TVD in Cancer Esophagus Radical Setting Primary & Nodal Volume Post op Tumor Bed

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Radiation Therapy

- Definitive - EBRT/Concurrent CRT
  - Radical
  - Preoperative (Neoadjuvant)
    - T3 or higher
    - N+
    - 45 – 50 Gy
  - Post operative (Adjuvant)
    - Rare; difficult to tolerate
    - 45 Gy
  - Palliative: Dysphagia 30 – 35Gy
- Brachytherapy

Radiation Therapy

- Computed tomography based planning utilizing conformal techniques is the standard of care for esophagus cancer

- Essential to accurately delineate
  - Target volumes
  - Critical normal structures

Importance of Target Volume Delineation

Journal of Medical Physics

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PMCID: PMC2772050

Tumor delineation: The weakest link in the search for accuracy in radiotherapy

C. F. Njeh

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Abstract

Go to:

Radiotherapy is one of the most effective modalities for the treatment of cancer. However, there is a high degree of uncertainty associated with the target volume of most cancer sites. The sources of these uncertainties include, but are not limited to, the motion of the target, patient setup errors, patient movements, and the delineation of the target volume. Recently, many imaging techniques have been introduced to track the motion of tumors. The treatment delivery using these techniques is collectively called image-guided radiation therapy (IGRT). Ultimately, IGRT is only as good as the accuracy with which the target is known. There are reports of interobserver variability in tumor delineation across anatomical sites, but the widest ranges of variations have been reported for the delineation of head and neck tumors as well as esophageal and lung carcinomas. Significant interobserver variability in target delineation can be attributed to many factors including the impact of imaging and the influence of the observer (specialty, training, and personal bias). The visibility of the target can be greatly improved with the use of multimodality imaging by co-registration of CT with a second modality such as magnetic resonance imaging (MRI) and/or positron emission tomography. Also, continuous education, training, and cross-collaboration of the radiation oncologist with other specialties can reduce the degree of variability in tumor delineation.

Tumor Delineation - the weakest link

- Imaging techniques to track the motion of tumors during treatment delivery - IGRT
- IGRT is only as good as the accuracy with which the target is defined
- Widest ranges of inter-observer variations reported for the delineation of
  - Head and neck tumors
  - Esophageal and lung carcinomas

Tumor Delineation - the weakest link

- Errors in TV localization & delineation occur early in the planning process and only once
- This generates systematic errors
  - Can produce the biggest deviation in the entire RT process
  - No level of image guidance will eliminate
- Potentially can alter outcome of treatment
- Once defined, this error is constant throughout the entire RT planning process

Simulation

- Immobilization
  - Vac Loc
- Position arms above head to maximize the number of beam arrangements
- Tattoos for daily Set-up

Simulation

- Four dimensional (4D) scanning
- If 4D study is not available following to estimate internal motion of intrathoracic structures
  - Slow helical CT scan or
  - Acquisition of CT images at maximal inspiration and expiration, with the difference being the total extent of motion of the target and critical structures

Simulation

- Tumors involving the distal esophagus
  - Nil per oral for at least 3 to 4 h prior to simulation and treatment
  - Limits variations in gastric bowel gas that may affect dose distribution

Nancy Y. Lee • Jiade J. Lu
Editors

Target Volume Delineation and Field Setup

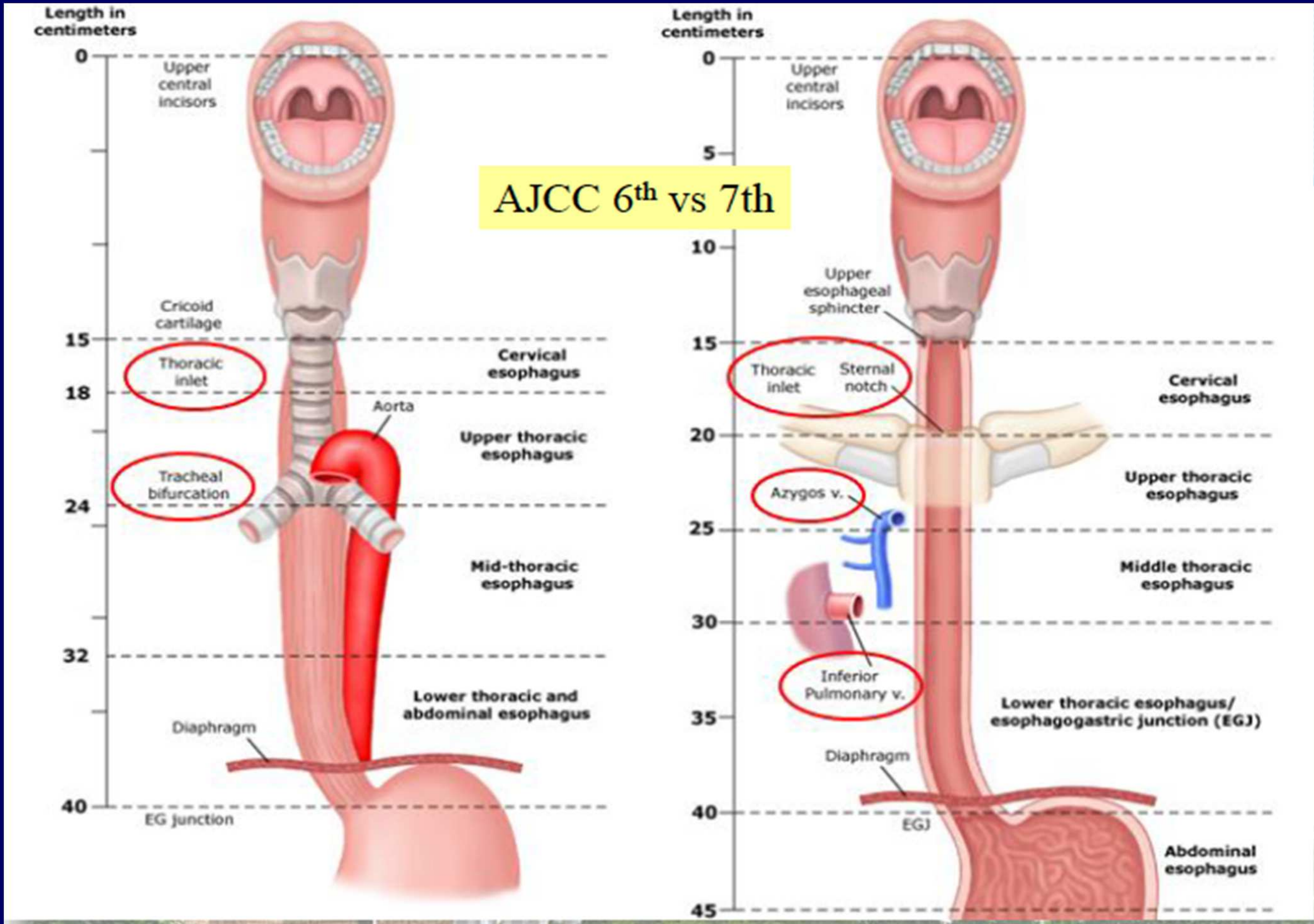
A Practical Guide for Conformal and Intensity-Modulated Radiation Therapy

Esophagus Cancer

13

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

AJCC 6th vs 7th



Guidelines for Contouring

- For contouring, esophageal malignancies divided anatomically into 2 regions
  - Upper esophagus tumors (including malignancies of the cervical esophagus)
  - Lower esophagus tumors (including tumors of the gastroesophageal [GE] junction)
- Tumors in the lower esophagus & upper esophagus - follow contouring guidelines of both subsets

