along the left gastric artery; 9, LN around the celiac artery; 11p, LN along the proximal splenic artery; 19, infradiaphragmatic LN; 20, LN in the oesophageal hiatus of the diaphragm; 110, paraoesophageal LN in the lower thorax; 111, supradiaphragmatic LN.

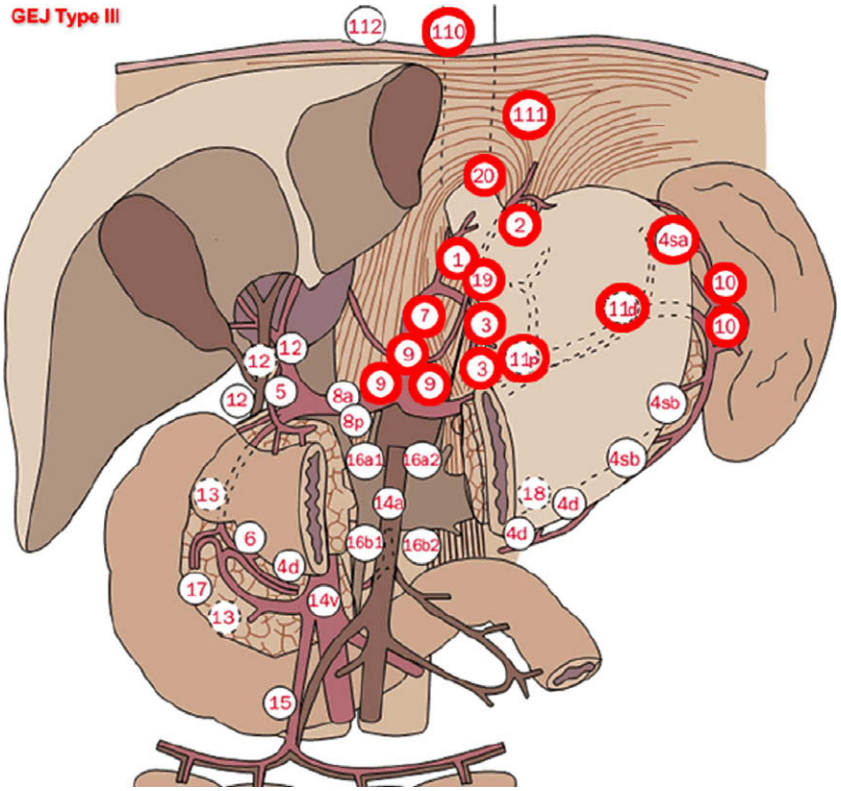


Fig. 6. Corresponding elective lymph node stations for tumours of the gastroesophageal junction. Type III: 1, right paracardial LN; 2, left paracardial LN; 3, LN along the lesser curvature 4sa LN along the short gastric vessels; 7; LN along the left gastric artery; 9, LN around the celiac artery; 10, LN at the splenic hilum; 11p, LN along the proximal splenic artery; 11d, LN along the distal splenic artery; 19, infradiaphragmatic LN; 20, LN in the oesophageal hiatus of the diaphragm; 110, paraoesophageal LN in the lower thorax; 111, supradiaphragmatic LN.

describe the current recommendation for incorporation of tumour motion into radiotherapy planning.

Therefore the planning target volume (PTV) is defined as the internal target volume (ITV) plus the set-up margin. The ITV takes into account physiologic organ motion, in particular motion caused by respiration, to ensure adequate CTV coverage throughout the respiratory cycle. Variations in the CTV position and shape are accounted for by using the internal margin (IM) [20,39].

Tumour imaging

Endoscopic ultrasound (EUS), CT and PET are all generally able to visualize the GTV. However the apparent longitudinal extent and location may vary between the different modalities. CT of chest and abdomen and EUS has been regarded as the best modality for staging GEJ and gastric tumours. More recently, the role of 18-fluorodeoxy-D-glucose positron emission tomography (FDG-PET) in staging and RT planning has been investigated.

