Taipei Veterans General Hospital
Practices Guidelines
Oncology
Esophageal Cancer
Principles of Radiotherapy

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General Radiation Information

General Radiation Information

- Treatment recommendations should be made after joint consultation and/or discussion by a multidisciplinary team including surgical, radiation, medical oncologists, radiologists, gastroenterologists, and pathologists.
- CT scans, barium swallow, endoscopic ultrasound (EUS), endoscopy reports and PET or PET/CT scans, when available, should be reviewed by the multidisciplinary team. This will allow an informed determination of treatment volume and field borders prior to simulation.

Simulation and Treatment Planning

- CT simulation and 3D treatment planning. Intensity-modulated radiation therapy (IMRT) may be used in clinical settings where reduction in dose to organs at risk (e.g. heart, lungs) is required that cannot be achieved by 3-D techniques.
- The patient should be instructed to avoid intake of a heavy meal 3 hours before simulation and treatment for lesions requiring therapy of the proximal stomach.
- When clinically appropriate, use IV contrast for CT simulation to aid in target localization.
- The slice thickness of CT simulation should be no more than 5 mm.
- Immobilization device is strongly recommended for reproducibility of daily set-up.
- When 4D CT planning or other motion management techniques are used, margins may be modified to account for observed motion and may also be reduced if justified. The 4D CT data may also be used to create an internal target volume (ITV) from which subsequent clinical target volume (CTV) and planning target volume (PTV) expansions can be made.

Principle of Target Volume Delineation

- **Gross Target Volume (GTV) delineation**
  - Target volume delineation based on CT simulation images. Diagnostic CT, barium, endoscopic ultrasound (EUS), endoscopic reports, and PET/CT scans should be reviewed, when available, for precise delineation of GTV
  - GTV should include the primary tumor and involved regional lymph nodes as identified on the planning scan and other pre-treatment diagnostic studies.
  - Esophageal wall thickness > 5mm, irregularity or asymmetric should be considered gross tumor
- **Clinical Target Volume (CTV) delineation**
  - The clinical target volume should include the areas at risk for microscopic disease
  - CTV_H: GTV of primary tumor and lymphadenopathy.
  - CTV_M: at least 3-4 cm superiorly and inferiorly expansion beyond the GTV; the nodal CTV should be 0.5-1.5 cm expansion from the nodal GTV.
  - CTV_M should also include coverage of elective nodal regions, depending on the location of the origin of primary tumor.
  - Recommended elective treatment of nodal regions:

Cervical esophagus	SCF lymph nodes, and consider higher echelon cervical nodes especially for N1 or greater
Proximal third of thoracic esophagus	Para-esophageal and SCF lymph nodes
Middle third of esophagus	Para-esophageal lymph nodes
Distal third of esophagus and GE junction	Para-esophageal lymph nodes, lesser curvature lymph nodes and celiac axis

Principle of Target Volume Delineation

- **Planning Target Volume (PTV) and Internal target delineation**
  - The margins of PTV should consider *respiratory motion* and *setup errors*
  - 4DCT may be used to create an ITV
  - PTV expansion should be 0.5 to 1 cm. The uncertainties arising from respiratory motion should also be taken into consideration.
- **Radiation dose**
  - Preoperative radiotherapy: 41.4 – 50.4Gy [a].
  - Definitive radiotherapy: 50.4 – 60Gy. A higher dose is suggested for tumors of cervical esophagus [b].
  - Postoperative radiotherapy: 45 – 50.4Gy
- **Radiation technique:** 3D-CRT, IMRT or VMAT, IGRT

[a] Patients who are at risk for not having surgery should receive radiation dose of 50 –50.4Gy.
[b] Published studies have reported radiation dose from 60-66Gy (no randomized evidence).

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- **Preoperative CCRT**
  - Candidate for preoperative CCRT
    - cT2N0 (high risk: LVI+, ≥3cm, poorly differentiated)
    - cT1b-cT2, N+
    - cT3-T4a, Any N
  - Radiation volume
    - The delineation of target volume follows the "***Principle of Target Volume Delineation"***
  - Radiation dose: 41.4 – 50.4Gy at 1.8-2Gy per fraction for primary tumors and regional LN
  - Evaluation: the possibility of surgical resection should be evaluated at 4-5 weeks after CCRT
    - Resectable: surgery should be done at the 6th weeks after preoperative CCRT
    - Unresectable (optional): boost to the gross tumor up to 59.4-66Gy in total

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- **Definitive chemoradiotherapy**
  - Candidate for definitive CCRT
    - Resectable disease but medically unfit for surgery, or patients refuse surgery
    - Unresectable disease: T4b
      - Consider chemotherapy alone in the setting of invasion of trachea, great vessels, vertebral body, or heart
    - Cervical esophageal cancer (tumor < 5 cm from cricopharyngeus)
  - Radiation volume
    - The delineation of target volume follows the "***Principle of Target volume delineation"***
  - Radiation dose:
    - 50.4-60Gy at 1.8-2Gy per fraction for all primary esophageal tumors and positive lymphadenopathy.
    - Higher dose up to 59.4-66Gy at 1.8-2Gy per fraction may be appropriate for tumors in cervical esophagus.

[Note]

1. The radiation dose of 50-50.4Gy as applied in the control arm in RTOG 9403 trial represents the "**evidence-based**' dose recommendation.
2. Most local failures after definitive chemoradiation for unresectable esophageal cancer occur in the GTV (Welsh *et al.* Cancer 2012;118:2632-40)
3. In recent clinical trials design, dose escalation successfully scheduled sum dose > 50Gy without excess morbidity (Bedenne et al. *J Clin Oncol* 2007;25:1160-1168).
4. For T4b disease, consider endoluminal stenting when appropriate. Chemotherapy alone may be considered in the setting of invasion of trachea, great vessels, or heart

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- **Postoperative chemoradiotherapy**
  - Candidate for postoperative CCRT
    - Positive or close margins (≤ 1mm) if not received CCRT preoperatively
    - Adenocarcinoma with positive lymph nodes or pT3-4a disease if not received CCRT preoperatively
    - Optional for squamous cell carcinoma with T3 or T4 and positive lymph nodes if not received CCRT preoperatively
  - Radiation volume
    - The delineation of target volume follows the "***Principle of Target volume delineation"***
    - The radiation volume is determined based on preoperative image findings
    - The anastomosis should be included in the radiation volume
  - Radiation dose: 45-50.4Gy at 1.8-2Gy per fraction

Charged Particle Therapy

- **Proton Therapy**
  - Proton therapy is appropriate in clinical settings where reduction in dose to organ at risk is required that cannot be achieved by 3D techniques, ideally within a clinical trial or registry study.
- **Carbon Ion Therapy**
  - Currently there is no role of carbon ion therapy in the primary treatment for esophageal cancer neither in preoperative nor definitive setting.

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