Guidelines for Contouring

- Significant involvement of gastric cardia or the stomach, consider as gastric origin rather than of esophageal
- Based on contouring guidelines of gastric cancers
  - Diagnostic laparoscopy and J-tube placement
  - Renal perfusion scan
  - Preoperative chemoradiation or
  - Postoperative chemoradiation

OARs

- For proper DVH analysis need to contour
  - Entire esophagus
  - Lung, Heart & Spinal Cord
- Upper esophageal tumors
  - Brachial plexus and Larynx
- Lower esophageal tumors
  - Liver & Kidneys

OARs

Heart

- Cranial border will include the infundibulum of the right ventricle and the apex of both atria & will exclude the great vessels as much as possible
- Caudal border will be defined as the lowest part of the left ventricle's inferior wall that is distinguishable from the liver

Target Volume Definitions

ICRU Definition

- Gross Tumor Volume (GTV Tumor + LN)
- Clinical Target Volume (CTV - microscopic dis)
- Internal Target Volume (ITV - eso movement upper - 0.5 cm, mid - 0.6 to 0.7 cm, lower - 0.8 to 0.9 cm)
- Planning Target Volume (PTV - accounts for setup error and intra-fraction motion)

Target Volume Delineation

- Upper esophagus – above carina
  - GTV → CTV margin longitudinal 3 to 5 cm
    radial 1 cm
  - CTV (or ITV) → PTV margin
    - No IGRT or Motion assessment (4DCT) 1 - 1.5 cm
    - IGRT or Motion assessment 0.5 - 1cm
    - Both 0.5 cm
  - Elective nodal
    - Peri – esophageal, Supraclavicular

Target Volume Delineation

- Lower esophagus – below carina
  - GTV → CTV margin - Same as upper
  - CTV (or ITV) → PTV margin – Same as upper
  - Elective nodal
    - Peri – esophageal, celiac
    - Based on extension to stomach - nodal regions
      - Perigastric, left gastric
      - Splenic hilum
      - Porta hepatis, SMA

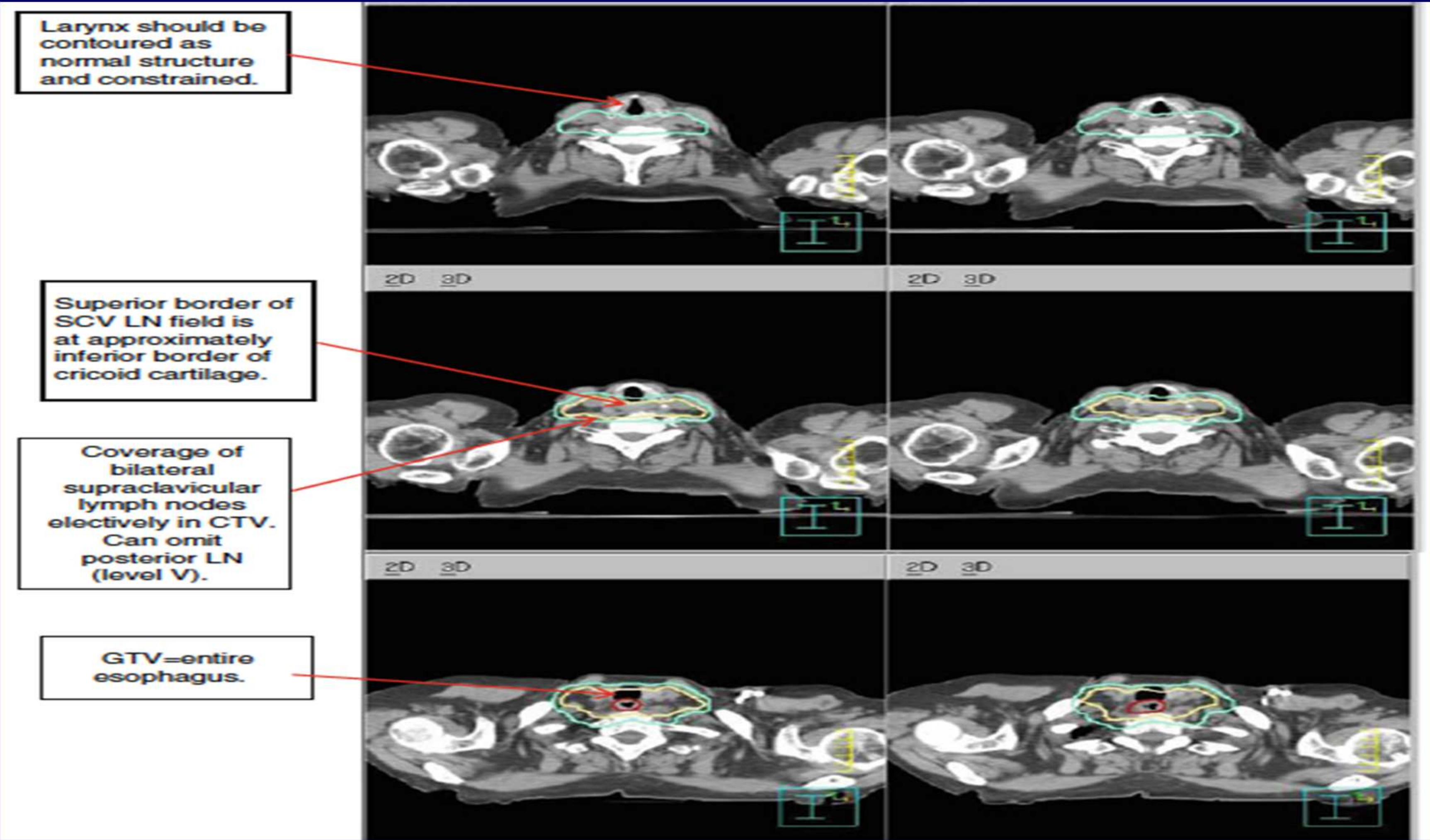
Target Volumes

- Standard GTV to CTV expansions are
  - Superior & inferior - 3 to 5 cm (CROSS Trial 4 cm, if extension into stomach distal margin 3 cm)
    - Submucosal spread, skip lesions
  - Radial - 1 cm (CROSS 2 cm subclinical disease & compensate for tumor motion & set-up variations)
  - Involved lymph nodes - 0.5 to1.0 cm