CT has a central role in the treatment volume definition as it is used for the RT dose calculation. EUS is a valuable addition in view of its accuracy in T and N staging [40,41] but it cannot be directly used for RT planning. Therefore, CT scan of the abdomen/thorax and EUS is mandatory for an exact preoperative tumour and node metastases staging [2,42].

The role of PET in the delineation of the primary tumour remains uncertain [43]. Key problems are the lack of studies using pathology as the reference and the lack of a standardized methodology to determine the extent of the primary tumour [44]. Both CT and PET have a poor sensitivity for detection of nodal involvement and should therefore not be used to exclude nodal volumes. On the other hand, PET-positive nodes outside the usual elective nodal volume should be included in the target volume in view of the high specificity of PET for nodal disease, [45].

In conclusion and at the present time, treatment volume selection and delineation should be based on a combination of all available imaging, with CT and EUS as mandatory and PET as recommended modalities [46].

Target volume delineation

The lack of randomized, controlled studies to determine details of radiation fields, resulted in the past in neoadjuvant radiation directed to the whole stomach and large lymph node areas [47]. Pilot studies with radiation individualized for the tumour location and a limited lymph node volume were not pursued [48].

The UICC TNM 6th ed. [49] classifies GEJ tumours as gastric cancers, but in the past they were classified inconsistently as either oesophageal or gastric cancers. Most clinical trials recruited patients with a mixture of histological types and anatomical locations. ACs of the junction (defined as tumours infiltrating the GEJ and having their tumour centres within 5 cm oral and aboral of the anatomical GEJ) have however clearly to be considered separately to the other tumours of the stomach or the oesophagus as their pathogenesis, pattern of spread as well as the surgical approach differ considerably [9,10,12–16]. The understanding that both location and histological type may influence the best treatment modality has led to increasing worldwide use of the "Siewert classification" of AC of the GEJ [10] (Fig. 1).

An individualized and standardized clinical treatment volume based on tumour location has to be defined in order to support a curative resection of gastroesophageal and GC. The reliability of

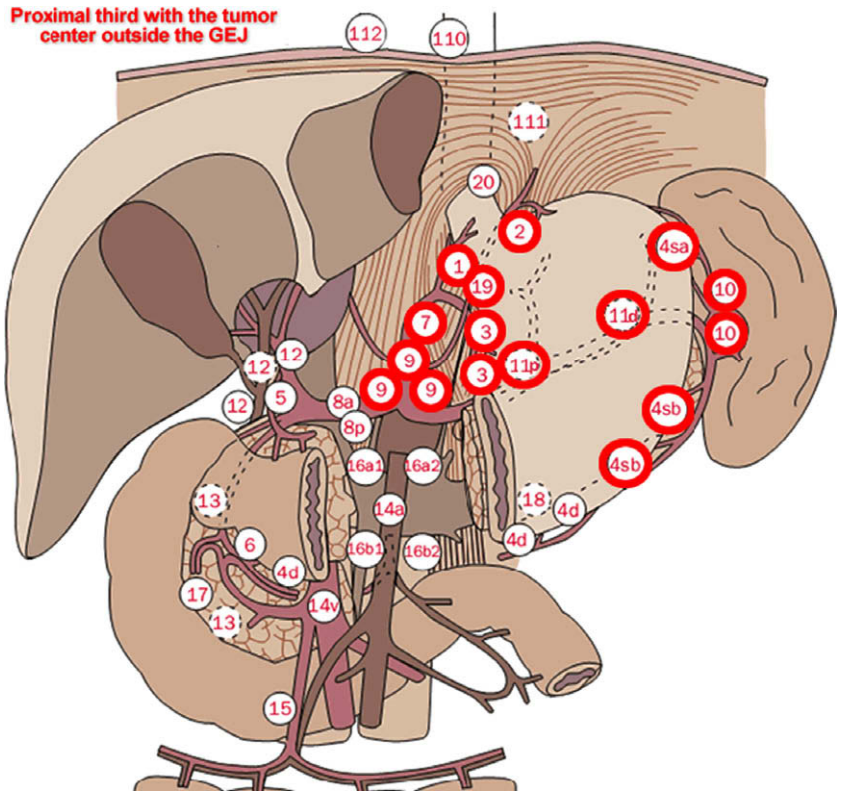


Fig. 7. Corresponding elective lymph node stations for GC tumours of the proximal third with their tumour centre outside of the gastroesophageal junction: 1, right paracardial LN; 2, left paracardial LN; 3, LN along the lesser curvature; 4sa, LN along the short gastric vessels; 4sb, LN along the left gastroepiploic vessels; 7, LN along the left gastric artery; 9, LN around the celiac artery; 10, LN at the splenic hilum; 11p, LN along the proximal splenic artery; 11d, LN along the distal splenic artery; 19, infradiaphragmatic LN.

pretherapeutic imaging to obtain information about lymphatic disease is however still limited in carcinomas of the oesophageal junction and of the stomach [41,50,51,46]. Therefore a preoperative clinical treatment volume has to be composed of the gross tumour volume and its potential extensions in the oesophageal and gastric wall, of the involved regional lymph nodes as well as of the draining lymph nodes areas [52–55].

The proposed elective lymph node areas of the GEJ I, II and III are derived from the 6th edition of the TNM Classification of the UICC [49].

- Tumours of the gastroesophageal junction (Fig. 1):
  - Type I, II, III.

The Japanese literature extensively investigated the pattern of lymph node spread [56,57]. They developed the concept of assigning tumours of the stomach to three anatomically defined tumour sites corresponding respectively to their different lymphatic spread patterns:

- Tumours of the stomach (Fig. 2):
  - Proximal, middle and distal third.

This grouping system is based on the results of studies of lymphatic flow at various tumour sites, together with the observed survival associated with metastasis at each nodal station [58]. The result of this extensive data is integrated in the 2nd English Edition of the Japanese Classification of Gastric Carcinoma of the Japanese Gastric Cancer Association (JGCA) [58].

This distribution of lymph node involvement according to the location of the primary tumour has been validated by many other pathological studies [59,52,56,60,12–15,61,62].

Gastric clinical target volume

The usual CTV in gastric cancer has always included the entire stomach from cardia to pylorus [53,54,63]. This volume definition was based on the consideration that gastric tumour position is difficult to be assessed with certainty and to be sure not to have a geographical miss. In order to avoid unnecessary toxicity, and in the framework of modern 3-D planning, the definition of this large volume should however be reconsidered in order to avoid toxicity. Surgical series show that less than 5% of the patients have tumour cells more than 3 cm from the macroscopic edge of the primary lesion [64].We propose therefore to define:

- $CTV_{stomach}$ for proximal GC: stomach without pylorus or antrum. A minimal margin of 5 cm from the GTV has however to be respected in order to have a comfortable security margin.
- $CTV_{stomach}$ for medial GC: entire stomach, including cardia and pylorus.
- $CTV_{stomach}$ for distal GC: stomach without cardia and fundus. A minimal margin of 5 cm from the GTV has however to be respected. In case of infiltration of the pylorus or the duodenum, CTV has to be expanded along the duodenum with a margin of 3 cm from the tumour.

Target volume motion

Tumours of the GEJ exhibit a significant respiration-induced motion. Only a few studies on GEJ tumour motion have been published [24,21,23,65,22]. Yaremko et al. studied 31 distal oesophageal cancer patients using 4D-CT during free breathing with feedback guidance. CTV–ITV margins of 0.8 cm radially