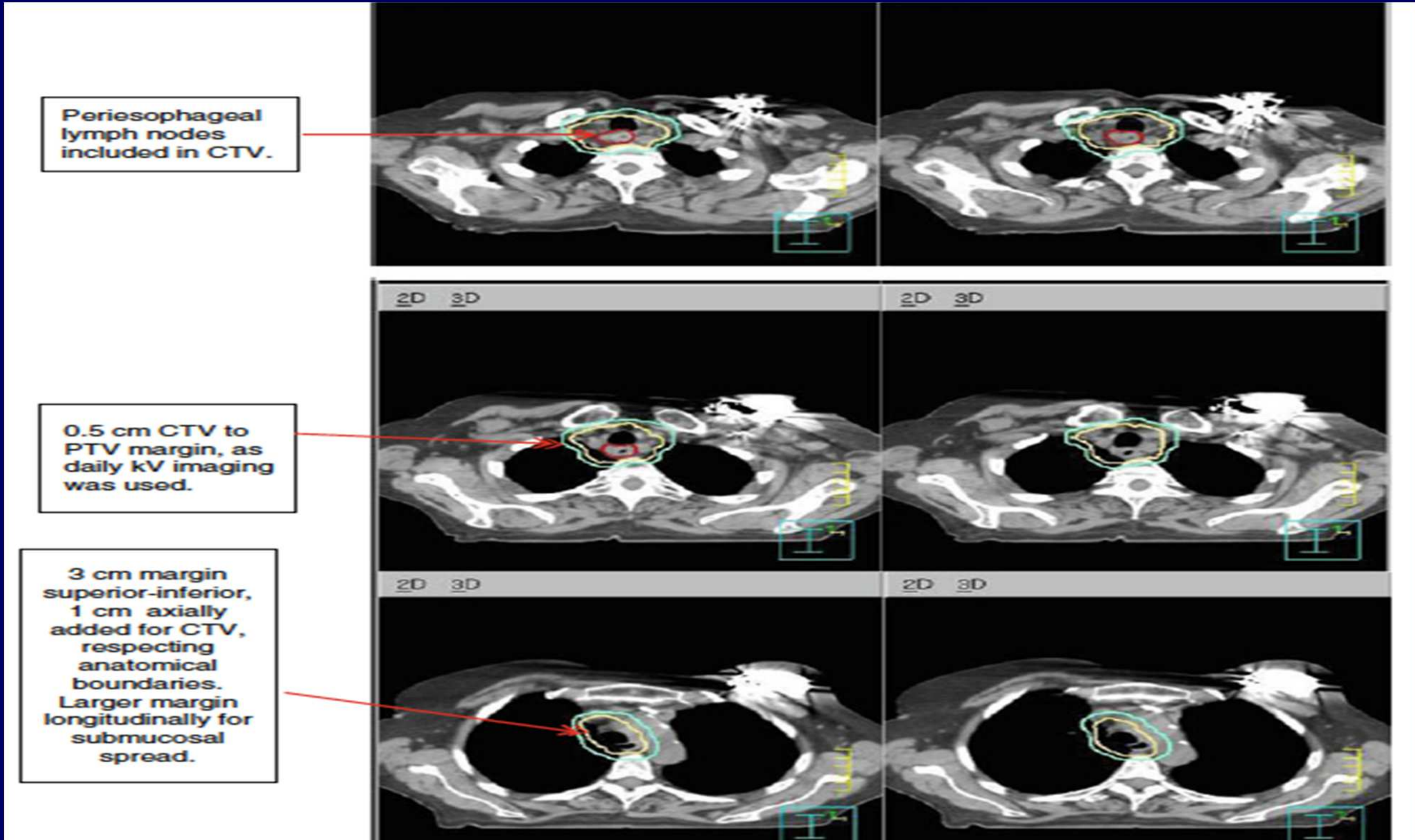
Target Volumes

- Margins can be adjusted based on
  - Use of motion assessment
  - Treating physician's confidence in knowing the extent of disease
  - Adjustment made according to anatomic barriers