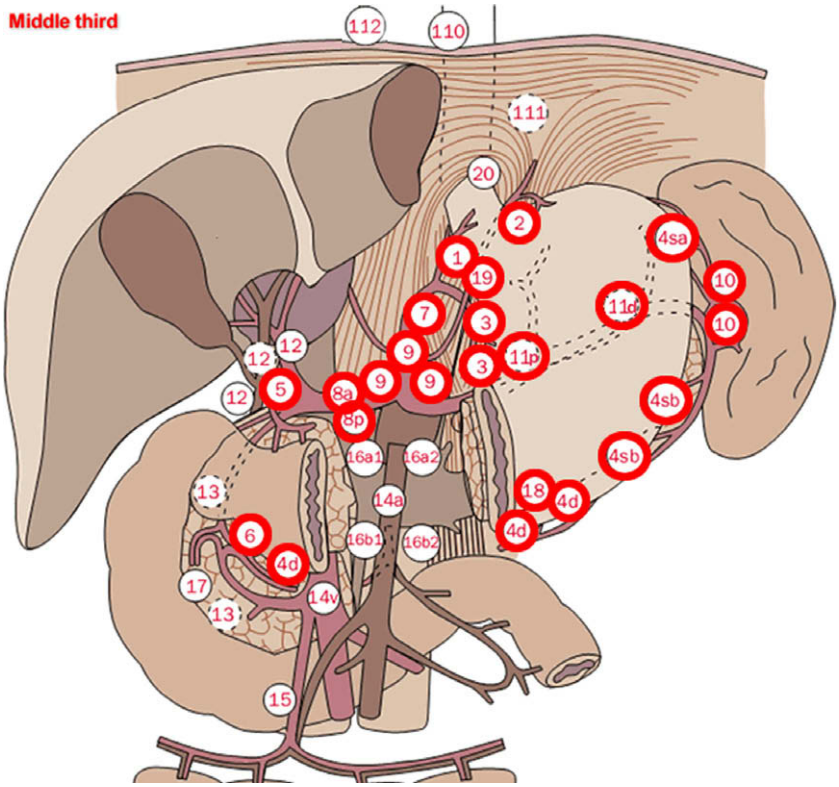


Fig. 8. Corresponding elective lymph node stations for GC tumours of the middle third: 1, right paracardial LN; 2, left paracardial; LN; 3, LN along the lesser curvature; 4sa, LN along the short gastric vessels; 4sb, LN along the left gastroepiploic vessels; 4d, LN along the right gastroepiploic vessels; 5, suprapyloric LN; 6, Infrapyloric LN; 7, LN along the left gastric artery; 8a, LN along the common hepatic artery (anterosuperior group); 8b, LN along the common hepatic artery (posterior group); 9, LN around the celiac artery; 10, LN at the splenic hilum; 11p, LN along the proximal splenic artery; 11d, LN along the distal splenic artery; 18, LN along the inferior margin of the pancreas; 19 infradiaphragmatic LN.