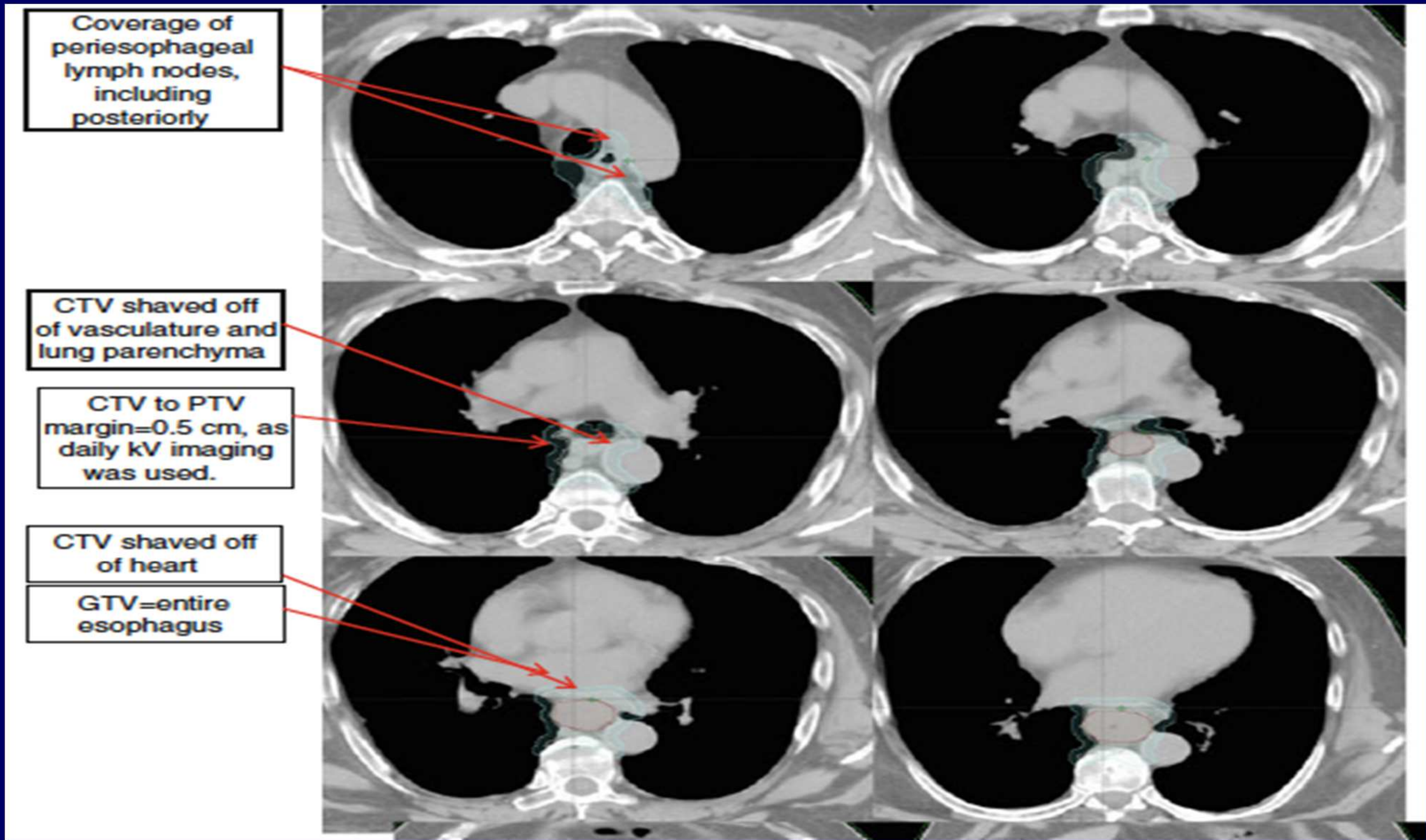
Upper Esophagus T3 N0



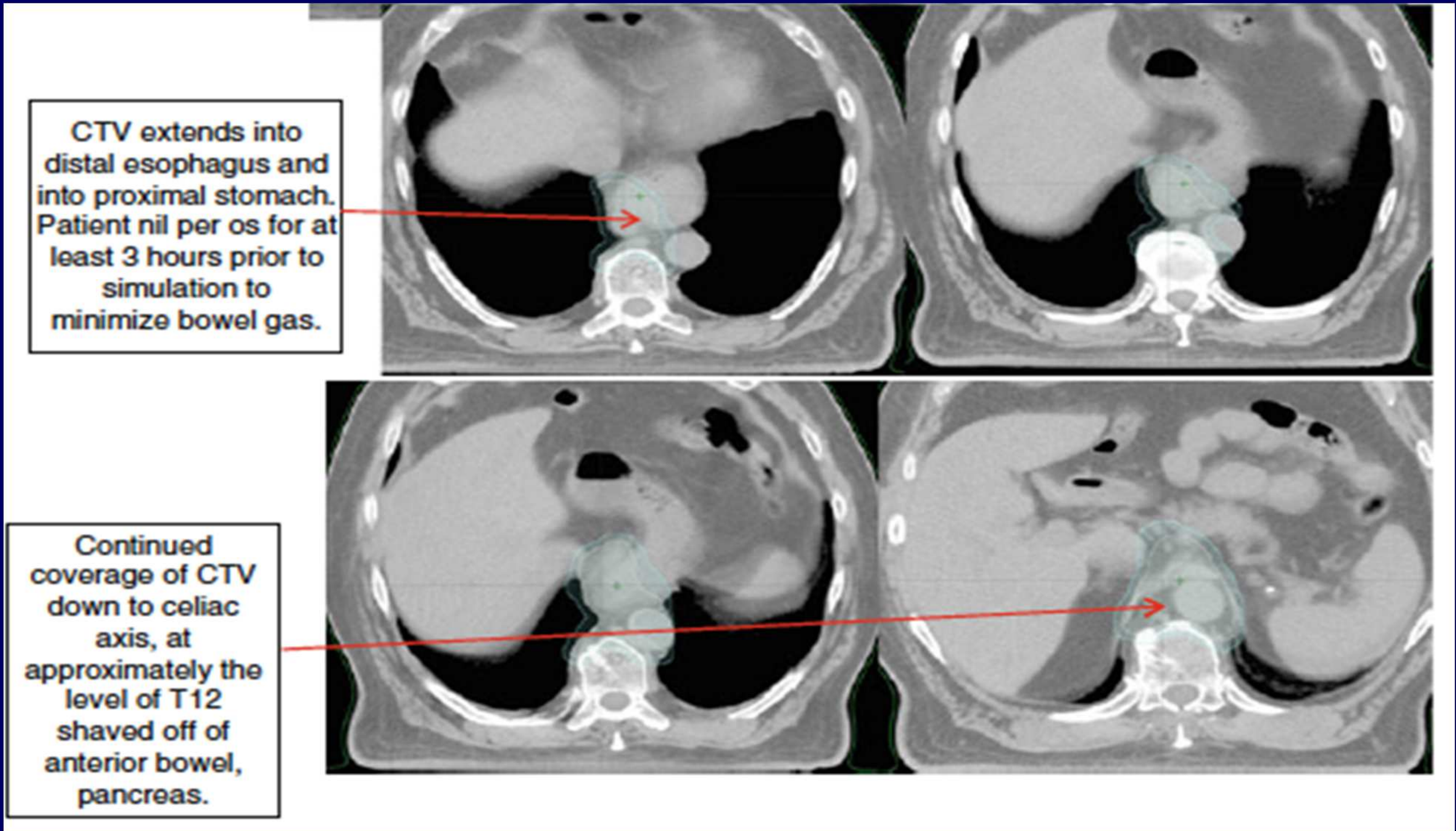
Upper Esophagus T3 N0



Distal Esophagus T3 N0



Distal Esophagus T3 N0



Chinese Journal of Cancer

·Esophageal Cancer Column·

Treatment guideline of radiotherapy for Chinese esophageal carcinoma (draft)

Esophageal Carcinoma Cooperative Group of Radiation Oncology Society of Chinese Medical Association

Drafted by Xian-Shu Gao

Target Volume

- No internationally unified opinion or high grade evidence on definition of CTV
- Gao et al did screening on esophageal carcinoma specimens the microscopic infiltration ranges were < 3 cm superior and inferior in 94%
  - Recommended margin of 3 cm along the vertical axis & 0.5 cm radial
  - Adjustment made according to anatomic barriers
  - Anatomic barriers should not be exceeded unless evidence proving disease has broken through

Target Volume

- CTV - LN
- No high grade evidence identifying the extent of lymphatic drainage in prophylactic radiation
- Extent of surgical lymphadenectomy is usually used when defining prophylactic radiation
- Radiation Therapy Oncology Group (RTOG) study – main reason of failure post radiotherapy was local failure

Target Volume

- Only tumor and positive lymph nodes were radiated, without elective lymph nodal areas
- Analysis on treatment failure
  - Isolated outfield recurrence rate of lymph nodes without tumor progression and distant metastasis was only 8%
- Concluded - elective prophylactic radiation to lymph nodes not necessary

Ji *et al. Radiation Oncology* 2012, **7**:200
http://www.ro-journal.com/content/7/1/200

RADIATION ONCOLOGY

RESEARCH **Open Access**

Three-dimensional conformal radiation for esophageal squamous cell carcinoma with involved-field irradiation may deliver considerable doses of incidental nodal irradiation

Kai Ji†, Lujun Zhao†, Chengwen Yang, Maobin Meng and Ping Wang*

3 D CRT - IFRT

- Nodal regions delineated using Japanese Society for Esophageal Diseases (JSED) guidelines & EORTC-ROG expert opinion
- The equivalent uniform dose (EUD) & other dosimetric parameters calculated for LN regions (metastasis rate > 5% were considered a high-risk lymph node subgroup)
- LN stations near Tumour - considerable incidental doses with IFRT – contribute to the elimination of subclinical lesions

Table 2 Terminology of regional lymph node in esophageal carcinoma by JSED

Numbering	Cervical and mediastinal lymph nodes	Numbering	Abdominal lymph nodes
101	Cervical paraesophageal	1	Right cardial
104	Supraclavicular	2	Left cardial
105	Upper thoracic paraesophageal	3	Lesser curvature
106rec-L	Left recurrent nerve	7	Left gastric arter
106rec-R	Right recurrent nerve	8	Common hepatic artery
106pre	Pretracheal		
106tb-L	Left tracheobronchial		
106tb-R	Right tracheobronchial		
107	Subcarinal		
108	Middle thoracic paraesophageal		
109	Main bronchus lymph nodes		
110	Lower thoracic paraesophageal		
111	Supradiaphragmatic		
112ao	Thoracic paraaortic		
112pul	Pulmonary ligament		
113	Ligamentum arteriosum		
114	Anterior mediastinal		

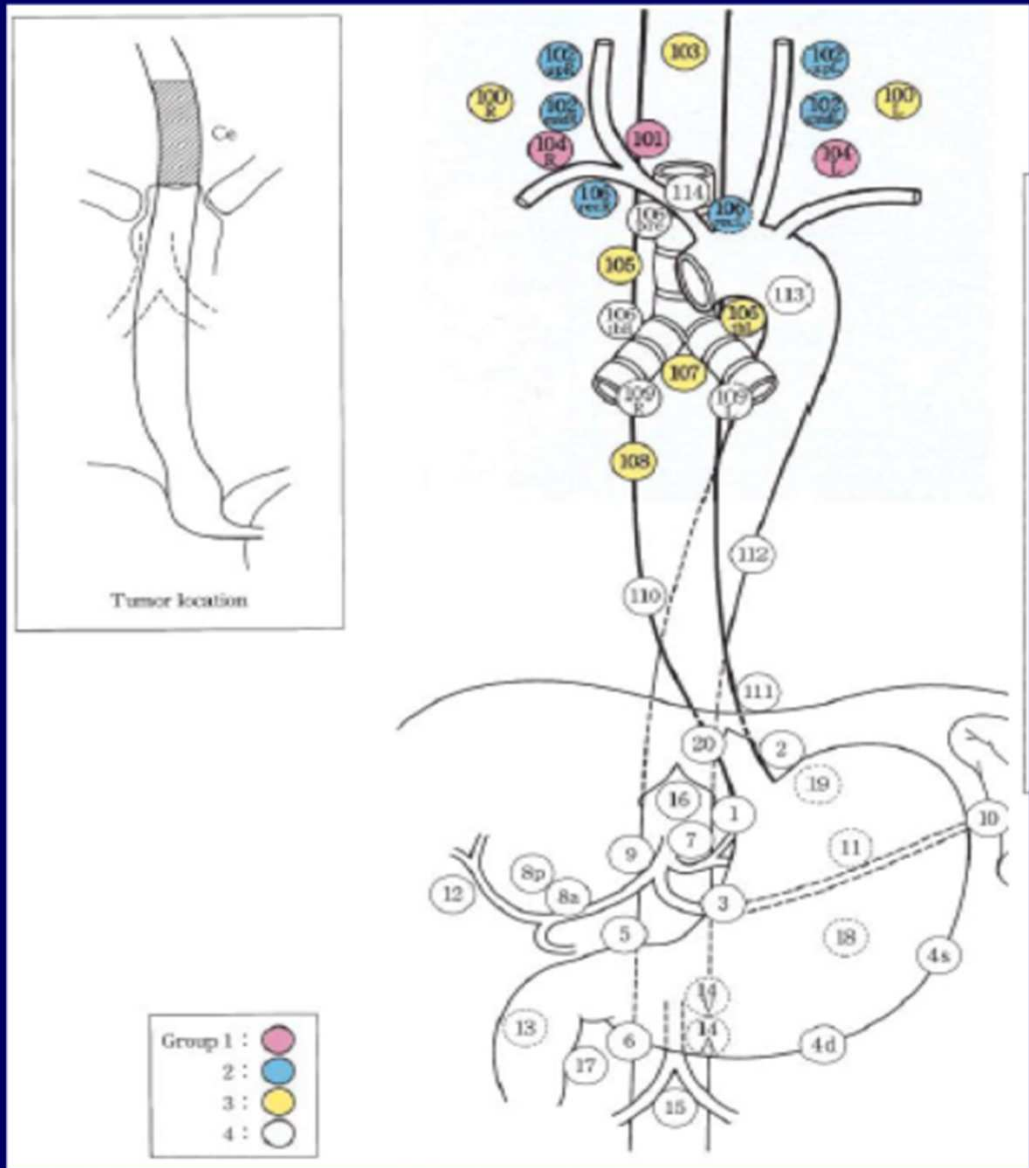
JSED: Japanese Society for Esophageal Diseases.

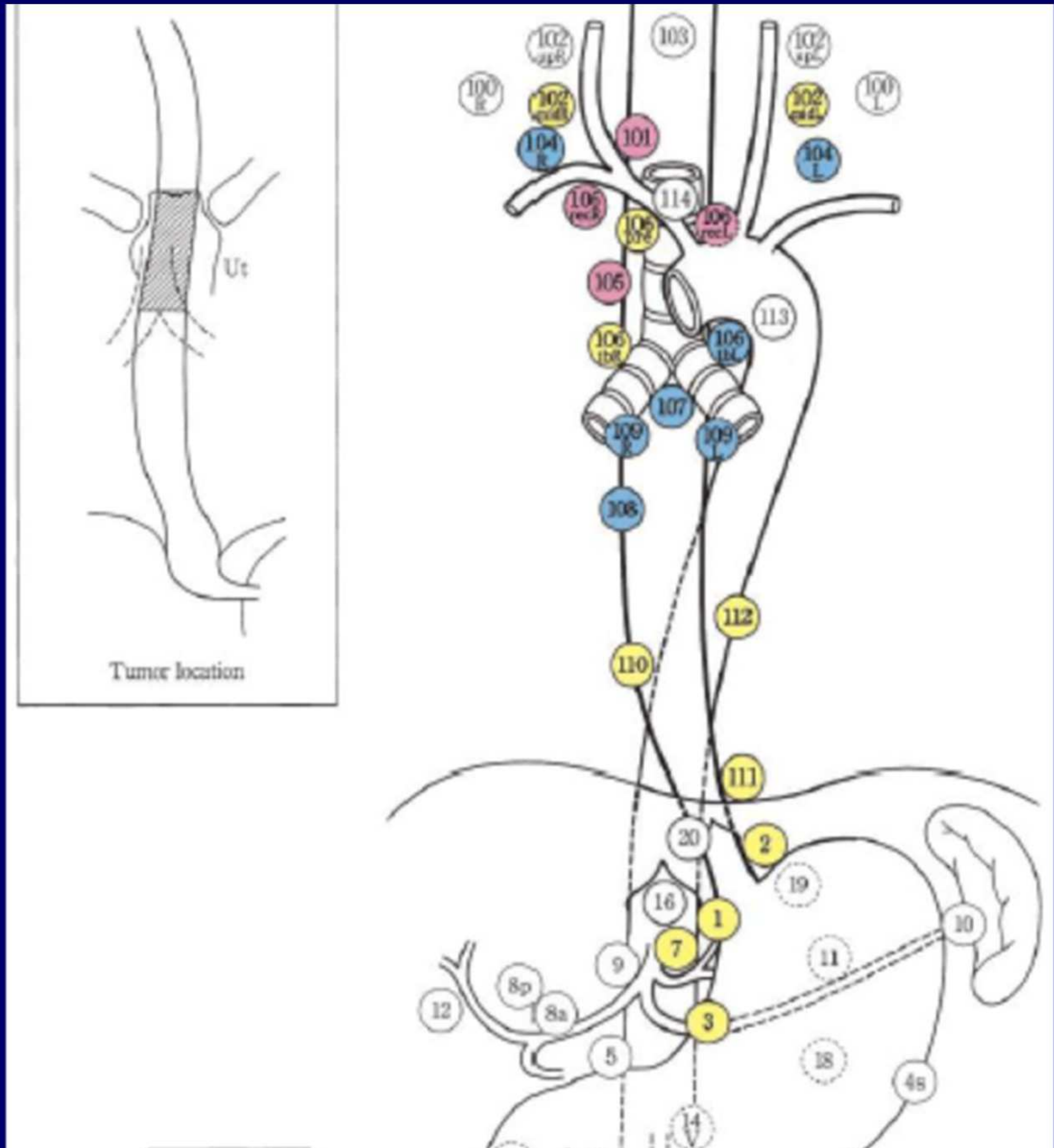
Table I-1. Naming of regional lymph nodes