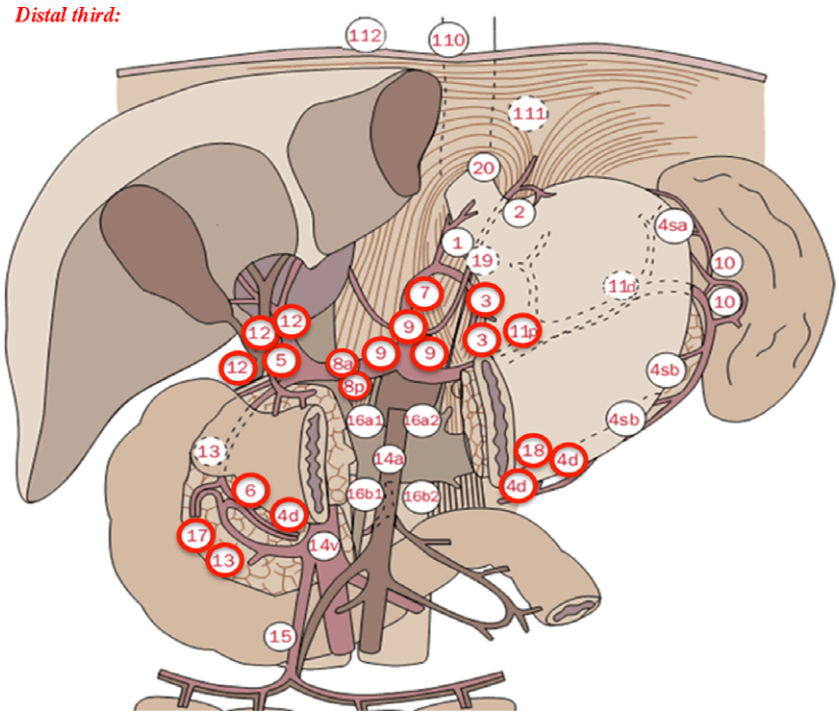


Fig. 9. Corresponding elective lymph node stations for GC tumours of the distal third: 3, LN along the lesser curvature; 4d, LN along the right gastroepiploic vessels; 5, suprapyloric LN; 6, infrapyloric LN; 7, LN along the left gastric artery; 8a, LN along the common hepatic artery (anterosuperior group); 8b, LN along the common hepatic artery (posterior group) 9, LN around the celiac artery; 11p, LN along the proximal splenic artery; 12a, LN in the hepatoduodenal ligament (along the hepatic artery); 12b, LN in the hepatoduodenal ligament (along the bile duct); 12p, LN in the hepatoduodenal ligament (behind the portal vein); 13, LN on the posterior surface of the pancreatic head; 17, LN on the anterior surface of the pancreatic head; 18, LN along the inferior margin of the pancreas.

Table 1
Elective lymph node stations corresponding to the different localization of GEJ and GT.

Tumour localization	Elective lymph node stations numbers and name	
GEJ type I	1	Right paracardial LN
	2	Left paracardial LN
(Figs. 3, 4 and 10)	7	LN along the left gastric artery
	9	LN around the celiac artery
	19	Infradiaphragmatic LN
	20	LN in the oesophageal hiatus of the diaphragm
	110	Paraoesophageal LN in the lower thorax
	111	Supradiaphragmatic LN
	112	Posterior mediastinal LN
GEJ type II	1	Right paracardial LN
	2	Left paracardial LN
(Figs. 3, 5 and 10)	3	LN along the lesser curvature
	4sa	LN along the short gastric vessels
	7	LN along the left gastric artery
	9	LN around the celiac artery
	11p	LN along the proximal splenic artery
	19	Infradiaphragmatic LN
	20	LN in the oesophageal hiatus of the diaphragm
	110	Paraoesophageal LN in the lower thorax
	111	Supradiaphragmatic LN
GEJ type III	1	Right paracardial LN
	2	Left paracardial LN
(Figs. 3, 6 and 10)	3	LN along the lesser curvature
	4sa	LN along the short gastric vessels
	7	LN along the left gastric artery
	9	LN around the celiac artery
	10	LN at the splenic hilum
	11p	LN along the proximal splenic artery
	11d	LN along the distal splenic artery
	19	Infradiaphragmatic LN
	20	LN in the oesophageal hiatus of the diaphragm
	110	Paraoesophageal LN in the lower thorax
	111	Supradiaphragmatic LN
GC: proximal third	1	Right paracardial LN
	2	Left paracardial LN
(Figs. 3, 7 and 10)	3	LN along the lesser curvature
	4sa	LN along the short gastric vessels
	4sb	LN along the left gastroepiploic vessels
	7	LN along the left gastric artery
	9	LN around the celiac artery
	10	LN at the splenic hilum
	11p	LN along the proximal splenic artery
	11d	LN along the distal splenic artery
	19	Infradiaphragmatic LN
GC: middle third	1	Right paracardial LN
	2	Left paracardial LN
(Figs. 3, 8 and 10)	3	LN along the lesser curvature
	4sa	LN along the short gastric vessels
	4sb	LN along the left gastroepiploic vessels
	4d	LN along the right gastroepiploic vessels
	5	Suprapyloric LN
	5	Infrapyloric LN
	7	LN along the left gastric artery
	8a	LN along the common hepatic artery (Anterosuperior group)
	8b	LN along the common hepatic artery (Posterior group)
	9	LN around the celiac artery
	10	LN at the splenic hilum
	11p	LN along the proximal splenic artery
	11d	LN along the distal splenic artery
	18	LN along the inferior margin of the pancreas
	19	infradiaphragmatic LN
GC: distal third	3	LN along the lesser curvature
	4d	LN along the right gastroepiploic vessels
(Figs. 3, 9 and 10)	5	Suprapyloric LN
	6	Infrapyloric LN
	7	LN along the left gastric artery
	8a	LN along the common hepatic artery (Anterosuperior group)
	8b	LN along the common hepatic artery (Posterior group)
	9	LN around the celiac artery
	11p	LN along the proximal splenic artery
	12a	LN in the hepatoduodenal ligament (along the hepatic artery)
	12b	LN in the hepatoduodenal ligament (along the bile duct)
	12p	LN in the hepatoduodenal ligament (behind the portal vein)
	13	LN on the posterior surface of the pancreatic head
	17	LN on the anterior surface of the pancreatic head
	18	LN along the inferior margin of the pancreas