(1) Cervical and mediastinal lymph nodes (Figs. I-5, 6, 7, and 8)	
100	Superficial lymph nodes of the neck
100-spf	Superficial cervical lymph nodes Lymph nodes along the external jugular veins and anterior jugular veins beneath the superficial cervical fascia.
100-sm	Submandibular lymph nodes Lymph nodes located around submandibular glands and parotid glands, and anterior to the myohyoid muscle.
100-tr	Cervical pretracheal lymph nodes Lymph nodes located in the pretracheal fatty tissue, extending from the hyoid bone superiorly, to the left brachiocephalic vein inferiorly, including prethyroidal lymph nodes and prelaryngeal lymph nodes.
100-ac	Accessory nerve lymph nodes Lymph nodes located along the accessory nerve(s), and anterior to the trapezius muscle.
101	Cervical paraesophageal lymph nodes Lymph nodes located around the cervical esophagus, including lymph nodes located along the recurrent laryngeal nerve and the cervical paratracheal lymph nodes. The lateral boundary is the medial border of the carotid sheath.
102	Deep cervical lymph nodes Lymph nodes located around the internal jugular vein and common carotid artery.
102-up	Upper deep cervical lymph nodes Lymph nodes located from the caudal border of the digastric muscle superior to the carotid artery bifurcation.
102-mid	Middle deep cervical lymph nodes Lymph nodes located from the carotid artery bifurcation superiorly to the lower border of the cricoid cartilage inferiorly.
103	Peripharyngeal lymph nodes Lymph nodes located medial to the carotid sheath, extending from the caudal border of the digastric muscle superiorly to the lower border of the cricoid cartilage inferiorly. Postpharyngeal and parapharyngeal lymph nodes are included.
104	Supraclavicular lymph nodes Lymph nodes located in the supraclavicular fossa, extending from the lower border of the cricoid cartilage superiorly, to the clavicle inferiorly, including the lower internal deep cervical lymph nodes. The medial boundary is the medial border of the carotid sheath.
105	Upper thoracic paraesophageal lymph nodes Lymph nodes located around the upper thoracic esophagus posterior to the right vagus nerve in the right side. Lymph nodes located along the azygos vein arch and the right bronchial artery are included. The superior boundary is drawn from the cephalic border of the subclavian arteries to the suprasternal notch.
106	Thoracic paratracheal lymph nodes Lymph nodes located along the anterior and lateral wall of the thoracic trachea.
106-rec	Recurrent nerve lymph nodes Lymph nodes located along the recurrent laryngeal nerves in the mediastinum. The superior boundary is drawn from the cephalic border of the subclavian arteries to the suprasternal notch, and the inferior boundary is the caudal border of the recurrent laryngeal nerve curving upward on both sides.
106-rec L	Left recurrent nerve lymph nodes Lymph nodes located along the left recurrent laryngeal nerve.
106-rec R	Right recurrent nerve lymph nodes Lymph nodes located along the right recurrent laryngeal nerve.
106-pre	Pretracheal lymph nodes Lymph nodes in front of the anterior wall of the thoracic trachea, and anterior to the right vagus nerve.
106-tb	Tracheobronchial lymph nodes Lymph nodes located in the tracheobronchial angle.
106-tb L	Left tracheobronchial lymph nodes The superior border is the inferior wall of the aortic arch, and the lymph nodes are located in the area surrounded by the medial wall of the aortic arch.
106-tb R	Right tracheobronchial lymph nodes The superior border is the inferior wall of the azygos vein.

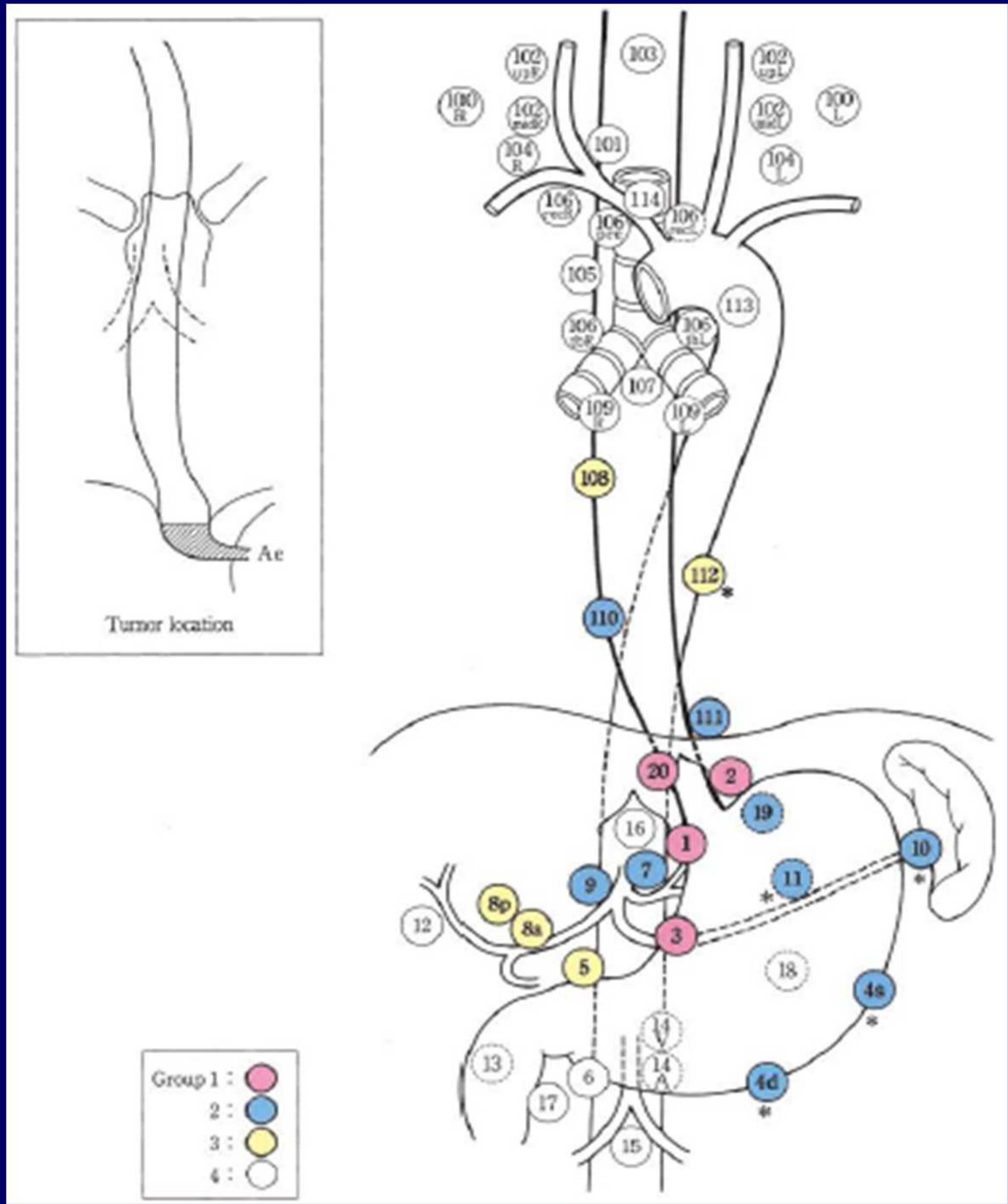
Table 1-1. *Continued*

107	Subcarinal lymph nodes Lymph nodes located caudal to the carina of the trachea. The lateral boundaries are the extended line of both lateral margins of the trachea.
108	Middle thoracic paraesophageal lymph nodes Lymph nodes located around the middle thoracic esophagus.
109	Main bronchus lymph nodes (formerly: pulmonary hilar lymph nodes) Lymph nodes located in the caudal area of the main bronchus. The internal boundary is the border of the 107 lymph nodes, and the external boundary is the lung.
110	Lower thoracic paraesophageal lymph nodes Lymph nodes located around the lower thoracic esophagus.
111	Supradiaphragmatic lymph nodes (formerly: diaphragmatic lymph nodes) Lymph nodes located in the area surrounded by the diaphragm, pericardium, and esophagus.
112	Posterior mediastinal lymph nodes Lymph nodes located in the area surrounded by the descending aorta, inferior pulmonary vein, and pericardium.
112-ao	Thoracic paraaortic lymph nodes Lymph nodes located around the descending aorta, including lymph nodes along the thoracic duct.
112-pul	Pulmonary ligament lymph nodes Lymph nodes located in the pulmonary ligament(s), including lymph nodes adjacent to the pericardium and the inferior pulmonary vein.
113	Ligamentum arteriosum lymph nodes (Botallo's lymph nodes) Lymph nodes located on the left side of the arterial ligament.
114	Anterior mediastinal lymph nodes Lymph nodes located anterior to the superior vena cava, including lymph nodes of the brachiocephalic venous angle and lymph nodes around the thymus gland.
(2) Abdominal lymph nodes (Fig. 1-5)	
1	Right cardial lymph nodes
2	Left cardial lymph nodes
3	Lymph nodes along the lesser curvature
4	Lymph nodes along the greater curvature
5	Suprapyloric lymph nodes
6	Infrapyloric lymph nodes
7	Lymph nodes along the left gastric artery
8	Lymph nodes along the common hepatic artery
9	Lymph nodes along the celiac artery
10	Lymph nodes at the splenic hilum
11	Lymph nodes along the splenic artery
12	Lymph nodes in the hepatoduodenal ligament
13	Lymph nodes on the posterior surface of the pancreatic head
14	Lymph nodes at the root of the mesentery
14A	Lymph nodes along the superior mesenteric artery
14V	Lymph nodes along the superior mesenteric vein
15	Lymph nodes along the middle colic artery
16	Lymph nodes around the abdominal aorta
17	Lymph nodes on the anterior surface of the pancreatic head
18	Lymph nodes along the inferior margin of the pancreas
19	Infradiaphragmatic lymph nodes
20	Lymph nodes in the esophageal hiatus of the diaphragm


Ce
Tumor location
Group 1 :
2 :
3 :
4 :
103
101
114
105
107
108
110
112
113
111
20
2
19
16
1
7
9
11
10
8p
8a
12
3
5
18
4s
13
6
14
4d
17
15



Ut
Tumor location
100 R
102 spR
102 midR
104 R
101
103
114
106 recR
106 pre
106 recL
102 spL
102 midL
100 L
104 L
105
113
106 tbR
106 tbL
107
109 R
109 L
108
112
110
111
20
2
19
16
1
7
9
10
11
8p
8a
12
3
5
18
4s
14



Tumor location
Ae
Group 1 :
2 :
3 :
4 :
100 L
100 R
101
102 up R
102 up L
102 mid R
102 mid L
103
104 R
104 L
105
107
108
109 R
109 L
110
111
112
113
114
1
2
3
4s
4d
5
6
7
8a
8p
9
10
11
12
13
14 A
14 V
15
16
17
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19
20

Table I-2. Lymph node groups

Tumor location		N1	N2	N3	N4
Cervical esophagus (Ce)		101, 104	102, 106-rec	100, 103, 105 106-tbL, 107, 108	106-pre, 106-tbR, 109, 110, 111, 112, 113, 114, 1, 2, 3, and others
Thoracic esophagus (Te)	Upper (Ut)	105, 101, 106-rec	104, 106-tbL 107, 108, 109	102-mid, 106-pre, 106-tbR, 110, 111 112, 1, 2, 3, 7	100, 102-up, 103, 113, 114, 4, 5, 6, 8, 9, 20, and others
	Middle (Mt)	108, 106-rec	101, 105, 106-tbL, 107, 109, 110, 1, 2, 3, 7	104, 111, 112, 20	100, 102, 103, 106-pre, 106-tbR, 113, 114, 4, 5, 6, 8, 9, and others
	Lower (Lt)	110, 1, 2	106-rec, 107, 108, 109, 111, 112, 3, 7, 20	101, 105, 106-tbL, 9, 19	100, 102, 103, 104, 106-pre, 106-tbR, 113, 114, 4, 5, 6, 8, 10, and others
Abdominal esophagus (Ae)		1, 2, 3, 20	110, 111, 7, 9, (4), (10), (11), 19	108, 5, 8, (112)	100, 101, 102, 103, 104, 105, 106, 107, 109, 113, 114, 6, and others
Esophagogastric junction	(EG E=G	1, 2, 3	7, 9, 10, 11 (110), (111), (4)	108, 5, 6, 8, (112), (12), (13),(14)	100, 101, 102, 103, 104, 105, 106, 107, 109,

Target Volume

- To delineate GTV
  - Physical examination
  - CT scan with IV contrast (Thorax/Abdomen)
  - Positron emission tomography (PET)
  - Upper endoscopy & Endoscopic ultrasound
    - Esophageal invasion & Lymph nodes
    - Endoscopic ultrasound - better classify small intrathoracic LN difficult to classify with CT or PET
  - MRI

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Systematic review

A systematic review on the role of FDG-PET/CT in tumour delineation and radiotherapy planning in patients with esophageal cancer

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A B S T R A C T

Purpose: FDG-PET/CT has proven to be useful in the staging process of esophageal tumours. This review analysed the role of FDG-PET/CT in tumour delineation and radiotherapy planning in comparison with CT alone among patients with esophageal cancer. Thereby we focused on the detection of the primary tumour and lymph nodes by FDG-PET/CT, changes in target volume (TV) delineation based on FDG-PET/CT and its validity, changes in inter- and intra-observer variability in TV delineation, consequences