Remark: The $CTV_{elective}$ volume should be defined by a 5 mm margin around the corresponding vessels.
The upper border of the CTV in GEJ tumours Type I and II is limited by a margin of 3 cm from the cranial extension of the primary tumour [68].
The upper border of the CTV in GEJ tumours type III is limited either by a margin of 3 cm from the cranial extension of the primary tumour or by the superior end of the oesophageal hiatus as defined by planning CT [68]. The most cranial of these two borders will define the upper border of the CTV and be delineated.

and 1.8 cm axially were recommended when 4D-CT is not available for planning. Zhao et al. studied 25 patients with oesophageal cancer near the GEJ. They used respiratory-correlated 4D-CT images. Their measured tumour mobility suggested the use of asymmetric margins: 1.0 cm left, 0.8 cm right, 1.1 cm anterior, 0.6 cm posterior, 1.0 cm superior and 1.6 cm inferior. Dieleman et al. [21] analysed the mobility for 29 non-oesophageal malignancy patients during normal respiration using normal breathing 4D-CT images. They concluded that 9-mm lateral and 8-mm AP margins were needed for the section of oesophagus 2-cm above the GEJ. However, they did not evaluate the superior–inferior motion.

Considering the above-mentioned data that are still sparse and that are still need to be confirmed by new studies, we propose to define in the meanwhile 1 cm radial; 1.5 cm distal and 1 cm proximal margins from CTV to ITV if no individualized identification of the target motion is available.

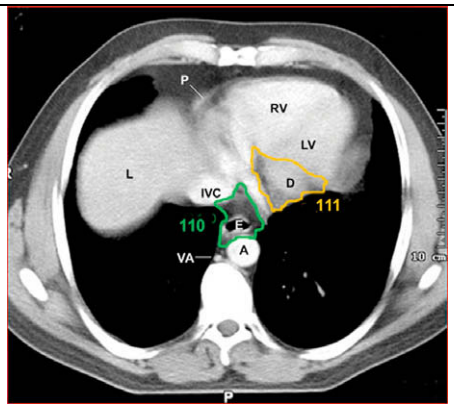
GC target volume definition continues to be the subject of research because of considerable intrafractional stomach motion and remarkable interfractional variability of gastric distension in response to variations in stomach filling and respiratory motion as confirmed by two recent studies [66,67].

Some centres advocate the use of respiratory gating devices to reduce intrafractional position variability. Daily cone-beam CT (image guided radiotherapy (IGRT)) could also be useful to assess interfractional variability.

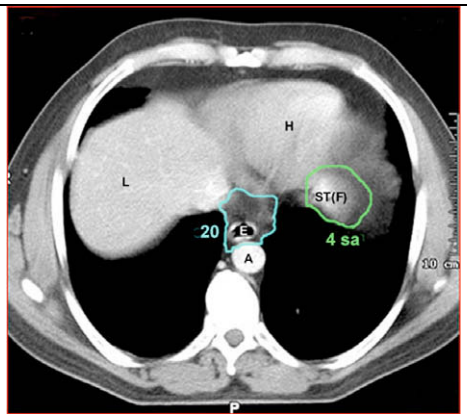
However no standard procedure can be recommended based on evidence until now. We recommend therefore a minimal 3-D margin of 1.5 cm in all directions to be added from the CTV to the ITV [21] if the centres do not perform routinely respiratory gating or IGRT.

Conclusion

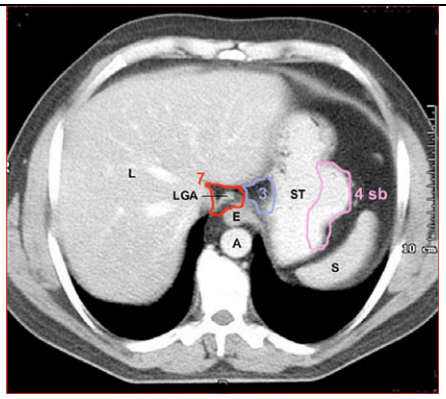
Preoperative radiochemotherapy is a promising development in the field of gastric and gastroesophageal tumours. The Gastro-Intestinal Working Party of the Radiation Oncology Group of the EORTC defined hereby a set of guidelines for preoperative irradiation of AC of the GEJ and the stomach. This consensus-based guideline should reduce inter-observer variability in target volume delineation as well as standardize the planning and the radiotherapy delivery in the framework of future clinical trials. Therein, particular attention will be given to the patterns of recurrence to ensure the appropriateness of our guidelines.



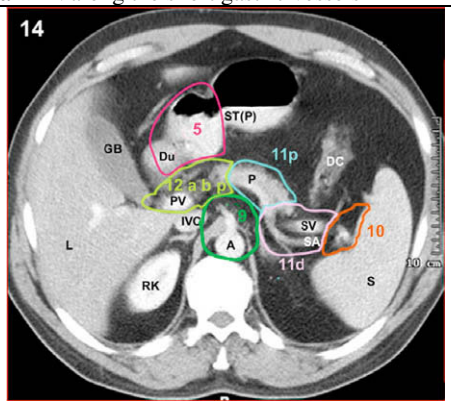
110 - Paraoesophageal LN
111 - Supradiaphragmatic LN



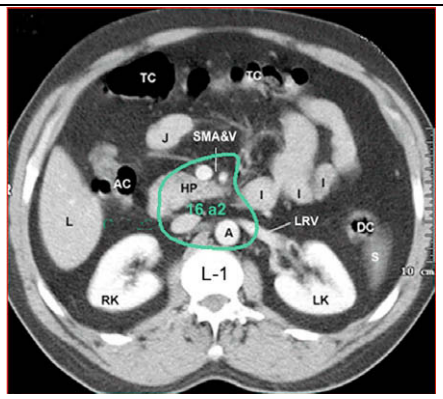
20 - LN in the oesophageal hiatus of the diaphragm
4sa - LN along the short gastric vessels



3 - LN along the lesser curvature
4sb - LN along the left gastroepiploic vessels
7 - LN along the left gastric artery



5 - Suprapyloric LN,
9 - LN around the celiac artery
10 - LN at the splenic hilum
11p - LN along the proximal splenic artery
11d - LN along the distal splenic artery
12 a, b, p - LN in the hepatoduodenal ligament



16 a2 LN around the abdominal aorta

LEGEND:
A – Aorta; AC – Ascending Colon; D - Diaphragma; DC – Descending Colon; Du – Duodenum; E – Oesophagus; GB – Gall Bladder; I – Ilium; H – Heart; J – Jejunum; IVC – Inferior Cava Vein; L – Liver; L-1 – First Lumbar Vertebra; LK – Left Kidney, LRV – Left Renal Vein; LV – Left Ventricle; P – Pancreas; PV – Portal Vein; RGA – Right Gastric Artery; RK – Right Kidney; RV – Right Ventricle; S – Spleen; SA – Splenic Artery; SMA&V – Superior Mesenteric Artery and Vein; SV – Splenic Vein; ST – Stomach; ST(F) – Stomach Fundus; ST(P) – Stomach Pylorus; TC - Transverse Colon; VA – Azygos Vein

Fig. 10. Examples of lymph node stations on the corresponding CT slices.

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