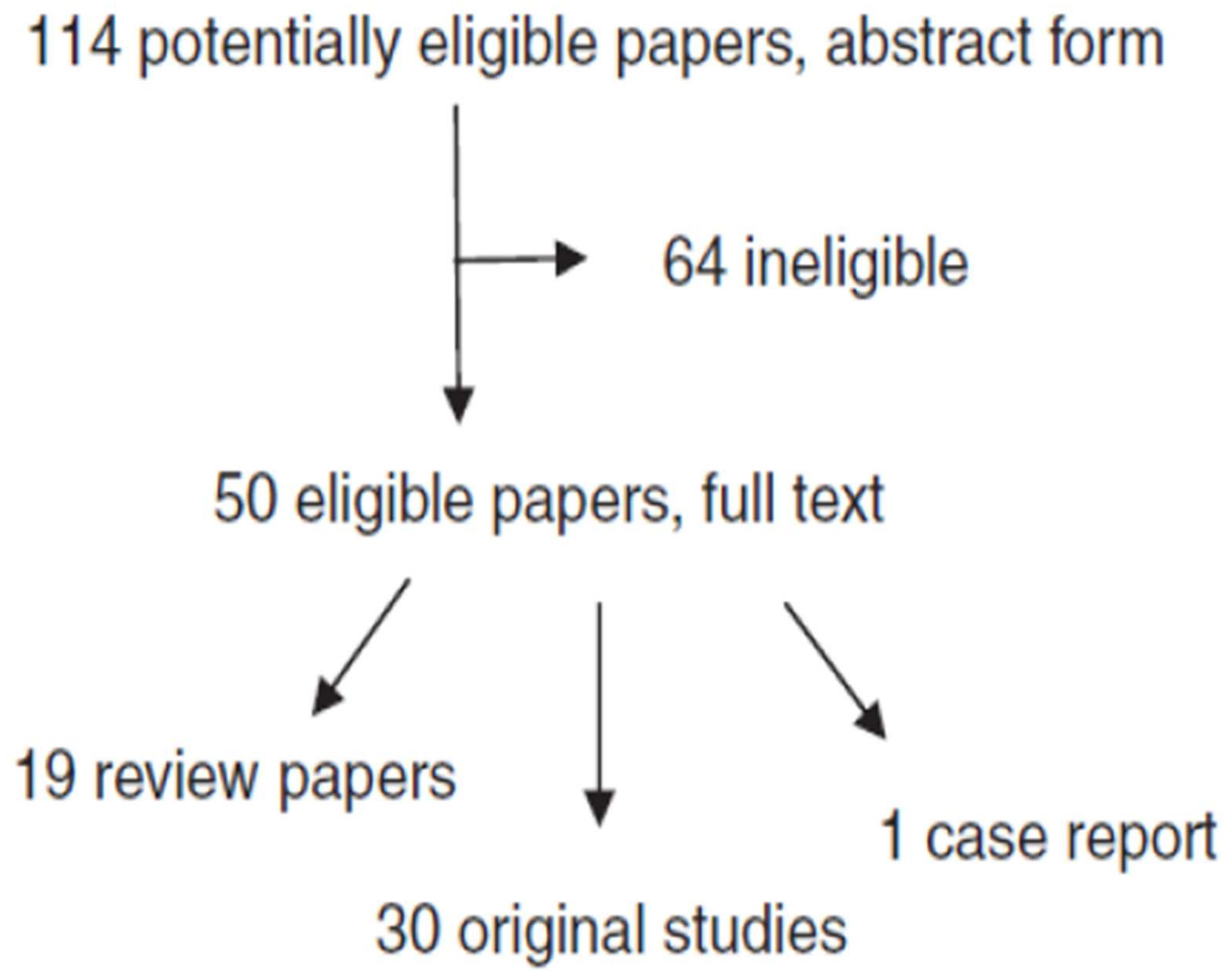

Fig. 1. The study selection process, both search strategies combined.

Table 1

Overview eligible original studies concerning the use of PET/CT for the detection of esophageal cancer.

Author	N	Primary tumour		Lymph node metastases						Remarks
		Detection rate on CT (%)	Detection rate on PET (%)	Sensitivity of PET for LN (%)	Specificity of PET for LN (%)	Sensitivity of CT for LN (%)	Specificity of CT for LN (%)	Sensitivity of PET/CT for LN (%)	Specificity of PET/CT for LN (%)	
Pfau et al. [28]	44	80	92	–	–	–	–	–	–	4 of 5 undetected were T1–T2
Rankin et al. [29]	19	95	100	–	–	–	–	–	–	
Salahudeen et al. [30]	25	–	100	–	–	–	–	–	–	
Wren et al. [43]	21	–	–	71	86	57	71	–	–	
Kato et al. [17]	149		80	32	99	23	97	–	–	Most undetected were T1
Kato et al. [16]	32	–	78	78	93	61	71	–	–	The not visible tumours were T1
Flamen et al. [10]	39		95	33	89	0	100	–	–	All false negative on PET were T1
Himeno et al. [13]	22	–	68	42	100	38	96	–	–	All undetected tumours were T1
Block et al. [3]	58	–	94	52	79	29	79	–	–	2 undetected lesions were T1a
Kato et al. [15]	167	–	74	33	99	27	98	–	–	Most undetected were T1–2
Kim et al. [18]	52	98	94	52	94	42	97	–	–	False negative on PET was T1 tumour
Meltzer et al. [23]	47	97	87	35–41	90	63–87	14–43	–	–	
Yoon et al. [44]	79	82	92	30	90	11	95	–	–	All undetected tumours were T1
Kole et al. [19]	26	81	96	92	88	38	100	–	–	
Sihvo et al. [33]	55	69	82	35	100	42	82	50	100	Of the false negative 7 T1 tumours and 3 T2 tumours
Yuan et al. [46]	45	–	–	82	87	–	–	94	92	
Schreurs et al. [32]	85	–	–	–	–	–	–	87	87	

Table 2
Overview eligible original studies concerning PET/CT in tumour delineation process.

Author	N	Fusion/integrated	Contour method	Conclusions
Tumour delineation and radiotherapy				
Gondi et al. [11]	16	Integrated	SBR (liver activity)/visual	Incorporation of PET led to GTV changes. Conformality index (CI) is recommended for more comprehensive comparison
Konski et al. [20]	25	Separately	$\geqslant$2.5 SUV	The PET-tumour length was significantly longer as measured by CT scans. PET-length correlated better with endoscopy than with CT
Vrieze et al. [40]	30	Separately	–	The irradiated volume should not be reduced based on negative PET findings, because of low sensitivity. However, thanks to the high specificity it is possible to adapt the treatment volume
Hong et al. [14]	25	Integrated	Visual/$\geqslant$mean activity of the liver + 2 SD	PET/CT appears to provide clinically meaningful data with a significant impact on target definition compared with CT alone
Moureau-Zabotto et al. [25]	34	Fusion	Visual	PET/CT had impact on treatment planning. Impact on treatment outcome remains to be demonstrated
Leong et al. [21]	16	Integrated	SBR (liver activity)/visual	PET/CT influences tumour delineation, with the potential to avoid geographic miss of tumour
Vesprini et al. [39]	10	Integrated	Visual	PET/CT decreased the inter- and intra-observer variability identification of the GTV
Schreurs et al. [31]	28	Fusion	SBR (liver activity)/visual	Combining FDG-PET and CT may improve target volume definition with less geographic misses, but without significant effects on inter-observer variability in esophageal cancer
Muijs et al. [26]	21	Fusion	SBR (liver activity)/visual	TVs based on CT might exclude PET-avid disease. Consequences are under dosing. The addition of PET in radiation planning might result in clinically important changes in NTCP
Comparison tumour length PET based vs. pathology				
Mamede et al. [22]	17	Integrated	SBR (liver activity), different SUV-thresholds	FDG-PET-tumour length of untreated esophageal carcinomas correlates well with surgical pathology results
Zhong et al. [47]	36	Integrated	$\geqslant$2.5 SUV/40% SUV_{max}/visual	The optimal PET method to estimate the length of gross tumour varies with tumour length and SUV_{max}, an SUV cutoff of 2.5 seems best
Han et al. [12]	22	Integrated	Visual/SUV-values for autocontouring	A standardised uptake value cutoff of 2.5 on FDG-PET/CT provided the closest estimation of GTV length
Yu et al. [45]	16	Integrated	SBR (liver activity)/SUV-values for autocontouring	The SUV_{bgd} + 20% (SUV_{max}(slice) – SUV_{bgd}) method optimally estimated gross tumour length, but only reached an unsatisfactory CI for GTV

Role of PET CT

- Sensitivity & Specificity
  - LN 30 to 93% & 79 to 100%
  - Primary 95 to 100% & 100%
- PET CT resulted in TV changes
- Evidence on validity of PETCT very limited
  - 3 studies significant correlation between PET based tumor lengths & Pathological findings
- No improved LR control or survival

Tumor Delineation

Weakest link in RT accuracy

- Significant inter-observer variability due to
  - Impact of imaging
  - Influence of observer (training, personal bias)
- Variability of targets can be minimized by
  - Multimodality imaging by co registration of CT with 2nd modality like MRI/PET
  - Continuous education & training
  - Collaboration of RO with other specialties
  - Concise contouring procedures and protocols